From: Flynn, William T </O=FDA/OU=FIRST ADMINISTRATIVE GROUP/CN=RECIPIENTS /CN=WFLYNN>
To: White, David G
Sent: 2/4/2016 3:10:39 PM
Subject: FW: EPA - Pending antibiotic request for Streptomycin, request for a teleconference

Hi Dave
It looks like she decided to reach out to me directly. I will pass this along to Jeff Gilbert
Thanks
Bill

From: Hill, Shaunta [mailto:Hill.Shaunta@epa.gov]
Sent: Thursday, February 04, 2016 9:59 AM
To: Flynn, William T
Cc: Jennings, Susan
Subject: EPA - Pending antibiotic request for Streptomycin, request for a teleconference

Hello Dr. William;
My name is Shaunta Hill and I am a Risk Assessor/Plant Pathologist with EPA's Office of Pesticide Programs – Registration Division.
I received your name from Dr. Jean Patel at CDC as a potential contact.
As EPA manages antibiotics for pesticidal use, we are interested in accessing the resistance risk potential along with human and environmental risks. We have previously worked with CDC and FDA (via David White) utilizing the FDA Guidance for Industry #152 for this purpose.
We have a number of applications currently pending and have scheduled a teleconference for **Wednesday Feb 10 at 11 am** to begin discussions.
I am hopefully that you are available to participate in this discussion as FDA input is valued. The primary application for consideration next week is Streptomycin sulfate use on grapefruit and tomatoes via FIFRA Section 3 Registration.
If you are available, I can provide additional background information in addition to our meeting agenda.
Should you have any questions, please let us know. I have cc'ed on this communication Susan Jennings, who serves as our Public Health Coordinator and is available to address questions on this meeting request as well.
Thank you for your time and I look forward to hearing from you.

Regards,
++

Shaunta Hill-Hammond, Ph. D.
Plant Pathologist
U.S. EPA: Office of Chemical Safety and Pollution Prevention
Registration Division/Fungicide Branch (PYS)
1200 Pennsylvania Avenue, NW (7505P)
Washington, DC 20460
Tel: 703.347.8961 l Fax: 703.305.6920
E-mail: hill.shaunta@epa.gov
URL Address: www.epa.gov/pesticides

From: Flynn, William T </O=FDA/OU=FIRST ADMINISTRATIVE GROUP/CN=RECIPIENTS /CN=WFLYNN>
To: White, David G
Sent: 2/4/2016 3:29:58 PM
Subject: RE: EPA - Pending antibiotic request for Streptomycin, request for a teleconference

I believe Erik was planning to participate in the premeeting – but I think it would be good if you could as well - if you are available
I will forward meeting info
Our desire is to have the meeting with Mike go as smoothly as possible – so some advance input from you and Erik would appreciated

---

From: White, David G
Sent: Thursday, February 04, 2016 10:15 AM
To: Flynn, William T
Subject: RE: EPA - Pending antibiotic request for Streptomycin, request for a teleconference
Hi, also, did you want me at the prebrief today on avilamycin/DG or just the meeting Monday?
Dave

From: Flynn, William T
Sent: Thursday, February 04, 2016 10:11 AM
To: White, David G
Subject: FW: EPA - Pending antibiotic request for Streptomycin, request for a teleconference
Hi Dave
It looks like she decided to reach out to me directly. I will pass this along to Jeff Gilbert
Thanks
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Sent: Thursday, February 04, 2016 9:59 AM
To: Flynn, William T
Cc: Jennings, Susan
Subject: EPA - Pending antibiotic request for Streptomycin, request for a teleconference
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Regards,
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1200 Pennsylvania Avenue, NW (7505P)

Washington, DC 20460
Tel: 703.347.8961 l Fax: 703.305.6920
E-mail: hill.shaunta@epa.gov
URL Address: www.epa.gov/pesticides

From:	White, David G </O=FDA/OU=FIRST ADMINISTRATIVE GROUP/CN=RECIPIENTS /CN=DWHITE>
To:	Flynn, William T
Sent:	2/4/2016 3:11:20 PM
Subject:	RE: EPA - Pending antibiotic request for Streptomycin, request for a teleconference

Thanks Bill, I had not reached out to her yet.
Dave

From: Flynn, William T
Sent: Thursday, February 04, 2016 10:11 AM
To: White, David G
Subject: FW: EPA - Pending antibiotic request for Streptomycin, request for a teleconference

Hi Dave
It looks like she decided to reach out to me directly. I will pass this along to Jeff Gilbert
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Plant Pathologist
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1200 Pennsylvania Avenue, NW (7505P)
Washington, DC 20460
Tel: 703.347.8961 l Fax: 703.305.6920
E-mail: hill.shaunta@epa.gov
URL Address: www.epa.gov/pesticides

From: Gilbert, Jeffrey M </O=FDA/OU=FIRST ADMINISTRATIVE GROUP/CN=RECIPIENTS /CN=JGILBERT>
To: Flynn, William T
CC: Vaughn, Steven D
Sent: 2/4/2016 6:21:07 PM
Subject: RE: EPA - Pending antibiotic request for Streptomycin, request for a teleconference

I'll handle it!!!!!

From: Flynn, William T
Sent: Thursday, February 04, 2016 10:49 AM
To: Gilbert, Jeffrey M
Cc: Vaughn, Steven D
Subject: FW: EPA - Pending antibiotic request for Streptomycin, request for a teleconference

Hi Jeff,
I know you have interacted with EPA before on their utilization of GFI 152. Would you mind following up with Shaunta Hill. I think it makes more sense that you be their point of contact on this issue rather than Dave White. I recently spoke to Dave White – so he is aware
Thanks
Bill

From: Hill, Shaunta [mailto:Hill.Shaunta@epa.gov]
Sent: Thursday, February 04, 2016 9:59 AM
To: Flynn, William T
Cc: Jennings, Susan
Subject: EPA - Pending antibiotic request for Streptomycin, request for a teleconference

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Washington, DC 20460
Tel: 703.347.8961 l Fax: 703.305.6920
E-mail: hill.shaunta@epa.gov
URL Address: www.epa.gov/pesticides

From: White, David G </O=FDA/OU=FIRST ADMINISTRATIVE GROUP/CN=RECIPIENTS /CN=DWHITE>
To: Flynn, William T
Sent: 2/4/2016 3:54:28 PM
Subject: RE: EPA - Pending antibiotic request for Streptomycin, request for a teleconference

B5

Dave

From: Flynn, William T
Sent: Thursday, February 04, 2016 10:49 AM
To: White, David G
Subject: RE: EPA - Pending antibiotic request for Streptomycin, request for a teleconference
I think B5

B5

– as I suspect B5

From: White, David G
Sent: Thursday, February 04, 2016 10:39 AM
To: Flynn, William T
Subject: RE: EPA - Pending antibiotic request for Streptomycin, request for a teleconference
Hi, quick question, B5

B5

Dave

From: Flynn, William T
Sent: Thursday, February 04, 2016 10:30 AM
To: White, David G
Subject: RE: EPA - Pending antibiotic request for Streptomycin, request for a teleconference
I believe Erik was planning to participate in the premeeting – but I think it would be good if you could as well - if you are available
I will forward meeting info

B5

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Sent: Thursday, February 04, 2016 10:15 AM
To: Flynn, William T
Subject: RE: EPA - Pending antibiotic request for Streptomycin, request for a teleconference
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To: White, David G
Subject: FW: EPA - Pending antibiotic request for Streptomycin, request for a teleconference
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Sent: Thursday, February 04, 2016 9:59 AM
To: Flynn, William T

Cc: Jennings, Susan
Subject: EPA - Pending antibiotic request for Streptomycin, request for a teleconference

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Should you have any questions, please let us know. I have cc'ed on this communication Susan Jennings, who serves as our Public Health Coordinator and is available to address questions on this meeting request as well.

Thank you for your time and I look forward to hearing from you.

Regards,

++

Shaunta Hill-Hammond, Ph. D.
Plant Pathologist
U.S. EPA: Office of Chemical Safety and Pollution Prevention
Registration Division/Fungicide Branch (PYS)
1200 Pennsylvania Avenue, NW (7505P)
Washington, DC 20460
Tel: 703.347.8961 l Fax: 703.305.6920
E-mail: hill.shaunta@epa.gov
URL Address: www.epa.gov/pesticides

From: Gilbert, Jeffrey M </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=80308E6A2328498ABB1E3BF85E99784C-JGILBERT>
To: Steel, Ashley; Flynn, William T
CC: Luddy, Elizabeth A; Long, Charli; Harbottle, Heather
Sent: 4/9/2019 1:06:14 PM
Subject: FW: letter for epa
Importance: High
Attachments: dietary exposure response tet strep march 6_JMG.docx

Here's the last email regarding a response to the EPA letter you asked about. Looks like it was winging its way to Beth for signature, but I do not know if it went out from her desk - maybe she can chime in?

From: Gilbert, Jeffrey M
Sent: Wednesday, March 7, 2018 8:36 AM
To: Harbottle, Heather <Heather.Harbottle@fda.hhs.gov>; Long, Charli <Charli.Long-Medrano@fda.hhs.gov>
Subject: RE: letter for epa

Attached – a few edits.

Do B5 B5 ? Is EPA B5 B5 ?

From: Harbottle, Heather
Sent: Tuesday, March 06, 2018 4:18 PM
To: Gilbert, Jeffrey M <Jeff.Gilbert@fda.hhs.gov>; Long, Charli <Charli.Long-Medrano@fda.hhs.gov>
Subject: letter for epa

Hi Charli and Jeff,
Here's the draft of the letter we can send back to EPA, with your edits, of course. The original letter from 2006 is almost identical B5 and I have provided it in case you want to read it. SDV signed that one, so I assume Beth would be signing this one?

Thoughts?
Thanks,
H

From: Gilbert, Jeffrey M
Sent: Tuesday, March 06, 2018 2:15 PM
To: Harbottle, Heather <Heather.Harbottle@fda.hhs.gov>; Long, Charli <Charli.Long-Medrano@fda.hhs.gov>
Subject: RE: check in on earlier email

Let's get it wrapped up an launch it!

From: Harbottle, Heather
Sent: Tuesday, March 06, 2018 9:29 AM
To: Long, Charli <Charli.Long-Medrano@fda.hhs.gov>; Gilbert, Jeffrey M <Jeff.Gilbert@fda.hhs.gov>
Subject: FW: check in on earlier email

B5

B5

From: Jennings, Susan [mailto:Jennings.Susan@epa.gov]
Sent: Tuesday, March 06, 2018 9:04 AM
To: Harbottle, Heather <Heather.Harbottle@fda.hhs.gov>; Long, Charli <Charli.Long-Medrano@fda.hhs.gov>
Cc: Gilbert, Jeffrey M <Jeff.Gilbert@fda.hhs.gov>
Subject: RE: check in on earlier email

Hi Heather,

Thanks for the information. If you could let me know as soon as you have a more firm date for completion, I'd appreciate it. As you know we are under a very tight legal deadline with this.

Thanks for all your help,

Susan.

Susan Jennings
Senior Advisor for Public Health
Office of Pesticide Programs
(706) 355-8574 (office)
(703) 216-8627 (cell)

From: Harbottle, Heather [mailto:Heather.Harbottle@fda.hhs.gov]
Sent: Monday, March 05, 2018 4:07 PM
To: Jennings, Susan <Jennings.Susan@epa.gov>; Long, Charli <Charli.Long-Medrano@fda.hhs.gov>
Cc: Gilbert, Jeffrey M <Jeff.Gilbert@fda.hhs.gov>
Subject: RE: check in on earlier email

Hi Susan,
I was just getting ready to email you. Our division director Charli is out of the office until tomorrow. I put forward a suggestion on how to handle this, since this isn't something we have done in the past (ourselves, other folks did it for you in 2005). I'm waiting for buy in or alternate suggestions. It's fair to say that management above our division will want to read and clear it, so I don't think March 7 is possible. I'm sorry about that.

We will get it back to you asap, once I've heard if my suggestion is the way that we should go. I'm sorry that I don't have a better estimate for when that might be.

Thanks,
Heather

From: Jennings, Susan [mailto:Jennings.Susan@epa.gov]
Sent: Monday, March 05, 2018 2:37 PM
To: Long, Charli <Charli.Long-Medrano@fda.hhs.gov>
Cc: Gilbert, Jeffrey M <Jeff.Gilbert@fda.hhs.gov>; Harbottle, Heather <Heather.Harbottle@fda.hhs.gov>
Subject: check in on earlier email

Dr. Long,

I just wanted to check on whether you received our earlier email requesting FDA input on tolerance decisions for oxytetracycline and streptomycin?

If so, do you think that FDA will be able to meet the March 7th deadline? Our Registration Division is finalizing their planning and hoping to schedule the publication date for the decision.

Thanks again for your help,

Susan.

Susan Jennings
Senior Advisor for Public Health
Office of Pesticide Programs
(706) 355-8574 (office)
(703) 216-8627 (cell)

From: Gilbert, Jeffrey M </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=80308E6A2328498ABB1E3BF85E99784C-JGILBERT>
To: Long, Charli
CC: Harbottle, Heather
Sent: 2/21/2018 10:17:39 PM
Subject: Fwd: letter on aggregate risk assessment

Look out for a letter from EPA!

From: Jennings, Susan <Jennings.Susan@epa.gov>
Date: February 20, 2018 at 8:22:33 AM CST
To: Gilbert, Jeffrey M <Jeff.Gilbert@fda.hhs.gov>, Harbottle, Heather <Heather.Harbottle@fda.hhs.gov>
Subject: RE: letter on aggregate risk assessment

Also, could you please let your Director know that the letter will be coming? We haven't sent it yet (needs more review), but they will likely request a pretty quick turnaround.

Thanks,

Susan.

Susan Jennings
Senior Advisor for Public Health
Office of Pesticide Programs
(706) 355-8574 (office)
(703) 216-8627 (cell)

From: Jennings, Susan
Sent: Thursday, February 15, 2018 12:34 PM
To: Gilbert, Jeffrey M <Jeff.Gilbert@fda.hhs.gov>; Harbottle, Heather <Heather.Harbottle@fda.hhs.gov>
Subject: RE: letter on aggregate risk assessment

Thanks.

From: Gilbert, Jeffrey M [mailto:Jeff.Gilbert@fda.hhs.gov]
Sent: Thursday, February 15, 2018 9:49 AM
To: Jennings, Susan <Jennings.Susan@epa.gov>; Harbottle, Heather <Heather.Harbottle@fda.hhs.gov>
Subject: Re: letter on aggregate risk assessment

Charli Long, Ph.D.
Director, Division of Human Food Safety
Center for Veterinary Medicine
US Food and Drug Administration
HFV-150, 7500 Standish Place

Rockville, MD 20855

From: Jennings, Susan <Jennings.Susan@epa.gov>
Date: February 15, 2018 at 9:43:13 AM EST
To: Harbottle, Heather <Heather.Harbottle@fda.hhs.gov>, Gilbert, Jeffrey M <Jeff.Gilbert@fda.hhs.gov>
Subject: letter on aggregate risk assessment

Hi Jeff and Heather,

Could one of you please provide me with the name of your division director, title, office, and address?

I think we'll just send the letter to them and they can forward it as appropriate.

Thanks,

Susan.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, DC 20460

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

February 27, 2018

Charli Long, Ph.D.
Director, Division of Human Food Safety
Center for Veterinary Medicine
U.S. Food and Drug Administration
HFV-150, 7500 Standish Place
Rockville, MD 20855

Dear Dr. Long:

The U.S. Environmental Protection Agency (EPA) currently has pending new use actions for the antibiotics oxytetracycline and streptomycin for certain pesticidal agricultural uses. For oxytetracycline, EPA has recently published a proposed decision for certain new uses, including publication of documents and assessments that support that decision (for reference, please see https://www.regulations.gov/ and Docket ID: EPA-HQ-OPP-2015-0820). For streptomycin, we have completed our assessments and expect to publish a proposed decision for certain new uses in the near future. Because these application of pesticides will result in residues of those pesticides in or on food, tolerances are required in order to register these new uses.

Under the Federal Food Drug and Cosmetic Act, EPA, when setting tolerances, must determine that the levels of allowed pesticide residues in food are safe, i.e. that there is a "reasonable certainty of no harm [resulting] from aggregate exposure to the pesticide chemical residue, including all anticipated dietary exposures and all other exposures for which there is reliable information." FFDCA §408(b)(2)(A)(ii). For substances that are used for pesticidal and pharmaceutical drug purposes, such as oxytetracycline and streptomycin, EPA has worked with FDA in the past to assess the safety of tolerances for those pesticides.

Under FFDCA section 505, FDA reviews human drugs for safety and effectiveness and may approve a drug notwithstanding the real possibility that some patients may experience adverse side effects. EPA does not believe that, for the purposes of section 408 dietary risk assessment, it is compelled to treat a pharmaceutical patient the same as a non-patient, or to assume that combined exposures to pesticide and pharmaceutical residues that lead to a physiological effect constitutes "harm" under the meaning of section 408. Rather, EPA believes the appropriate way to harmonize sections 408 and 505 is to examine the impact that the additional non-occupational pesticide exposures would have to a pharmaceutical patient exposed to a similar (or, in some cases, the same) compound. Where the additional pesticide exposure has not more than a minimal impact on the pharmaceutical patient, EPA could make a reasonable certainty of no harm finding for the pesticide tolerances of that compound under section 408. If the potential impact on the pharmaceutical user as a result of co-exposure from pesticide use is not deemed to be minimal, then the Agencies could discuss appropriate measures to reduce exposure from one or both sources.

Under this approach, EPA must look to FDA's authority to determine the safety of a pharmaceutical patient who may be additionally exposed to oxytetracycline and/or streptomycin pesticide residues under conditions of co-exposure.

The information below is being provided to FDA for consideration in determining whether the additional pesticide exposure to oxytetracycline and streptomycin results in no more than a minimal impact on the pharmaceutical patient. EPA requests that, following your review of this information, FDA provide a letter summarizing your conclusions, as this will be an important part of EPA's public record on this issue. EPA previously had a similar request during Reregistration of oxytetracycline and FDA's written determination was appreciated [http://www.regulations.gov; EPA-HQ-OPP-2005-0492-0028 and EPA-HQ-OPP-2005-0492-0031]. We request that FDA provide your written determination to EPA by March 7, 2018, if possible.

The EPA's Health Effects Division considered typical human daily dosages of both oxytetracycline and streptomycin as human drugs to determine how these doses compared to the worst case exposures potentially incurred as a result of the food plus drinking water exposures resulting from pesticidal uses of the chemicals. To assure a conservative assessment, the pesticide exposures were calculated using tolerance-level residues and an assumption that 100% of the relevant crops are treated so to represent screening-level values, which will far exceed any exposures likely to actually occur from use of oxytetracycline or streptomycin as pesticides.

This assessment is summarized below:

Chemical	Age	Drug Dosage (mg/kg/day)	Dietary exposure from pesticide use (mg/kgbw/day)	Drug dose to dietary exposure ratio
Oxytetracycline	Adult	15	0.0079	1900X
	Child > 8 y/o	1.6	0.0164	100X
Streptomycin	Adult	15	0.019	790X
	Child > 8 y/o	15	0.02	750X

As you can see, the typical drug dosage is significantly higher (100 to 1900 times higher) than the conservatively estimated dietary (i.e., food and drinking water) exposures from pesticidal use of oxytetracycline and streptomycin. Based on these estimates, EPA poses the following two questions to FDA:

1. Does FDA have any concern that the additional dose of oxytetracycline from the pesticide uses of oxytetracycline – estimated to range from 0.0079 mg/kgbw/day to 0.0164 mg/kgbw/day – would result in more than a minimal impact on an individual who may be treated therapeutically with oxytetracycline?

2. Does the FDA have any concern that the additional dose of streptomycin from the pesticide uses of streptomycin – estimated to range from 0.019 mg/kgbw/day to 0.02 mg/kgbw/day – would result in more than a minimal impact on an individual who may be treated therapeutically with streptomycin?

Again, we request FDA to provide your written determination to EPA by March 7, 2018, if possible. If you have comments on the information provided, or need any further documentation, please let us know and we will schedule a conference call or meeting to exchange comments and discuss FDA's assessment. You may contact me at 703-308-8157 or goodis.michael@epa.gov. Thank you in advance!

Sincerely,

Michael L. Goodis, P.E.
Director, Registration Division (RD)
Office of Pesticide Programs (OPP)

From: Long, Charli </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=8F7E70AD08E1478F894C497C6F992133-CHARLI.LONG>
To: Gilbert, Jeffrey M; Harbottle, Heather
Sent: 3/6/2018 9:05:18 PM
Subject: RE: check in on earlier email

Agree. B6 You can send out without waiting for my feedback, but please cc me on it so I have a copy of what gets sent out.

Thanks,

Charli M. Long, Ph.D.
Director
Division of Human Food Safety (HFV-150)
Office of New Animal Drug Evaluation
Center for Veterinary Medicine
7500 Standish Place
Rockville, MD 20855
VOIP #: (240) 402-0850

From: Gilbert, Jeffrey M
Sent: Tuesday, March 06, 2018 2:15 PM
To: Harbottle, Heather <Heather.Harbottle@fda.hhs.gov>; Long, Charli <Charli.Long-Medrano@fda.hhs.gov>
Subject: RE: check in on earlier email

Let's get it wrapped up an launch it!

From: Harbottle, Heather
Sent: Tuesday, March 06, 2018 9:29 AM
To: Long, Charli <Charli.Long-Medrano@fda.hhs.gov>; Gilbert, Jeffrey M <Jeff.Gilbert@fda.hhs.gov>
Subject: FW: check in on earlier email

I have a draft ready, which is pretty much word for word what was sent in 2006. The only difference is the estimates they provided for oxytet and streptomycin (no changes in tolerances for tets or strep). As I pointed

B5

From: Jennings, Susan [mailto:Jennings.Susan@epa.gov]
Sent: Tuesday, March 06, 2018 9:04 AM
To: Harbottle, Heather <Heather.Harbottle@fda.hhs.gov>; Long, Charli <Charli.Long-Medrano@fda.hhs.gov>
Cc: Gilbert, Jeffrey M <Jeff.Gilbert@fda.hhs.gov>
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We will get it back to you asap, once I've heard if my suggestion is the way that we should go. I'm sorry that I don't have a better estimate for when that might be.

Thanks,
Heather

From: Jennings, Susan [mailto:Jennings.Susan@epa.gov]
Sent: Monday, March 05, 2018 2:37 PM
To: Long, Charli <Charli.Long-Medrano@fda.hhs.gov>
Cc: Gilbert, Jeffrey M <Jeff.Gilbert@fda.hhs.gov>; Harbottle, Heather <Heather.Harbottle@fda.hhs.gov>
Subject: check in on earlier email

Dr. Long,

I just wanted to check on whether you received our earlier email requesting FDA input on tolerance decisions for oxytetracycline and streptomycin?

If so, do you think that FDA will be able to meet the March 7th deadline? Our Registration Division is finalizing their planning and hoping to schedule the publication date for the decision.

Thanks again for your help,

Susan.

Susan Jennings
Senior Advisor for Public Health
Office of Pesticide Programs
(706) 355-8574 (office)
(703) 216-8627 (cell)

From: Harbottle, Heather </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=55429E94C1CE44C4B031B4CFEE99A90F-HHARBOTT>
To: Zhou, Tong; Long, Charli; Gilbert, Jeffrey M
CC: Friedlander, Lynn G
Sent: 3/6/2018 4:37:42 PM
Subject: RE: FDA Input on Tolerance Decisions for Oxytetracycline and Streptomycin - response quested by March 7

Thanks Tong! Agreed on all of your points below. B5

B5

Thanks again,
Heather

From: Zhou, Tong
Sent: Tuesday, March 06, 2018 11:32 AM
To: Harbottle, Heather <Heather.Harbottle@fda.hhs.gov>; Long, Charli <Charli.Long-Medrano@fda.hhs.gov>; Gilbert, Jeffrey M <Jeff.Gilbert@fda.hhs.gov>
Cc: Friedlander, Lynn G <Lynn.Friedlander@fda.hhs.gov>
Subject: RE: FDA Input on Tolerance Decisions for Oxytetracycline and Streptomycin - response quested by March 7

Hi Heather,

B5

Tong

From: Harbottle, Heather
Sent: Monday, March 05, 2018 4:18 PM
To: Zhou, Tong <Tong.Zhou@fda.hhs.gov>; Long, Charli <Charli.Long-Medrano@fda.hhs.gov>; Gilbert, Jeffrey M <Jeff.Gilbert@fda.hhs.gov>
Cc: Friedlander, Lynn G <Lynn.Friedlander@fda.hhs.gov>
Subject: RE: FDA Input on Tolerance Decisions for Oxytetracycline and Streptomycin - response quested by March 7

Thanks for the reply, Tong.

I do think that what you are suggesting is what EPA is asking – B5

B5

B5

B5

B5 I don't believe that the tolerances have changed for tet or strep since 2006, but I'll double check.

Thanks again,
Heather

From: Zhou, Tong
Sent: Monday, March 05, 2018 2:09 PM
To: Harbottle, Heather <Heather.Harbottle@fda.hhs.gov>; Long, Charli <Charli.Long-Medrano@fda.hhs.gov>; Gilbert, Jeffrey M <Jeff.Gilbert@fda.hhs.gov>
Cc: Friedlander, Lynn G <Lynn.Friedlander@fda.hhs.gov>
Subject: RE: FDA Input on Tolerance Decisions for Oxytetracycline and Streptomycin - response quested by March 7

Hi Heather,

I think the FDA's 2006 response is acceptable.

EPA asks B5

B5

Tong

From: Harbottle, Heather
Sent: Thursday, March 01, 2018 10:21 AM
To: Long, Charli <Charli.Long-Medrano@fda.hhs.gov>; Gilbert, Jeffrey M <Jeff.Gilbert@fda.hhs.gov>

Cc: Friedlander, Lynn G <Lynn.Friedlander@fda.hhs.gov>; Zhou, Tong <Tong.Zhou@fda.hhs.gov>
Subject: FW: FDA Input on Tolerance Decisions for Oxytetracycline and Streptomycin - response quested by March 7
Importance: High

Hi Jeff, Charli, Lynn, and Tong,
I looked up the previous example that is listed in EPA's request (attached) for our group. Just to remind you,

B5

Please let me know if you all would like a quick call for me to bring you up to speed on this issue. I assume that we will need office management sign off on this, and maybe Urvi's blessing? Unfortunately, they ask for a very short turn around of March 7.

Thanks,
Heather

From: Jennings, Susan [mailto:Jennings.Susan@epa.gov]
Sent: Tuesday, February 27, 2018 3:42 PM
To: Long, Charli <Charli.Long-Medrano@fda.hhs.gov>
Cc: Goodis, Michael <Goodis.Michael@epa.gov>; Gilbert, Jeffrey M <Jeff.Gilbert@fda.hhs.gov>; Harbottle, Heather <Heather.Harbottle@fda.hhs.gov>; Giles-Parker, Cynthia <Giles-Parker.Cynthia@epa.gov>; Johnson, Hope <Johnson.Hope@epa.gov>
Subject: FDA Input on Tolerance Decisions for Oxytetracycline and Streptomycin

Dr. Long:

Thank you for allowing Drs. Jeffrey Gilbert and Heather Harbottle to collaborate with us on our registrations for new uses for antibiotic pesticides. They have provided valuable input into our draft decisions and analyses and, along with our colleagues at CDC and USDA, helped EPA's decision be more robust and balanced.

While working on these decisions, B5 n
B5
B5 . EPA is required by the Federal Food, Drug and Cosmetic Act to consider this information when establishing tolerances on agricultural commodities. The attached letter, signed by Michael Goodis (Director, Registration Division) provides more information and serves as the official request. If it all possible, we would appreciate receiving a response to this letter by March 7, 2018. If this is not possible, please let us know so that we can readjust our schedules accordingly.

Again, thank you for your time and consideration, as well as your division's continued collaboration on antibiotic pesticide activities.

Susan Jennings
Senior Advisor for Public Health
Office of Pesticide Programs
(706) 355-8574 (office)
(703) 216-8627 (cell)

From:	Harbottle, Heather </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=55429E94C1CE44C4B031B4CFEE99A90F-HHARBOTT>
To:	Jennings, Susan; Long, Charli
CC:	Goodis, Michael; Gilbert, Jeffrey M; Giles-Parker, Cynthia; Johnson, Hope
Sent:	3/15/2018 7:19:15 PM
Subject:	RE: FDA Input on Tolerance Decisions for Oxytetracycline and Streptomycin - Revised FDA response
Attachments:	dietary exposure response tet strep final march 14.pdf

Dear Dr. Jennings,
Per your February 27, 2018 request, we have attached an edited response to your request letter. We hope this letter satisfies your request, as it is modeled after our previous response to your request in 2006. Please feel free to contact us with any further questions.

B5

https://www.fda.gov/downloads/AnimalVeterinary/GuidanceComplianceEnforcement/GuidanceforIndustry/UCM124674.pdf

We look forward to collaborating with you in the future in this respect and regarding the risk for the development of antimicrobial resistance.

Best regards,
Heather Harbottle

Heather Harbottle, Ph.D.
Microbiologist
Microbial Food Safety Team
Division of Human Food Safety
Office of New Animal Drug Evaluation
Center for Veterinary Medicine, FDA
240-402-0791

From: Jennings, Susan [mailto:Jennings.Susan@epa.gov]
Sent: Tuesday, February 27, 2018 3:42 PM
To: Long, Charli <Charli.Long-Medrano@fda.hhs.gov>
Cc: Goodis, Michael <Goodis.Michael@epa.gov>; Gilbert, Jeffrey M <Jeff.Gilbert@fda.hhs.gov>; Harbottle, Heather <Heather.Harbottle@fda.hhs.gov>; Giles-Parker, Cynthia <Giles-Parker.Cynthia@epa.gov>; Johnson, Hope <Johnson.Hope@epa.gov>
Subject: FDA Input on Tolerance Decisions for Oxytetracycline and Streptomycin

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To: Long, Charli; Gilbert, Jeffrey M
Sent: 3/7/2018 3:59:13 PM
Subject: RE: letter for epa - conversation with Susan at EPA

Hi Jeff and Charli,
I was able to get Susan Jennings from EPA on the phone B5

B5

Thanks again,
Heather

From: Long, Charli
Sent: Wednesday, March 07, 2018 9:30 AM
To: Harbottle, Heather <Heather.Harbottle@fda.hhs.gov>; Gilbert, Jeffrey M <Jeff.Gilbert@fda.hhs.gov>
Subject: RE: letter for epa

Hi,

Yes, I would want Beth to sign off on this one….my only edit to the letter is that her title should be Acting Director.

Thanks,

Charli M. Long, Ph.D.
Director
Division of Human Food Safety (HFV-150)
Office of New Animal Drug Evaluation
Center for Veterinary Medicine
7500 Standish Place
Rockville, MD 20855
VOIP #: (240) 402-0850

From: Harbottle, Heather
Sent: Wednesday, March 07, 2018 8:44 AM
To: Gilbert, Jeffrey M <Jeff.Gilbert@fda.hhs.gov>; Long, Charli <Charli.Long-Medrano@fda.hhs.gov>
Subject: RE: letter for epa

Hey Jeff,

B5

B5

And we agree Beth needs to sign?

Thanks,
H

From: Gilbert, Jeffrey M
Sent: Wednesday, March 07, 2018 8:36 AM
To: Harbottle, Heather <Heather.Harbottle@fda.hhs.gov>; Long, Charli <Charli.Long-Medrano@fda.hhs.gov>
Subject: RE: letter for epa

Attached – a few edits.

B5

From: Harbottle, Heather
Sent: Tuesday, March 06, 2018 4:18 PM
To: Gilbert, Jeffrey M <Jeff.Gilbert@fda.hhs.gov>; Long, Charli <Charli.Long-Medrano@fda.hhs.gov>
Subject: letter for epa

Hi Charli and Jeff,
Here's the draft of the letter we can send back to EPA, with your edits, of course. B5 B5, and I have provided it in case you want to read it. SDV signed that one, so I assume Beth would be signing this one?

Thoughts?
Thanks,
H

From: Gilbert, Jeffrey M
Sent: Tuesday, March 06, 2018 2:15 PM
To: Harbottle, Heather <Heather.Harbottle@fda.hhs.gov>; Long, Charli <Charli.Long-Medrano@fda.hhs.gov>
Subject: RE: check in on earlier email

Let's get it wrapped up an launch it!

From: Harbottle, Heather
Sent: Tuesday, March 06, 2018 9:29 AM
To: Long, Charli <Charli.Long-Medrano@fda.hhs.gov>; Gilbert, Jeffrey M <Jeff.Gilbert@fda.hhs.gov>
Subject: FW: check in on earlier email

B5

From: Jennings, Susan [mailto:Jennings.Susan@epa.gov]
Sent: Tuesday, March 06, 2018 9:04 AM
To: Harbottle, Heather <Heather.Harbottle@fda.hhs.gov>; Long, Charli <Charli.Long-Medrano@fda.hhs.gov>
Cc: Gilbert, Jeffrey M <Jeff.Gilbert@fda.hhs.gov>
Subject: RE: check in on earlier email

Hi Heather,

Thanks for the information. If you could let me know as soon as you have a more firm date for completion, I'd appreciate it. As you know we are under a very tight legal deadline with this.

Thanks for all your help,

Susan.

Susan Jennings
Senior Advisor for Public Health
Office of Pesticide Programs
(706) 355-8574 (office)
(703) 216-8627 (cell)

From: Harbottle, Heather [mailto:Heather.Harbottle@fda.hhs.gov]
Sent: Monday, March 05, 2018 4:07 PM
To: Jennings, Susan <Jennings.Susan@epa.gov>; Long, Charli <Charli.Long-Medrano@fda.hhs.gov>
Cc: Gilbert, Jeffrey M <Jeff.Gilbert@fda.hhs.gov>
Subject: RE: check in on earlier email

Hi Susan,
I was just getting ready to email you. Our division director Charli is out of the office until tomorrow. I put forward a suggestion on how to handle this, since this isn't something we have done in the past (ourselves, other folks did it for you in 2005). I'm waiting for buy in or alternate suggestions. It's fair to say that management above our division will want to read and clear it, so I don't think March 7 is possible. I'm sorry about that.

We will get it back to you asap, once I've heard if my suggestion is the way that we should go. I'm sorry that I don't have a better estimate for when that might be.

Thanks,
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Cc: Gilbert, Jeffrey M <Jeff.Gilbert@fda.hhs.gov>; Harbottle, Heather <Heather.Harbottle@fda.hhs.gov>
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If so, do you think that FDA will be able to meet the March 7th deadline? Our Registration Division is finalizing their planning and hoping to schedule the publication date for the decision.

Thanks again for your help,

Susan.

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From: Steel, Ashley </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=C235284C0D224496BE223A2F6B7E8C1F-ASTEEL>
To: Harbottle, Heather; Gilbert, Jeffrey M
CC: Luddy, Elizabeth A; Long, Charli; Flynn, William T
Sent: 4/9/2019 2:04:08 PM
Subject: RE: letter for epa
Attachments: Letter From CDER to EPA.pdf

Hi all - Thank you for looking into this. The explanation makes sense and is in line with the CDER response

B5

Best,
Ashley

From: Harbottle, Heather
Sent: Tuesday, April 09, 2019 9:16 AM
To: Gilbert, Jeffrey M <Jeff.Gilbert@fda.hhs.gov>; Steel, Ashley <Ashley.Steel@fda.hhs.gov>; Flynn, William T <William.Flynn@fda.hhs.gov>
Cc: Luddy, Elizabeth A <Elizabeth.Luddy@fda.hhs.gov>; Long, Charli <Charli.Long-Medrano@fda.hhs.gov>
Subject: RE: letter for epa

Hi everyone,
This letter was sent to EPA; B5

B5

Thanks,
Heather

From: Gilbert, Jeffrey M
Sent: Tuesday, April 09, 2019 9:06 AM
To: Steel, Ashley <Ashley.Steel@fda.hhs.gov>; Flynn, William T <William.Flynn@fda.hhs.gov>
Cc: Luddy, Elizabeth A <Elizabeth.Luddy@fda.hhs.gov>; Long, Charli <Charli.Long-Medrano@fda.hhs.gov>; Harbottle, Heather <Heather.Harbottle@fda.hhs.gov>
Subject: FW: letter for epa
Importance: High

Here's the last email regarding a response to the EPA letter you asked about. B5

B5

From: Gilbert, Jeffrey M
Sent: Wednesday, March 7, 2018 8:36 AM
To: Harbottle, Heather <Heather.Harbottle@fda.hhs.gov>; Long, Charli <Charli.Long-Medrano@fda.hhs.gov>
Subject: RE: letter for epa

Attached – a few edits.

B5

From: Harbottle, Heather
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To: Gilbert, Jeffrey M <Jeff.Gilbert@fda.hhs.gov>; Long, Charli <Charli.Long-Medrano@fda.hhs.gov>
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B5

Thoughts?
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B5

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(703) 216-8627 (cell)

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Sent: Monday, March 05, 2018 4:07 PM
To: Jennings, Susan <Jennings.Susan@epa.gov>; Long, Charli <Charli.Long-Medrano@fda.hhs.gov>
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Heather

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Cc: Gilbert, Jeffrey M <Jeff.Gilbert@fda.hhs.gov>; Harbottle, Heather <Heather.Harbottle@fda.hhs.gov>
Subject: check in on earlier email

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Thanks again for your help,

Susan.

Susan Jennings
Senior Advisor for Public Health
Office of Pesticide Programs
(706) 355-8574 (office)
(703) 216-8627 (cell)

From:	Jennings, Susan <Jennings.Susan@epa.gov>
To:	Carl Schultze; Fajardo, Julius; Harbottle, Heather; Patel, Jean (CDC); Gilbert, Jeffrey M; Craig, Michael R (CDC); Rose Hammond
CC:	Johnson, Marion; Maignan, Tawanda; Giles-Parker, Cynthia; Johnson, Marion; Garvie, Heather; Jones, Arnet; Chandgoyal, Tara; Yourman, Leonard; Britton, Cathryn; Manupella, Matthew; Leshin, Jonathan; Collins, Samantha; Conrath, Andrea B; Kaul, Monisha; Herndon, George; Kough, John
Sent:	9/30/2016 3:08:23 PM
Subject:	Action Items from AR Interagency Meeting
Attachments:	Antibiotic Resistance Interagency Meeting Minutes 09-28-16.docx

Hi,

Thanks to all for helping to make Wednesday's meeting so productive. I have attached a copy of the meeting minutes. If everyone could please review and make sure that I have not overlooked, misinterpreted, or erred on anything I would truly appreciate it.

The minutes detail the action items (highlighted with ***), but for clarity I am also going to include them here (again, please let me know if this list can be improved):

B5

I'm looking forward to working with all of you on this.

Thanks,

Susan.

Susan Jennings
Senior Advisor for Public Health
Office of Pesticide Programs
(706) 355-8574 (office)
(703) 216-8627 (cell)

Antibiotic Resistance Interagency Meeting Minutes

September 30, 2016

FDA Report Out:

FDA presented an overview of their efforts to minimize the impact of antibiotics in livestock from promoting antibiotic resistance. By January, 2017, they expect to have no antibiotics licensed for weight gain. FDA looks at all compounds for antibiotic resistance, not only antibiotics (they presented an example of hydrogen peroxide). FDA also relies up Guideline 159 to evaluate potential residues consumed by humans through meat, milk, or eggs from treated livestock. (Dr. Jeffrey Gilbert and Dr. Heather Hardbottle from FDA participated).

USDA Report Out:

Discussed use of bacterial static compounds and the role of suppressing bacteria in the host organism. USDA also discussed some of the research being conducted into the various types of control, including: injection and phage research (1 is registered in BPPD). (Dr. Rose Hammon, Dr. Carl Shultze, Dr. Julius Fajardo from USDA participated).

CDC Report Out

CDC discussed their various surveillance measures and the importance of antibiotic stewardship. NARMS tracks bacterial pathogens in animal food. Includes shigella, MRSA and other healthcare and community spread pathogens. CDC also captures antibiotic-resistant infections in hospitals, characterizes bacterial isolates, and measures antibiotic use in the healthcare system. CDC has seen increasing threats from antibiotic resistance and new types of resistance mechanisms. There is also concern about hospital effluent into the environment. (Dr. Michael Craig and Dr. Jean Patel participated from CDC).

Discussion about how to assess potential for antibiotic resistance from antibiotics used in crops

Current levels of persistence: about 25 day half-life for aminoglycosides and 12 – 26 days for streptomycin.

B5

Risk in Greenhouse: Group believes that it is only a concern to the extent that it's a risk directly to humans or in a transfer from greenhouse to real world.

Limitations for yearly restriction (do not use on same land in less than a four year cycle to encourage rotation and other physical means of control) was determined not to be feasible. Challenges discussed included enforceability, compliance, and even whether the growers would know if it had been used in

EPAREF2656-000032

the previous year. USDA pointed out that these diseases are frequently transmitted via the seed so that even if a field is clear one year, the bacteria could be reintroduced the next. CDC felt that putting something unenforceable on the label could lead to a false sense of accomplishment.

Monitoring Data

The group discussed the feasibility and benefit of monitoring data. CDC does not believe any of the monitoring data submitted thus far have been very useful. EPA scientists for the most part concurred. Most powerful tool is sequencing; however, sequencing will not detect novel modes of resistance, the researcher needs to know what they are looking for.

B5

B5

(FDA may have a template to start with).

EPAREF2656-000033

EPAREF2656-000034

Document properties

Author: Jennings, Susan
Template: Normal.dotm
Page count: 2
Paragraph count: 31
Line count: 71
Word count: 770
Character count (spaces excluded): 4142
Character count (spaces included): 4890

From: Harbottle, Heather </O=FDA/OU=FIRST ADMINISTRATIVE GROUP/CN=RECIPIENTS /CN=HHARBOTT>
To: Jennings, Susan; Gilbert, Jeffrey M
CC: Johnson, Hope; Garvie, Heather
Sent: 7/31/2017 9:51:11 PM
Subject: AR Comments - Streptomycin

Hi Susan and all,
Please find below our comments on the Streptomycin application and the addendum summarizing the CDC MIC data. I'll get back to you with comments on the tetracycline and kasugamycin application by Weds/Thurs. Although, unless something jumps out at us regarding the kasugamycin application, B5

B5

Comments for Streptomycin 152 Firewall 50WP 07032017 Document and the Addendum summarizing CDC MIC data on streptomycin:

B5

B5

B5

Thank you for giving us the opportunity to comment on these assessments. I will send our comments on oxytetracycline (and kasugamycin, if any) on Weds/Thurs at the latest.

Let us know if you have questions!

Best,
Heather

From: Jennings, Susan [mailto:Jennings.Susan@epa.gov]
Sent: Monday, July 31, 2017 11:33 AM
To: Harbottle, Heather; Gilbert, Jeffrey M
Cc: Johnson, Hope; Garvie, Heather
Subject: RE: AR Comments

Ok. thanks.

From: Harbottle, Heather [mailto:Heather.Harbottle@fda.hhs.gov]
Sent: Monday, July 31, 2017 11:31 AM
To: Jennings, Susan <Jennings.Susan@epa.gov>; Gilbert, Jeffrey M <Jeff.Gilbert@fda.hhs.gov>
Subject: RE: AR Comments

Hi Susan,
I'll look them over today and get back to you asap. We do have some comments.
Thanks!
Heather

From: Jennings, Susan [mailto:Jennings.Susan@epa.gov]
Sent: Monday, July 31, 2017 11:29 AM
To: Harbottle, Heather; Gilbert, Jeffrey M
Subject: AR Comments

Hi,

Did you have any comments on the antibiotic assessments from EPA? Or are you OK with them?

Thanks,

Susan.

From: Jennings, Susan <Jennings.Susan@epa.gov>
To: Long, Charli
CC: Gilbert, Jeffrey M; Harbottle, Heather
Sent: 3/5/2018 7:36:38 PM
Subject: check in on earlier email

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Susan.

Susan Jennings
Senior Advisor for Public Health
Office of Pesticide Programs
(706) 355-8574 (office)
(703) 216-8627 (cell)

From: Jennings, Susan <Jennings.Susan@epa.gov>
To: Patel, Jean (CDC); Harbottle, Heather; Gilbert, Jeffrey M; Rose Hammond; Julius Fajardo
CC: Garvie, Heather; Johnson, Hope
Sent: 10/10/2017 1:49:06 PM
Subject: Draft Decision Document Interagency discussion

Hi all,

Below is some language that we would like to include in the draft risk management decision. I pulled the language for each of your agencies from the web, link is provided at the end of each paragraph.

Could each of you please read through this and let me know if there are any issues? I want to stick as closely to web language as possible since we don't have time for interagency concurrence.

Thanks,

Susan.

==========
Other agencies in the federal government (CDC, FDA, USDA) are aware of the potential for resistance to develop from the use of antibiotics in agriculture and have been working within their areas of expertise to address the problem. CDC cites "Improving Antibiotic Prescribing/Stewardship" as one of its Four Core Actions to Fight Resistance. CDC believes antibiotic stewardship is the "commitment to always use antibiotics appropriately and safely -- only when they are needed to treat disease, and to choose the right antibiotics and to administer them in the right way in every case." For more on CDC's views, see https://www.cdc.gov/drugresistance/about.html/.

FDA is committed to further advancing antimicrobial stewardship by focusing on the following key initiatives: (1) aligning antimicrobial drug products with the principles of antimicrobial stewardship in veterinary settings; (2) supporting efforts to foster stewardship of antimicrobials in veterinary settings; and (3) assessing the impact of strategies intended to curb the emergence of antimicrobial resistance associated with the use of antimicrobial drugs in veterinary settings. For more on FDA's views, see https://www.fda.gov/AnimalVeterinary/SafetyHealth/AntimicrobialResistance /JudiciousUseofAntimicrobials/ucm535158.htm]

USDA is funding research where the focus addresses studying the role of agriculture in antimicrobial resistance, reducing potential negative impacts from the use of antibiotics, and identifying alternative strategies for mitigating AMR in the food chain. The goal is to reduce or negate any potential negatively adverse impact of antimicrobials used in agriculture that may have potentially adverse effects on the treatment of human diseases. For more on USDA's views, see https://nifa.usda.gov /antimicrobial-resistance]

EPA believes that the management of pesticide resistance development is an important part of sustainable pest management and, in conjunction with alternative pest management strategies and IPM programs, can make significant contributions to reducing risks to humans and the environment. In support of these goals, EPA is assessing the potential development of antibiotic resistance as an adverse effect under FIFRA.

==========

From: Hill, Shaunta <Hill.Shaunta@epa.gov>
To: Harbottle, Heather; Jennings, Susan
CC: Gilbert, Jeffrey M
Sent: 2/10/2016 11:34:13 AM
Subject: EPA - Pending antibiotic request for Streptomycin, request for a teleconference
Attachments: 6. FL Citrus Greening Section 18 Antimicrobial Request petition and lett....pdf; 7. FDA 152 FireWall Resistance Risk Assessment HLB and Canker 10-19-15.pdf; 8. FDA 152, FireLine Resistance Risk Assessment, 10-2-15.pdf

This is the second email for Wednesday's teleconference.
If you have any questions / trouble with the files, please let me know.
Thank you

Regards,
****

Shaunta Hill-Hammond, Ph. D.
Plant Pathologist
U.S. EPA: Office of Chemical Safety and Pollution Prevention
Registration Division/Fungicide Branch (PYS)
1200 Pennsylvania Avenue, NW (7505P)
Washington, DC 20460

Tel: 703.347.8961 I Fax: 703.305.6920
E-mail: hill.shaunta@epa.gov
URL Address: www.epa.gov/pesticides

From: Harbottle, Heather [mailto:Heather.Harbottle@fda.hhs.gov]
Sent: Tuesday, February 09, 2016 4:58 PM
To: Hill, Shaunta <Hill.Shaunta@epa.gov>; Jennings, Susan <Jennings.Susan@epa.gov>
Cc: Gilbert, Jeffrey M <Jeff.Gilbert@fda.hhs.gov>
Subject: RE: EPA - Pending antibiotic request for Streptomycin, request for a teleconference

Hi Shaunta,
We'll be happy to call in. Is there a call in number and agenda yet for the teleconference tomorrow at 11am?
Thanks!
Heather

From: Hill, Shaunta [mailto:Hill.Shaunta@epa.gov]
Sent: Monday, February 08, 2016 12:16 PM
To: Harbottle, Heather; Jennings, Susan
Cc: Gilbert, Jeffrey M
Subject: RE: EPA - Pending antibiotic request for Streptomycin, request for a teleconference

Hello Heather,
We did meet during the IR-4 meeting. Happy to hear that you and Jeff will be joining our discussion.

The meeting agenda will be finalized shortly and I will forward it along with several reference documents for our discussion.
In the meantime, I wanted to provide some background information on pesticide registrations.

The type of registrations permitted under FIFRA (i.e. Section 3 and Section 18) can be found here: http://www.epa.gov/pesticide-registration/types-registrations-under-fifra

Information on the general registration process can be found here: http://www.epa.gov/pesticide-registration/pesticide-registration-manual-chapter-1-overview-requirements-pesticide

I hope you find this initial information helpful.
If you have any questions, please let me know.

Regards,
****

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Tel: 703.347.8961 I Fax: 703.305.6920
E-mail: hill.shaunta@epa.gov
URL Address: www.epa.gov/pesticides

From: Harbottle, Heather [mailto:Heather.Harbottle@fda.hhs.gov]
Sent: Friday, February 05, 2016 8:35 AM
To: Hill, Shaunta <Hill.Shaunta@epa.gov>; Jennings, Susan <Jennings.Susan@epa.gov>
Cc: Gilbert, Jeffrey M <Jeff.Gilbert@fda.hhs.gov>
Subject: FW: EPA - Pending antibiotic request for Streptomycin, request for a teleconference
Importance: High

Good morning Ms. Hill and Ms. Jennings,

My name is Heather Harbottle and I believe we met during the IR-4 Bacterial Challenges Mini-Summit meeting "Understanding the ABCs (Awareness of Bacterial Challenges) with Antibiotics In Crops" in September of 2014. As you may remember, I delivered a presentation regarding FDA's use of GFI #152 due to our extensive use of this guidance assessing risk for the use of antimicrobials in food producing animals. I've been asked by Bill Flynn and my team leader, Dr. Jeff Gilbert, to get in touch with you regarding your email below. Dr. Gilbert and I would be happy to attend the teleconference on Wednesday, and provide any assistance with GFI #152 as it pertains to your application for streptomycin or any other antimicrobial.

Please let us know how we can be of help.

Best,
Heather Harbottle

From: Hill, Shaunta [mailto:Hill.Shaunta@epa.gov]
Sent: Thursday, February 04, 2016 9:59 AM
To: Flynn, William T
Cc: Jennings, Susan
Subject: EPA - Pending antibiotic request for Streptomycin, request for a teleconference

Hello Dr. William;

My name is Shaunta Hill and I am a Risk Assessor/Plant Pathologist with EPA's Office of Pesticide Programs – Registration Division.
I received your name from Dr. Jean Patel at CDC as a potential contact.

As EPA manages antibiotics for pesticidal use, we are interested in accessing the resistance risk potential along with human and environmental risks. We have previously worked with CDC and FDA (via David White) utilizing the FDA Guidance for Industry #152 for this purpose.

We have a number of applications currently pending and have scheduled a teleconference for **Wednesday Feb 10 at 11 am** to begin discussions.
I am hopefully that you are available to participate in this discussion as FDA input is valued.
The primary application for consideration next week is Streptomycin sulfate use on grapefruit and tomatoes via FIFRA Section 3 Registration.

If you are available, I can provide additional background information in addition to our meeting agenda.
Should you have any questions, please let us know. I have cc'ed on this communication Susan Jennings, who serves as our Public Health Coordinator and is available to address questions on this meeting request as well.

Thank you for your time and I look forward to hearing from you.

Regards,
****

Shaunta Hill-Hammond, Ph. D.
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U.S. EPA: Office of Chemical Safety and Pollution Prevention
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Tel: 703.347.8961 | Fax: 703.305.6920
E-mail: hill.shaunta@epa.gov
URL Address: www.epa.gov/pesticides

From: Hill, Shaunta <Hill.Shaunta@epa.gov>
To: Harbottle, Heather; Jennings, Susan
CC: Gilbert, Jeffrey M
Sent: 2/10/2016 11:33:52 AM
Subject: EPA - Pending antibiotic request for Streptomycin, request for a teleconference
Attachments: 1. Resistance Monitoring Protocol Draft 11-13-14.pdf; 2. 2014 Testing and Field Monitoring for Streptomycin Resistance under F....pdf; 3. 4921332-02-XX.PDF; 4. image2016-02-01-085505.pdf; 5. 080990-00003.20151123.revised Master Label.pdf; Meeting agenda.pdf

Good Morning Heather and Jeff,
Please see the attached agenda and support files for our teleconference Wednesday – Feb 10, 2016 at 11 am.
The conference line information is noted on the agenda.

**Due to the file sizes, two emails will be sent.*

If you would not mind, could you please provide contact information and title for both you and Jeff.
Thank you

From: Harbottle, Heather [mailto:Heather.Harbottle@fda.hhs.gov]
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To: Hill, Shaunta <Hill.Shaunta@epa.gov>; Jennings, Susan <Jennings.Susan@epa.gov>
Cc: Gilbert, Jeffrey M <Jeff.Gilbert@fda.hhs.gov>
Subject: FW: EPA - Pending antibiotic request for Streptomycin, request for a teleconference
Importance: High

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Washington, DC 20460

Tel: 703.347.8961 | Fax: 703.305.6920
E-mail: hill.shaunta@epa.gov
URL Address: www.epa.gov/pesticides

Ceres International LLC

November 13, 2014

Document Processing Desk
Office of Pesticide Programs
U.S. Environmental Protection Agency
Room S-4900, One Potomac Yard
S. 2777 Crystal Drive
Arlington, Virginia 22202-4501

Attention: Tawanda Maignan, Minor Use & Emergency Response Team (Sect.18)

Subject: **FireWall™ 50 WP; EPA Re. No. 80990-3,**
Submission of Protocol for Resistance Monitoring

Dear Ms. Maignan:

On June 12, 2014 EPA issued a specific exemption according to the provision of Section 18 under FIFRA to the Florida Department of Agriculture and Consumer Service (FDACS) for the use of FireWall 50 WP (65.8% streptomycin sulfate) on grapefruit to control citrus canker. As a condition of this approval, the Agency requested FDACS and its partners (AgroSource) to conduct testing and field monitoring for resistant populations of *Xanthomonas citri* subsp. *Citri* in grapefruit groves treated with FireWall 50 WP.

AgroSource, in cooperation with USDA/ARS and FDACS, hereby submits its resistance monitoring protocol relative to the above. If you have any questions or comments, please do not hesitate to contact me at 610-793-3222 or by e-mail at bertvolger@ceresinternational.com.

Sincerely,

Bert Volger
Agent for AgroSource, Inc.

Enclosure

Cc: T. Richardson, AgroSource
R. Amundson, AgroSource
Charlie Clark -FDACS
Bob Moore: -FDACS
Mike Aerts -FFVA

1087 Heartsease Drive ■ West Chester, PA 19382 ■ 610-793-3222

Monitoring *Xanthomonas citri* subsp. *citri* for risk of streptomycin resistance in Florida grapefruit groves following treatment with FireWall™ 50 WP for canker management - Protocol

Background:

FireWall 50 WP (65.8% streptomycin sulfate; AgroSource, Inc.) was granted a specific exemption by EPA on June 12, 2014 under the provisions of section 18 of FIFRA for control of citrus canker in Florida grapefruit. The Section 18 label for FireWall restricts use to no more than two applications at 11 oz./Ac, each application. As a condition for use of FireWall registration, EPA requires monitoring of *Xanthomonas citri* subsp. *citri* (Xcc) for streptomycin resistance in treated groves. This survey will apply the published protocol (Behlau et al., 2012) for sampling canker-infected grapefruit leaves for detection streptomycin resistance.

Overview:

The Project Coordinator (PC, Dr. Morgan) will contact and identify Florida grapefruit grower who plan to use FireWall in their canker management program. PC will identify five locations, based on knowledge of past canker problems in area and ability to obtain required samples from location. Growers and grove managers will determine timing of applications. For each FireWall treated grove, the PC will identify a portion of the grapefruit grove that will not be treated with FireWall to act as the untreated area. The untreated grove area will be selected to be comparable to the treated grove in tree management and productivity. Selection of locations will be reviewed and agreed upon with Project Directors from USDA/ARS (Drs. Shatters and Stover) and AgroSource (Dr. Trimmer).

All samples will be collected in parallel from the FireWall treated and untreated groves. Evaluations and sampling from each site will include the following:

Sampling

- Leaf samples for bacterial monitoring
- Soil samples for bacterial monitoring
- Fruit samples for FireWall residue analysis (including whole fruit, juice, and oil)

Sampling Procedure:

All samples should be collected from 5 trees within the treated and 5 trees from within the untreated area of the grove.

Bacterial Resistant Monitoring:

Resistance monitoring sampling procedure for the Firewall Section 18 program is outlined below. Samples should be collected prior to Firewall application and following Firewall application at approximately monthly intervals for at least three months. Both leaf and soil samples should be collected and analyzed, as described in the procedure(s) below. **All samples should be handled using aseptic (sterile) technique.**

Leaf selection:

1. Select five representative trees in the treated area and five representative trees in the untreated area, randomly distributed in the grove.
2. Using sterile gloves, from each tree, sample four, canker free, mature, fully expanded leaves from the most recent flush. One leaf should be sampled from each quadrant (North, South, East, and West) of the tree.
3. Place four leaves from each tree into a single labeled sampling bag and place in cooler immediately after sampling.
4. Upon return to lab, store samples in refrigerator prior to analysis.

Leaf Wash/Plating Analysis:

1. Weigh the leaves in a sterile container (e.g. Petri dish) to determine the weight of the leaves
2. Place the leaves (combined) into a 50 mL sterile conical vial.
3. Add 10 mL of MGY Broth per gram of leaf material to the 50 mL conical vial.
4. Place conical vials on their side with leaves in a horizontal position in line with the MGY broth on a shaker with vigorous shaking 'wash' (perform at room temperature for 2 hours).
5. After 1 hour flip the vials and continue shaking.
6. After 2 hours take conical vials off and plate out serial dilutions by adding 100 uL of wash broth to 900 uL of tap water (per Belhau et al, 2011) forming a 10^{-1} dilution, and perform for 2 more dilutions (10^{-2} and 10^{-3}).
7. Plate 100 uL of each serial dilution onto MGY agar with Streptomycin (@ 100 µg/mL) + Cycloheximide (@ 50 µg/mL) and onto MGY plates without streptomycin (e.g. MGY + Cycloheximide [50 µg/mL]) for all samples.
8. Place plates on a tray and incubate at 28 C for 96 hours.
9. At 96 hours count colonies on each plate and also designate the number of unique types of colony morphology and record this information.

10. Following colony and colony type counts, select a representative colony from each morphology type and streak these on an MGY + Cycloheximide (50 µg/mL) plate.
11. Place these at 28°C for 24-48 hours to grow.
12. Screen these bacteria using a standard Gram stain protocol to determine the gram-negative bacteria populations and harvest from the streak plate and store in MGY Broth with 15% glycerol in labeled tubes at -70 C.

Soil selection:

1. From the same five representative trees used for leaf sampling in the treated and untreated areas, sample soil from each quadrant (N, S, E, W) under the dripline at a depth of 7.5 cm using a sterile implement and collect these as a bulk sample into a single sterile labeled bag.
2. Place in a cooler immediately after sampling.

Soil Plating Analysis:

1. Upon returning to the lab, mix the bulk soil within the bag by shaking.
2. Open the bag and using a sterile implement weigh out 2 grams of soil into a sterile Petri dish.
3. Aseptically transfer the 2 g of soil and place into a sterile 50 mL conical vial and add 20 mL chilled 0.5X phosphate buffered saline (PBS).
4. Place 50 mL sample vials into an ice water bath and place a sonication probe into the center of the ice water bath to sonicate at setting #9 for 8 minutes.
5. After 4 minutes, rotate the soil vials and continue to sonicate.
6. After sonication, vortex the 50 mL tubes for 3-5 seconds and pipette out 100 µL into 900 µL of 0.5X PBS forming a 10^{-1} dilution
7. Perform sequential serial dilutions 1/10 (transfer 100 µL into 900 µL) out to 10^{-5}.
8. Plate 100 µL of 10^{-1} through 10^{-5} onto MGY agar with Streptomycin (@ 100 µg/mL) + Cycloheximide (@ 50 µg/mL) and onto MGY plates without streptomycin (e.g. MGY + Cycloheximide [50 µg/mL]) for all samples.
9. Place plates on a tray and incubate at 28 C for 96 hours.
10. At 96 hours count colonies on each plate and also designate the number of unique types of colony morphology and record this information.
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12. Place these at 28°C for 24-48 hours to grow.

13. Screen these bacteria using a standard Gram stain protocol to determine the gram-negative bacteria populations and harvest these individually from the streak plate and store in MGY Broth with 15% glycerol in labeled tubes at -70 C.

To Make 10 mL Stock Solution of Streptomycin Sulfate:

Weigh out 1 gram of technical Streptomycin Sulfate (not FireWall) and bring the volume up to 10 mL in sterile H_2O and mix to dissolve. Add 1 mL of stock solution to 1 Liter of MGY Agar to obtain a final concentration of 100 µg/mL.

To Make 10 mL Stock Solution of Cycloheximide:

Weigh out 0.5 grams of technical Cycloheximide and bring the volume up to 10 mL in 95% ethanol and mix to dissolve. Add 1 mL of stock solution to 1 Liter of MGY Agar to obtain a final concentration of 50 µg/mL.

To Make 1 Liter of MGY Agar or MGY Broth (leave out the Agar for the Broth) add:

- 10.0 g of Mannitol
- 2.0 g L-glutamic acid
- 0.5 g KH_2PO_4
- 0.2 g NaCl
- 0.2 g $MgSO_4$
- 1.0 g yeast extract
- 15.0 g agar (leave out for broth)

Autoclave to sterilize at 121°C for 15 min – 20 min (e.g. use the L3 setting on USHRL autoclaves)

Add antimicrobials as needed (streptomycin and or Cycloheximide) to agar once the liquid agar has cooled to ~40-50°C and swirl to mix. Take care not to introduce bubbles to the medium.

CFU and Monitoring Resistance Plan:

Total aerobic bacterial Colony Forming Units (CFUs) per gram of leaf tissue (washate) or total aerobic bacterial CFU's per gram of soil (washate) will be calculated following standard methods for serial dilution computations of CFU's from the countable bacterial plates (e.g. 25-250 colonies) from both agar plate types: MGY supplemented only with Cycloheximide and MGY supplemented with both Cycloheximide and streptomycin. The pre-treatment

(T0) samples along with a comparison of treated verses non-treated sites (from all five locations in the study) will be used for relative comparisons to determine both the native streptomycin resistance present at onset of the study in these environments before streptomycin treatment and to monitor for any potential newly acquired streptomycin non-susceptibility trends. Relative significant changes in bacterial populations over time on the bacterial plates with supplemented streptomycin may indicate an increase in streptomycin resistance in these environments. Any indication of acquired streptomycin resistance in the native aerobic bacterial populations will be further analyzed to determine if specifically *Xanthomonas citri* subsp. *citri* colonies are implicated in streptomycin acquired resistance.

Reference

Behlau F., Jones, J.B., Myers, M.E. and Graham, J.H. 2012. Monitoring for resistant populations of *Xanthomonas citri* subsp. *citri* and epiphytic bacteria on citrus trees treated with copper or streptomycin using a new semi-selective medium. European Journal of Plant Pathology 132:259–270.

EPA – FDA – CDC Teleconference Discussion of pending agricultural antibiotic applications **Feb 10, 2016. 11 am**	**Teleconference Information:** **Dial:** **Code** B6

Meeting Lead: Shaunta Hill-Hammond EPA – OPP-RD (703-347-8961, hill.shaunta@epa.gov)
A list of participants will be provided with the MOU following the teleconference.

Agenda:

1. Introductions
2. Purpose of the meeting
3. Section 3 request: Streptomycin sulfate use on grapefruit and tomato (greenhouse and field)
   a. **Risk Management Summary:**

Target dates	
Last Science Due Date:	7/15/15
CDC/FDA teleconference	2/10/16
Public Participation Period:	3/24/16
PRIA Due Date:	5/16/16

   b. Relevant documents: files 1-5
   c. Grapefruit Considerations
      i. Currently approved via Section 18 (use granted 2013-2015)
      ii. One season of monitoring data available
   d. Tomato Considerations
      i. Current use is limited to greenhouse seedlings
      ii. No monitoring data available
      iii. No restrictions against treatment both in the greenhouse and field

TIME PERMITTING:

4. Section 18 request: Streptomycin sulfate and Oxytetracycline hydrochloride use on citrus-lemons, grapefruit and oranges (Florida limited)
   a. Relevant documents: files 6-8
   b. Considerations
      i. Streptomycin currently approved for Section 18 use on grapefruit.

Attachments:

1. Streptomycin monitoring protocol
2. Streptomycin monitoring report (2014 use season)
3. Applicant 152 document (49213202)
4. EPA review memo (image2016-02-01)
5. Proposed label (080990-00003.20151123. revised Master Label)
6. FL Citrus greening Section 18 petition
7. Applicant 152 – Streptomycin – citrus
8. Applicant 152 – Oxytetracycline hydrochloride –citrus

From:	Jennings, Susan <Jennings.Susan@epa.gov>
To:	Patel, Jean (CDC); Gilbert, Jeffrey M; Harbottle, Heather; Fajardo, Julius; Hammond, Rose; Tichenor, Robert H - APHIS; Carl.P.Schulze@aphis.usda.gov
CC:	Britton, Cathryn; Johnson, Hope; Manupella, Matthew; Garvie, Heather
Sent:	9/27/2016 3:22:43 PM
Subject:	EPA AR Assessment Interagency Meeting
Attachments:	interagency agenda 09-28-16.doc

Hi all,

Attached is an agenda for tomorrow's meeting. We will have several new players in the room from USDA (welcome!) and you'll notice an agenda item starting at 10:15 for each of the agencies to tell the group your agency's role in antimicrobial resistance and to provide us with any new updates or changes in the past year or so.

If you have any questions, please let me know. When you arrive in the building, you can wait in the lobby and we'll be down to escort you up. Please bring your federal badges, as it will help the process move quickly.

I'm looking forward to our meeting tomorrow and please let me know if you have any questions. This will be a fairly casual meeting, so please come as you are.

Thanks,

Susan.

Susan Jennings
Senior Advisor for Public Health
Office of Pesticide Programs
(706) 355-8574 (office)
(703) 216-8627 (cell)

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

Antimicrobial Resistance Assessment Interagency
Room S-7100, seventh floor, Potomac Yards South
No conference line until 3:30
September 28, 2016

Agenda (all times are approximations)

9:00	Arrival/Welcome/Introductions
9:15	Brief history of EPA's process and goals for the day
9:30	Brief history of FDA/CDC/USDA, current processes and updates
10:15	Goals for the day of workgroup, problem definition
10:30	Guideline 152 (what is its value and what is not helpful)
11:00	Presentation of assessment elements (followed by discussion of each) - Efficacy, environmental fate and half-life in the environment, application technique, pathogens to control, class of proposed compound, importance in human disease control, extent of use area, agricultural alternatives to pesticides, cross-resistance, existing resistance, others?
12:00	Lunch
1:00	Discussion of importance/weight of assessment elements (continued)
2:00	Discussion of feasibility/potential of mitigation options - Treatment intervals (based on crop rotation to eliminate disease), time limited registrations, prescription use only, others?
3:30	Teleconference with CDC on aspergillus resistance from use of azoles in agriculture
4:30	Next steps and conclusions of the day

Document properties

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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, DC 20460

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

February 27, 2018

Charli Long, Ph.D.
Director, Division of Human Food Safety
Center for Veterinary Medicine
U.S. Food and Drug Administration
HFV-150, 7500 Standish Place
Rockville, MD 20855

Dear Dr. Long:

The U.S. Environmental Protection Agency (EPA) currently has pending new use actions for the antibiotics oxytetracycline and streptomycin for certain pesticidal agricultural uses. For oxytetracycline, EPA has recently published a proposed decision for certain new uses, including publication of documents and assessments that support that decision (for reference, please see https://www.regulations.gov/ and Docket ID: EPA-HQ-OPP-2015-0820). For streptomycin, we have completed our assessments and expect to publish a proposed decision for certain new uses in the near future. Because these application of pesticides will result in residues of those pesticides in or on food, tolerances are required in order to register these new uses.

Under the Federal Food Drug and Cosmetic Act, EPA, when setting tolerances, must determine that the levels of allowed pesticide residues in food are safe, i.e. that there is a "reasonable certainty of no harm [resulting] from aggregate exposure to the pesticide chemical residue, including all anticipated dietary exposures and all other exposures for which there is reliable information." FFDCA §408(b)(2)(A)(ii). For substances that are used for pesticidal and pharmaceutical drug purposes, such as oxytetracycline and streptomycin, EPA has worked with FDA in the past to assess the safety of tolerances for those pesticides.

Under FFDCA section 505, FDA reviews human drugs for safety and effectiveness and may approve a drug notwithstanding the real possibility that some patients may experience adverse side effects. EPA does not believe that, for the purposes of section 408 dietary risk assessment, it is compelled to treat a pharmaceutical patient the same as a non-patient, or to assume that combined exposures to pesticide and pharmaceutical residues that lead to a physiological effect constitutes "harm" under the meaning of section 408. Rather, EPA believes the appropriate way to harmonize sections 408 and 505 is to examine the impact that the additional non-occupational pesticide exposures would have to a pharmaceutical patient exposed to a similar (or, in some cases, the same) compound. Where the additional pesticide exposure has not more than a minimal impact on the pharmaceutical patient, EPA could make a reasonable certainty of no harm finding for the pesticide tolerances of that compound under section 408. If the potential impact on the pharmaceutical user as a result of co-exposure from pesticide use is not deemed to be minimal, then the Agencies could discuss appropriate measures to reduce exposure from one or both sources.

Under this approach, EPA must look to FDA's authority to determine the safety of a pharmaceutical patient who may be additionally exposed to oxytetracycline and/or streptomycin pesticide residues under conditions of co-exposure.

The information below is being provided to FDA for consideration in determining whether the additional pesticide exposure to oxytetracycline and streptomycin results in no more than a minimal impact on the pharmaceutical patient. EPA requests that, following your review of this information, FDA provide a letter summarizing your conclusions, as this will be an important part of EPA's public record on this issue. EPA previously had a similar request during Reregistration of oxytetracycline and FDA's written determination was appreciated [http://www.regulations.gov; EPA-HQ-OPP-2005-0492-0028 and EPA-HQ-OPP-2005-0492-0031]. We request that FDA provide your written determination to EPA by March 7, 2018, if possible.

The EPA's Health Effects Division considered typical human daily dosages of both oxytetracycline and streptomycin as human drugs to determine how these doses compared to the worst case exposures potentially incurred as a result of the food plus drinking water exposures resulting from pesticidal uses of the chemicals. To assure a conservative assessment, the pesticide exposures were calculated using tolerance-level residues and an assumption that 100% of the relevant crops are treated so to represent screening-level values, which will far exceed any exposures likely to actually occur from use of oxytetracycline or streptomycin as pesticides.

This assessment is summarized below:

Chemical	Age	Drug Dosage (mg/kg/day)	Dietary exposure from pesticide use (mg/kgbw/day)	Drug dose to dietary exposure ratio
Oxytetracycline	Adult	15	0.0079	1900X
	Child > 8 y/o	1.6	0.0164	100X
Streptomycin	Adult	15	0.019	790X
	Child > 8 y/o	15	0.02	750X

As you can see, the typical drug dosage is significantly higher (100 to 1900 times higher) than the conservatively estimated dietary (i.e., food and drinking water) exposures from pesticidal use of oxytetracycline and streptomycin. Based on these estimates, EPA poses the following two questions to FDA:

1. Does FDA have any concern that the additional dose of oxytetracycline from the pesticide uses of oxytetracycline – estimated to range from 0.0079 mg/kgbw/day to 0.0164 mg/kgbw/day – would result in more than a minimal impact on an individual who may be treated therapeutically with oxytetracycline?

2. Does the FDA have any concern that the additional dose of streptomycin from the pesticide uses of streptomycin – estimated to range from 0.019 mg/kgbw/day to 0.02 mg/kgbw/day – would result in more than a minimal impact on an individual who may be treated therapeutically with streptomycin?

Again, we request FDA to provide your written determination to EPA by March 7, 2018, if possible. If you have comments on the information provided, or need any further documentation, please let us know and we will schedule a conference call or meeting to exchange comments and discuss FDA's assessment. You may contact me at 703-308-8157 or goodis.michael@epa.gov. Thank you in advance!

Sincerely,

Michael L. Goodis, P.E.
Director, Registration Division (RD)
Office of Pesticide Programs (OPP)

U.S. ENVIRONMENTAL PROTECTION AGENCY

OFFICE OF INSPECTOR GENERAL

Ensuring the safety of chemicals

Measures and Management Controls Needed to Improve EPA's Pesticide Emergency Exemption Process

Report No. 18-P-0281 **September 25, 2018**

Report Contributors:

Ming Chang
Jeffrey Harris
Lauretta Joseph
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Abbreviations

CFR	Code of Federal Regulations
EPA	U.S. Environmental Protection Agency
FIFRA	Federal Insecticide, Fungicide, and Rodenticide Act
OCSPP	Office of Chemical Safety and Pollution Prevention
OIG	Office of Inspector General
OMB	Office of Management and Budget
OPP	Office of Pesticide Programs
SLA	State Lead Agency
SOP	Standard Operating Procedure
U.S.C.	United States Code

Cover Photo: Citrus greening (a bacterial disease) occurring on a Florida citrus tree. (U.S. Department of Agriculture)

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U.S. Environmental Protection Agency
Office of Inspector General

18-P-0281
September 25, 2018

At a Glance

Why We Did This Project

We conducted this audit to determine whether the U.S. Environmental Protection Agency (EPA) has a comprehensive pesticide emergency exemption approval process that maintains environmental and human health safeguards.

Under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), all pesticides distributed and sold in the United States must be registered by the EPA for each specific use. Per Section 18 of FIFRA, the EPA can grant federal and state lead agencies the authority to approve—in certain emergency situations—the limited application of a pesticide not registered for that particular use. These short-term pesticide use approvals are called *emergency exemptions*.

This report addresses the following:

- *Ensuring the safety of chemicals.*

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Measures and Management Controls Needed to Improve EPA's Pesticide Emergency Exemption Process

What We Found

The EPA needs outcome measures to demonstrate the benefits or risks of pesticide emergency exemptions on human health and the environment.

The EPA's Office of Pesticide Programs (OPP) does not have outcome measures in place to determine how well the emergency exemption process maintains human health and environmental safeguards. The program office also does not have comprehensive internal controls to manage the emergency exemption data it collects. Finally, the OPP does not consistently communicate emergency exemption information with its stakeholders.

Specifically, we found that the OPP collects human health and environmental data through its emergency exemption application process, including the total acres affected, the proposed and actual quantities of the exempted pesticide applied, and the estimated economic losses. Yet, we found that the OPP does not use these data to support outcome-based performance measures that capture the scope of each exemption or to measure the potential benefits or risks of each exemption.

We also found significant deficiencies in the OPP's online database management, in its draft Section 18 emergency exemption standard operating procedure and application checklist, and in its reports to Congress and the Office of Management and Budget. Some state lead agencies and extension agents that we interviewed also reported that additional guidance is needed to support the preparation of emergency exemption applications, including whether data can be used from applications submitted by other state lead agencies.

Furthermore, we found that the OPP previously sent a "year in review" letter to states that summarized the emergency exemption activity for that year and provided additional information regarding the emergency exemption process. However, the OPP has not sent this letter since 2015.

Recommendations and Planned Agency Corrective Actions

We recommend that the Assistant Administrator for Chemical Safety and Pollution Prevention develop outcome-based performance measures; develop or update procedures on data collection, database management and the re-use of data submitted by state lead agencies; and communicate changes to the emergency exemption processes in a timely manner. Of our eight recommendations, the EPA agreed with four, neither agreed nor disagreed with two, and disagreed with two. For three recommendations, the agency proposed corrective actions that meet the intent of the recommendations. The remaining five recommendations are unresolved.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

THE INSPECTOR GENERAL

September 25, 2018

MEMORANDUM

SUBJECT: Measures and Management Controls Needed to Improve EPA's Emergency Pesticide Exemption Process
Report No. 18-P-0281

FROM: Arthur A. Elkins Jr.

TO: Charlotte Bertrand, Acting Principal Deputy Assistant Administrator
Office of Chemical Safety and Pollution Prevention

This is our report on the subject audit conducted by the Office of Inspector General (OIG) of the U.S. Environmental Protection Agency (EPA). The project number for this evaluation was OPE-FY17-0024. This report contains findings that describe the problems the OIG has identified and corrective actions the OIG recommends. This report represents the opinion of the OIG and does not necessarily represent the final EPA position. Final determinations on matters in this report will be made by EPA managers in accordance with established audit resolution procedures.

The office responsible for issues evaluated in this report is the EPA's Office of Pesticide Programs within the Office of Chemical Safety and Pollution Prevention.

In accordance with EPA Manual 2750, your office provided acceptable corrective actions and milestone dates in response to Recommendations 2, 3 and 4. These recommendations are resolved and no final response is required.

Action Required

Recommendations 1, 5, 6, 7 and 8 are unresolved. In accordance with EPA Manual 2750, the resolution process begins immediately with the issuance of this report. We are requesting a meeting within 30 days between the acting Principal Deputy Assistant Administrator for Chemical Safety and Pollution Prevention and the OIG's Assistant Inspector General for Audit and Evaluation. If resolution is still not reached, the EPA is required to complete and submit a dispute resolution request to the Chief Financial Officer to continue resolution.

We will post this report to our website at www.epa.gov/oig.

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Purpose

The U.S. Environmental Protection Agency's (EPA's) Office of Inspector General (OIG) conducted this audit to determine whether the EPA has a comprehensive emergency exemption process that maintains environmental and human health safeguards.

Background

Pesticides are chemicals used to curb unwanted vegetation, insects, animals or bacteria. Pesticide use has contributed to increased agricultural production and improved public health through control of disease-ridden pests. However, pesticides are poisons. Acute and chronic issues affecting human health and causing environmental harm can be associated with exposure to many pesticides.

The Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) was enacted in part to reduce the negative impacts of pesticides on human health and the environment. All pesticides distributed or sold in the United States must be registered (licensed) by the EPA. Before the EPA may register a pesticide under FIFRA, the manufacturer or formulator (also known as the *registrant*) must show, among other things, that using the pesticide according to specifications "will not generally cause unreasonable adverse effects on the environment."[1] Under the normal, nonemergency registration requirements of FIFRA, a registrant of a pesticide must register that product for each specific use. Registrants must submit a new application each time they register a new pesticide active ingredient, register a new product for an existing pesticide active ingredient, or add a new use to an existing product registration.

Emergency Exemptions

Unexpected pests, invasive species or resistant strains of insect, weed, microbe or other type of pests that cannot be eliminated or controlled with registered pesticide products are periodically identified. Section 18 of FIFRA allows the EPA to grant federal and state agencies the authority to approve the limited application of a pesticide not currently registered for that use. These short-term pesticide use approvals are called *emergency exemptions*.

Regulations that govern the implementation of Section 18 of FIFRA are found at 40 CFR Part 166. These regulations identify four types of emergency exemptions: specific, quarantine, public health and crisis. As shown in Table 1, each type addresses a different emergency situation, and each has a corresponding allowable time frame for the emergency exemption.

[1] EPA, "Summary of the Federal Insecticide, Fungicide, and Rodenticide Act" webpage, and 7 U.S.C. § 136a(c)(5)(D).

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Table 1: Types of emergency exemptions

Type	Maximum duration	Description of emergency exemption
Specific	1 year	The most common emergency exemption. May be authorized in an emergency condition to avert a significant economic loss or a significant risk to endangered species, threatened species, beneficial organisms or the environment.
Quarantine	3 years	May be authorized in an emergency condition to control the introduction or spread of any pest that is an invasive species or not known to be widely prevalent or distributed within the United States and its territories.
Public health	1 year	May be authorized in an emergency condition to control a pest that will cause a significant risk to human health.
Crisis	15 days	May be utilized in an emergency condition when the time from discovery of the emergency to the time when the pesticide use is needed is insufficient to allow for the authorization of a specific, quarantine or public health exemption.

Source: 40 CFR § 166.2(a–d).

The purpose of an emergency exemption is to allow the application of a pesticide not currently registered for the requested use. Most emergency exemption applications are *specific* types, and nearly all of those applications address impacts to agricultural crops.

Emergency Exemption Process

State and federal agencies can apply for emergency exemptions when a serious pest problem jeopardizes public health or the production of agricultural goods. If the emergency exemption is based on current crop loss, applicants must demonstrate that a significant economic loss will or has occurred and that the pest cannot be countered by a pesticide currently approved for that use. In conjunction with growers and extension agents, a state lead agency (SLA) submits an emergency exemption application to the EPA.[2] The application specifies the estimated significant economic loss without the expanded use, the total requested application acreage, the requested application rate and other parameters of use, and numerous other information points.

In most instances, an emergency exemption applicant requests approval for the expanded use of a pesticide that has already been registered by the EPA for other uses. Because of the existing registration, the review time for the short-term emergency use is significantly reduced compared to the full registration process under Section 3 of FIFRA. In addition, as shown in Table 1, crisis exemptions can only be approved for 15 days, requiring the EPA's Office of Pesticide Programs

[2] *Extension agents* are employed by land-grant universities and serve the citizens of that state as experts or teachers on topics related to economics, community development, agriculture, family, animal production, diet or nutrition. An example of an *SLA* that would apply for an emergency pesticide exemption is a state department of agriculture.

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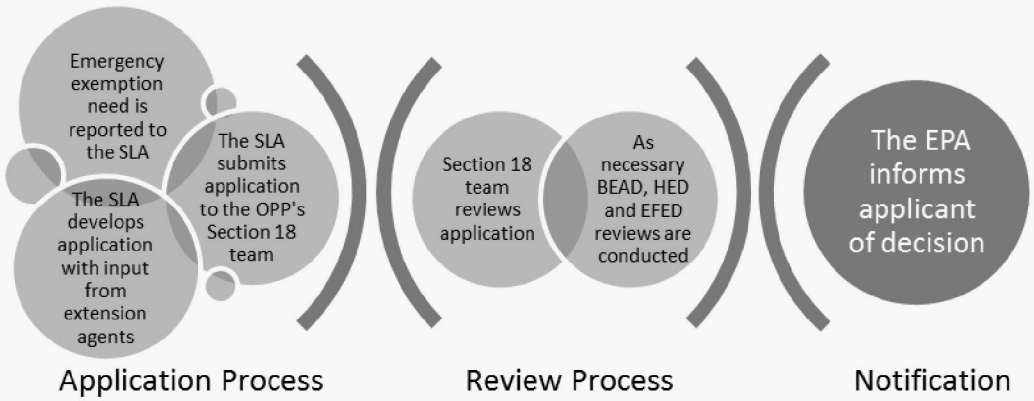
(OPP) to review those applications as quickly as possible. The other types of emergency exemptions have different review time frames. OPP staff informed us that their goal is to review and approve most emergency exemption applications (other than *crisis* types) within 50 calendar days of receipt. Reviews can take longer if the OPP needs to request more information from the SLA.

Once the OPP receives an emergency exemption application, the office's Section 18 team starts the review process (Figure 1). As a part of the review, the Section 18 team determines whether the emergency exemption request requires public notice in the Federal Register.[3] Then the Section 18 team forwards the applicant's request to the OPP's Biological and Economic Analysis Division, Health Effects Division, and Environmental Fate and Effects Division for economic, health effect and/or ecological risk assessments.[4] The OPP uses these assessments to determine whether the situation is a valid emergency and the efficacy of the requested use. At the end of the review process, the Section 18 team recommends to OPP management whether an emergency exemption should be approved or denied, and the applicant is informed of the final decision. According to the OPP, the agency processes an average of 140 emergency exemption applications annually. The OPP publishes information regarding approved emergency exemptions in a database publicly available on its Section 18 website.

Figure 1: Section 18 emergency exemption process



Acronyms: *BEAD*—Biological and Economic Analysis Division; *EFED*—Environmental Fate and Effects Division; *HED*—Health Effects Division; *SLA*—State Lead Agency

Source: OIG-generated image.

When an emergency exemption is granted, the OPP issues an approval to the SLA that contains general use instructions, use limitations and the emergency

[3] When an exemption request meets the following criteria outlined in 40 CFR § 166.24(1–8), the EPA is required to publish a notice of that request in the Federal Register: the proposed use of a new (unregistered) chemical, the first food use of a chemical, if the chemical's use is currently suspended or cancelled, and other instances where the public can provide comments on the requested exemption.

[4] When an exemption request is for an antimicrobial or biological pesticide, after the Biological and Economic Analysis Division completes its initial evaluation of the emergency economic-loss claim, the request will then be forwarded to the Antimicrobial Division and/or the Biopesticides Pollution Prevention Division.

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exemption expiration date. Because FIFRA provides states with primary enforcement authority for pesticide violations, the EPA does not usually conduct oversight of approved emergency exemptions. Instead, approved exemptions require the SLA to conduct implementation and oversight and to submit an end-of-use report to the OPP 6 months after the exemption expires. This end-of-use report details the amount of pesticide used, the total acres treated, any adverse effects reported and other information required by the EPA.

As long as the situation continues to meet the emergency exemption criteria, SLAs have the option of reapplying for a repeat emergency exemption. Based on the regulations governing emergency exemptions, to repeatedly gain approval for a specific or public health emergency exemption use, the registrant must demonstrate progress toward permanent registration of that pesticide use under Section 3 of FIFRA. If after 3 years (or 5 years for some small volume uses) the manufacturer has not made an effort to register the exempted use, the OPP may deny a repeat specific or public health emergency exemption.

Potential Human Health and Environmental Risks

Emergency exemptions to address urgent and nonroutine pest situations can create human health and environmental risks. Issues such as herbicide resistance, the Zika virus and citrus greening (Figure 2) have required emergency exemptions to protect public health and help prevent significant economic loss. However, environmental groups have argued that emergency exemptions have become a mechanism for protecting growers' profit margins while placing human health and the environment at risk.

Figure 2: Examples of emergency exemption situations

Herbicide resistance, Zika virus concerns and citrus greening have required emergency exemptions. Sources *(from left to right)*: the OIG, Centers for Disease Control and Prevention, and U.S. Department of Agriculture.

For example, citrus greening is a bacterial disease spread by the Asian Citrus Psyllid, for which there is no known cure. A 2012 study by the University of Florida estimated that approximately 80 percent of Florida citrus trees are currently infected, and some affected groves no longer produce any fruit. The study further estimated the direct revenue loss to citrus growers to be $1.66 billion over 5 years, or $331 million annually, representing 19 percent of the average grower revenues. Emergency exemption applications related to citrus greening have requested approval to treat the problem by applying antibiotics. However,

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misuse and overuse of antibiotics can result in the spread of bacteria that are resistant to them, triggering concern about the continuing long-term ability of these drugs to tackle disease. The Centers for Disease Control and Prevention estimates that more than 2 million people in the United States are infected with antibiotic-resistant organisms each year, leading to 23,000 deaths. Some environmental groups have also expressed concern that exposure to antibiotics can have serious unintended side effects for wildlife, including adverse drug reactions. They further claim that antibiotics used in the environment can cause changes in the chemical composition and pH of waters and soils, with potentially serious consequences.

Responsible Office

The OPP, within the Office of Chemical Safety and Pollution Prevention (OCSPP), is responsible for administering FIFRA and for all regulatory activities associated with the emergency exemption issues evaluated in this report. The OPP's Section 18 team manages the emergency exemption process.

Scope and Methodology

We conducted our work from September 2017 through July 2018. We conducted this audit in accordance with generally accepted government auditing standards. Those standards require that we plan and perform the audit to obtain sufficient, appropriate evidence to provide a reasonable basis for our findings and conclusions based on our audit objective. We believe that the evidence obtained provides a reasonable basis for our findings and conclusions based on our audit objective.

The scope of this audit focused on the emergency exemption management process and the internal controls necessary to consistently implement and administer it. We did not evaluate the science used to review emergency exemptions or the subsequent emergency exemption application decisions.

During our interviews, we obtained information about the EPA's emergency exemption process, including the application, review, approval, implementation and oversight of emergency exemptions. We reviewed the universe of emergency exemption applications[5] that were received by the EPA between January 1, 2010, and September 5, 2017. We also determined the five states with the highest percentage of emergency exemption applications between those dates and interviewed SLA representatives regarding their emergency exemption experiences. In addition, we performed the following steps:

[5] According to the Section 18 database, there were 1,033 applications from SLAs during this period. Federal agencies requested 71 emergency exemptions during this period, bringing the total application number to 1,104.

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- Reviewed and analyzed relevant EPA regulations, as well as statutory and policy requirements governing the agency's measurement and internal management controls environment.

- Conducted a review of emergency exemption-related reports and articles.

- Interviewed extension agents from three states to discuss their roles, responsibilities and experiences regarding emergency exemptions.

- Interviewed nongovernmental organization stakeholders with interests in pesticides (e.g., Pesticide Action Network, Center for Biological Diversity, Beyond Pesticides and Crop Life America).

Results

The OPP's emergency exemption process provides flexibility to growers and other pesticide applicators during emergency situations. However, the OPP does not have outcome measures in place to determine how well the emergency exemption process maintains human health and environmental safeguards. The program office also does not have comprehensive internal controls to manage the emergency exemptions data it collects. Finally, the OPP does not consistently communicate emergency exemption information to its stakeholders. Without outcome measures, better data management and consistent communication, the EPA cannot demonstrate the benefits or risks of emergency pesticide exemptions on human health and the environment.

Poor Data Use Prevents OPP from Developing Meaningful Performance Measures

The OPP currently has no measures in place to demonstrate how human health or environmental safeguards for the emergency exemption process are being maintained. The OPP informed us that the annual number of emergency exemption applications has fallen over the years. OPP staff said that they believe this reduction shows improved outcomes.

The GPRA Modernization Act of 2010 requires federal programs and activities to develop measures to attain outcome-oriented goals and collect data that support outcome measures.[6] However, as of March 2018, the only official measure for the emergency exemption process was the average number of days to review applications. Information on progress toward the full registration of the pesticide's expanded use is not required to be collected, and the OPP does not

[6] GPRA stands for *Government Performance and Results Act*. The GPRA Modernization Act of 2010 requires every federal agency to have performance measures that "reflect the highest priorities of the agency." Outcome-oriented goals are identified as more impactful than output goals, and output goals are identified as more impactful than customer service goals.

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currently report on whether the exempted uses approved under the emergency exemption process later obtain full approval for use under FIFRA.
We found that the OPP collects outcome data through its emergency exemption application process that are not used to describe the human health and environmental impacts of the process, nor are these data reported in the Section 18 public database. Only the following application data are available on the EPA Section 18 database public website:

• Chemical	• Site	• Pest	• Applicant
• Status	• Received Date	• Response Date	• Expiration Date

However, none of these reported data allow the OPP or the public to track any potential risks or benefits to human health or the environment, or even to track and understand the scope of any individual exempted use.

The OPP collects outcome data through its emergency exemption process, but it is not using these data or making these data publicly available on its website. For example, emergency exemption applicants are required to calculate the potential significant economic loss that the exemption will prevent or reduce. The OPP also requires applicants to submit the number of affected acres that the pest is impacting, as well as the number of acres that the exempted pesticide could potentially be applied to. In addition, at the end of the exemption period, applicants must report the number of acres that the exempted pesticide was applied to during the exemption period.

Yet the OPP does not use these data to measure the impacts or potential risks of the pesticides it exempts, nor does it report the total application acres of those pesticides in its emergency exemption database to inform the public of the scope of their risks. As a result, the public is currently unable to determine whether an exempted pesticide was applied to 1,000 acres or 1,000,000 acres because the Section 18 database does not report or measure outputs or outcomes.

Case Study

- In 2014, the EPA denied a pesticide emergency exemption request for the use of a potential endocrine disruptor on a major field crop.
- This decision prevented the environmental and human health exposure to a higher-risk pesticide across as many as 3 million acres of cropland.
- This benefit could be more transparent to the public in the Section 18 database if potential application acreage data were available.

The OPP should use its data to measure outputs and outcomes to determine whether its decisions are protective of human health and the environment. In discussing program outcomes, OPP staff indicated that one factor that suggests that the emergency exemption program has been successful is a decrease in the number of emergency exemption applications over the years. However, the decline in the number of applications does not measure whether there were reductions in risks or increases in benefits to human health or the environment. Without meaningful outcome-based measures in place, the OPP does not know whether a decline in applications also resulted in changes to human health and environmental impacts.

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OPP Lacks Internal Controls to Manage Emergency Exemption Data

The OPP does not have comprehensive internal controls to manage the emergency exemption data it collects. We found deficiencies within its online public database, internal guidance documents, and annual progress reports to the Office of Management and Budget (OMB) and Congress.

During our review, we found that the OPP's Section 18 database webpage stated, "Our Emergency Exemption Database provides information about actions received since October 1997. This database is updated approximately every two weeks." We found that neither of these statements was accurate. During interviews, OPP staff confirmed that data collected before 2010 were not included in the version of the Section 18 database that we reviewed and that the database was only updated quarterly.[7] During our interviews with the OPP and SLAs, we were also told that there can be significant lags in data entry. Several SLAs said they did not use the database at all or did not find it useful.

Internal guidance documents that address the emergency exemption process lack controls to require accurate and consistent data collection. We found numerous steps in the OPP's internal guidance documents that mention data collection, but these steps lack sufficient specificity to demonstrate consistent control of either data entry or data management. We also found that the OPP does not have a formal method of ensuring consistency in the review process, such as a process flowchart or application checklist. When asked, the OPP did provide an informal Section 18 Application Checklist that was developed by a member of the Section 18 team, but that document is incomplete and not consistently used. For example, there are nine specific line items in the Section 18 Application Checklist that identify data management actions. However, each of those steps has a note stating "TBA, directions," "TBA specific directions" or "TBA Process." Based on our review of the document, we determined that "TBA" indicates a process that is "To Be Announced" and has not yet been developed. These gaps leave staff with incomplete direction and guidance regarding data collection and database management.

We found that these gaps are mirrored in the draft Section 18 standard operating procedure (SOP) document, with numerous steps that expect data to be collected but that do not provide any procedures or specific descriptions regarding what, how and when data points are to be recorded. Based on our discussions with the OPP, we determined that these deficiencies have existed for nearly a decade. Specifically, we identified these gaps in a still-draft SOP document first developed 10 years ago, which was written to update procedures based on regulatory changes made in January 2006, over 12 years ago. Without a finalized

[7] In response to our concerns, the OPP changed the language on its website in March 2018 to reflect that the database only contains information starting from 2010 and that updates are made quarterly rather than biweekly.

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SOP document or specific data points defined, the OPP is at risk of not collecting or reporting consistent and accurate data.

Lastly, we found inconsistencies in the way the OPP's emergency exemption implementation is reported to the OMB and Congress. The OPP's 2017 Annual Performance Goal, which was submitted to OMB and Congress as part of the EPA's annual performance plan, states that the OPP's goal is to process emergency exemption applications in an average of 45 days. During our interviews, OPP staff indicated that they strive to achieve a 50-day maximum application processing time frame. This 50-day approval time frame is further reinforced by the EPA's Pesticide Emergency Exemption website. However, this performance target is not mentioned in the emergency exemption draft SOP or Section 18 Application Checklist documents.

In fiscal year 2016, the OPP reported an average application review time of 48 days to the OMB and Congress. This level of performance meets the OPP's internal goal of 50 days but fails to meet the Annual Performance Goal commitment of 45 days. Since emergency exemption requests are based on the urgent need for a solution, this discrepancy could result in SLAs and growers waiting longer to obtain solutions to emergencies than if the OPP worked to meet the Annual Performance Goal reported to the OMB and Congress. It also means that OPP staff are working to meet an internal goal (50 days) that is not consistent with the performance target (45 days) that the OMB and Congress are expecting them to achieve.

EPA Needs to Improve Communication Regarding Its Emergency Exemption Process

The OIG has previously reported on the value of increased communication to stakeholders and the public regarding the EPA's management of chemicals and pesticides.[8] OPP staff stated that the Section 18 team communicates often with emergency exemption applicants. However, SLAs and extension agents with whom we spoke stated that communication could be further improved with better guidance and timely emergency exemption updates.

Pesticide efficacy data and potential economic loss calculations are a required part of emergency exemption applications. Invasive species and diseases can migrate from state to state, and SLAs may try to proactively address an emergency that they expect to impact their state. For example, once trees contract citrus greening,

[8] The OIG previously issued three reports related to this topic:

- EPA OIG, *EPA Needs a Coordinated Plan to Oversee Its Toxic Substances Control Act Responsibilities,* Report No. 10-P-0066, February 17, 2010.
- EPA OIG, *Changes Needed to Improve Public Confidence in EPA's Implementation of the Food Quality Protection Act,* Report No. 2006-P-00003, October 19, 2005.
- EPA OIG, *EPA Needs Policies and Procedures to Manage Public Pesticide Petitions in a Transparent and Efficient Manner,* Report No. 16-P-0019, October 27, 2015.

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there is no cure, so SLAs may look to prevent the disease from even reaching their state. However, because the "emergency" does not yet exist in their state, these SLAs do not have access to state-specific pesticide efficacy data. One stakeholder was concerned that the lack of state-specific data would prevent an SLA from proactively requesting an emergency exemption. In addition, one extension agent we interviewed said that it is unclear whether the OPP allows applicants to use data for the same pest and same pesticide use from another SLA's application. The OPP needs to clarify the guidance regarding whether states must use efficacy data only from their state to justify an emergency exemption request.

Staff within the OPP stated that the office's online training module is its main tool for communicating with applicants about the emergency exemption process. Yet, some of the various stakeholders with whom we spoke were unfamiliar with the training module. One SLA that was aware of the module stated that it would prefer shorter guidance. However, the OPP does not provide concise emergency exemption guidance for applicants. Applicants are directed to either use the online training module, which contains 174 slides, or contact the Section 18 team with any questions. We also found that the emergency exemption training module provides general information about the entire emergency exemption process but does not provide specific data requirements or answers to frequently asked questions. Conversely, on another OPP-managed pesticide website focused on FIFRA Section 24(c) registrations, there are quick links to relevant information and specific examples of how to submit applications. In addition, this OPP website has links to general policies and a question-and-answer webpage.

Lastly, the SLAs we spoke with indicated that communication from the Section 18 team regarding the status of the emergency exemption applications could be improved. The OPP previously sent an annual "year in review" letter that summarized the emergency exemption activity for that year. The letter also provided additional information from the Section 18 team regarding the emergency exemption process. According to the OPP, the most recent letter was sent in 2015. Some SLAs with whom we spoke requested that the OPP reinstate this end-of-the-year letter.

Conclusion

Emergency exemptions represent a necessary element in a grower's toolbox to handle nonroutine and urgent situations caused by unexpected pests, invasive species or pesticide resistance. However, we found that the OPP does not have outcome measures in place to determine whether the emergency exemption process protects human health and the environment. The OPP is missing key data management controls that would support its ability to manage its emergency exemption process. The OPP's emergency exemption process also faces challenges regarding the collection and dissemination of reliable emergency exemption information. To mitigate these challenges, the OPP needs meaningful

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measures, better data management and consistent communication to increase the agency's ability to manage its emergency exemption process.

Recommendations

We recommend that the Assistant Administrator for Chemical Safety and Pollution Prevention:

1. Develop and implement applicable outcome-based performance measures to demonstrate the human health and environmental effects of the EPA's emergency exemption decisions.

2. Determine which application review performance target for emergency exemption applications the Office of Pesticide Programs plans to meet, and make that target consistent between its Annual Performance Goal and its internal controls governing the emergency exemption process.

3. Update and finalize the draft standard operating procedure that the Office of Pesticide Programs uses to guide the emergency exemption process.

4. Develop formal emergency exemption application review procedures that detail specific data collection, management and reporting control steps, as well as procedures that require specific management controls for accurately and consistently updating the Office of Pesticide Programs Section 18 database.

5. Develop concise emergency exemption application guidance that specifies the minimum requirements of an application submission and is available on the Office of Pesticide Programs Section 18 website.

6. Provide clear guidance to state lead agencies on how and when they can use efficacy data from other state lead agencies to satisfy the emergency exemption application criteria.

7. Expand the data presented in the Office of Pesticide Programs Section 18 database by considering additional data points, such as application acreage requested, actual acreage applied and registration status of each exempted pesticide.

8. Provide an annual update and information summary to state lead agencies to better inform them about any changes to the emergency exemption application-and-review process.

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Agency Response and OIG Evaluation

In the EPA's official comments regarding the draft report, the agency agreed with Recommendations 3, 4, 7 and 8; neither agreed nor disagreed with Recommendations 2 and 5; and disagreed with Recommendations 1 and 6. The OIG accepts the proposed corrective actions and scheduled completion dates for Recommendations 2, 3 and 4. During our exit conference and other discussions with OCSPP staff, the OIG tried to reach resolution on sufficient corrective actions for Recommendations 1, 5, 6, 7 and 8; however, no resolution was reached, and these recommendations remain unresolved. The following list summarizes the status of our recommendations:

- The OCSPP concurred with Recommendations 3 and 4, and it provided acceptable planned corrective actions and completion dates. Although the agency did not agree or disagree with Recommendation 2, it provided an acceptable corrective action "to avoid future confusion." This corrective action meets the intent of the recommendation. These three recommendations are therefore resolved with corrective actions pending.

- The EPA disagreed with Recommendations 1 and 6. Regarding Recommendation 1, the OCSPP stated that the development of an outcome-based performance measure for the Section 18 emergency exemption process was neither appropriate nor feasible. Although we attempted to reach resolution on Recommendations 1 and 6, the EPA did not formally propose corrective actions. Recommendations 1 and 6 remain unresolved.

- The OCSPP neither agreed nor disagreed with Recommendation 5. Based on our analysis of the emergency exemption application guidance, as well as stakeholder comments regarding that guidance, we believe that a corrective action is warranted. The agency did propose corrective action for this recommendation, but it was insufficient to meet the intent of the recommendation. This recommendation remains unresolved.

- Although the EPA agreed with Recommendations 7 and 8, the proposed corrective actions were insufficient to meet the intent of the recommendations. For Recommendation 7, the OCSPP proposed only that it "will consider additional data points" and did not commit to expanding the data presented in the Section 18 database. For Recommendation 8, the EPA proposed to "develop a strategy which details the activities that might be conducted to provide periodic and useful program updates to applicants." However, the agency needs to clarify the term "periodic" before we can determine whether the proposed corrective action is acceptable. Therefore, both recommendations remain unresolved.

The agency provided technical comments on the draft report, which we incorporated into our final report as appropriate. Appendix A includes the agency's official response to the draft report.

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Status of Recommendations and Potential Monetary Benefits

RECOMMENDATIONS

Rec. No.	Page No.	Subject	Status[1]	Action Official	Planned Completion Date	Potential Monetary Benefits (in $000s)
1	11	Develop and implement applicable outcome-based performance measures to demonstrate the human health and environmental effects of the EPA's emergency exemption decisions.	U	Assistant Administrator for Chemical Safety and Pollution Prevention		
2	11	Determine which application review performance target for emergency exemption applications the Office of Pesticide Programs plans to meet, and make that target consistent between its Annual Performance Goal and its internal controls governing the emergency exemption process.	R	Assistant Administrator for Chemical Safety and Pollution Prevention	7/31/19	
3	11	Update and finalize the draft standard operating procedure that the Office of Pesticide Programs uses to guide the emergency exemption process.	R	Assistant Administrator for Chemical Safety and Pollution Prevention	7/31/19	
4	11	Develop formal emergency exemption application review procedures that detail specific data collection, management and reporting control steps, as well as procedures that require specific management controls for accurately and consistently updating the Office of Pesticide Programs Section 18 database.	R	Assistant Administrator for Chemical Safety and Pollution Prevention	7/31/19	
5	11	Develop concise emergency exemption application guidance that specifies the minimum requirements of an application submission and is available on the Office of Pesticide Programs Section 18 website.	U	Assistant Administrator for Chemical Safety and Pollution Prevention		
6	11	Provide clear guidance to state lead agencies on how and when they can use efficacy data from other state lead agencies to satisfy the emergency exemption application criteria.	U	Assistant Administrator for Chemical Safety and Pollution Prevention		
7	11	Expand the data presented in the Office of Pesticide Programs Section 18 database by considering additional data points, such as application acreage requested, actual acreage applied and registration status of each exempted pesticide.	U	Assistant Administrator for Chemical Safety and Pollution Prevention		
8	11	Provide an annual update and information summary to state lead agencies to better inform them about any changes to the emergency exemption application-and-review process.	U	Assistant Administrator for Chemical Safety and Pollution Prevention		

[1] C = Corrective action completed.
R = Recommendation resolved with corrective action pending.
U = Recommendation unresolved with resolution efforts in progress.

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Agency Response to Draft Report

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

JUL - 3 2018

MEMORANDUM

SUBJECT: Response to Draft Report entitled "Measures and Management Controls Needed to Improve EPA's Emergency Pesticide Exemption Process."

FROM: Charlotte Bertrand
Acting Principal Deputy Assistant Administrator

TO: Arthur A. Elkins
Inspector General

This memorandum is in response to the Office of Inspector General's (OIG's) June 5, 2018 Draft Report entitled "Measures and Management Controls Needed to Improve EPA's Emergency Pesticide Exemption Process," Project No. OPE-FY17-0024.

OCSPP's Responses to OIG's Recommendations:

The Draft Report contains eight recommendations for the Office of Chemical Safety and Pollution Prevention's (OCSPP's) Office of Pesticide Programs (OPP):

Recommendation 1. Develop and implement applicable outcome-based performance measures to demonstrate the human health and environmental effects of the EPA's emergency exemption decisions.

> **OCSPP Response:** OCSPP does not agree that outcome-based performance measures to demonstrate the human health and environmental impacts of EPA's emergency exemption decisions are appropriate or feasible. Requests for FIFRA Section 18 emergency exemptions are reviewed in accordance with the specific statutory criteria of the Federal Food, Drug, and Cosmetic Act (FFDCA) and the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA). OPP assesses all emergency exemptions for human and environmental safeguards consistent with these statutory requirements. In addition, each emergency exemption decision details the conclusions of OPP's

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assessment and the public safety requirements necessary to support the approved use. As a result, the decision to authorize an emergency exemption under FIFRA Section 18 ensures that the pesticide can be used safely, in accordance with Federal law. The human health and environmental risk assessments that are done for all Section 18 exemptions are based on the best available data and assessment procedures, and must ensure the same safety findings are made as for uses covered by Section 3 registrations. As such, OPP believes that emergency exemption decisions, which are scientifically supported by risk assessments, show that EPA has adequately met its obligations under our regulatory statutes.

Proposed Corrective Action and Timeframe for Completion: OCSPP disagrees with this recommendation and is not providing a timeframe for completion.

Recommendation 2. Determine which application review performance target for emergency exemption applications the Office of Pesticide Programs plans to meet, and make that target consistent between its Annual Performance Goal and its internal controls governing the emergency exemption process.

OCSPP Response: EPA's Annual Performance Plan has a performance metric of 45 days for completing emergency exemption applications. OCSPP has historically advised applicants to allow 50 days for EPA to render a decision on an emergency exemption request, but to avoid future confusion, OCSPP will state 45 days as the timeframe for completion whether referring to estimated processing time, target completion, or performance goals.

Proposed Corrective Action and Timeframe for Completion: By July 2019, OCSPP will consistently reference the 45-day decision period, as is reflected in EPA's Annual Performance Assessment (https://www.epa.gov.sites.production/files/2018-03/documents/fy19-cj-14-program-performance.pdf). In particular, internal control documents and public-facing discussion of the processing timelines will cite 45 days.

Recommendation 3. Update and finalize the draft standard operating procedure that the Office of Pesticide Programs uses to guide the emergency exemption process.

OCSPP Response: OCSPP agrees with OIG's recommendation that the standard operating procedure (SOP) guidance for emergency exemptions needs to be updated and finalized.

Proposed Corrective Action and Timeframe for Completion: OCSPP will update and finalize the standard operating procedures and/or guidance for emergency exemptions by July 2019.

Recommendation 4. Develop formal emergency exemption application review procedures that detail specific data collection, management and reporting control steps, as well as procedures that require specific management controls for accurately and consistently updating the Office of Pesticide Programs Section 18 database.

OCSPP Response: OCSPP agrees with OIG's recommendation to develop formal emergency exemption application review procedures that detail specific data collection,

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management and reporting control steps, as well as procedures that require specific management controls for accurately and consistently updating the OPP Section 18 database. As part of the updates to the standard operating procedures guidance cited in recommendation 3, OCSPP will also incorporate recommendation 4.

Proposed Corrective Action and Timeframe for Completion: OCSPP will update and finalize the standard operating procedures and/or guidance for emergency exemptions by July 2019.

Recommendation 5. Develop concise emergency exemption application guidance that specifies the minimum requirements of an application submission and is available on the Office of Pesticide Programs Section 18 website.

OCSPP Response: Section 18 application and training materials are currently available through several sources, including the EPA Section 18 website, periodic and regular group training sessions with State Lead Agency personnel, and one-on-one sessions between EPA staff and the State Lead Agencies. The most recent update to the EPA Section 18 website was on March 22, 2018. The updated site provides links to Section 18 training materials, and links to the regulatory language in 40 CFR 166.20, which provide a precise description of the requirements for a specific, quarantine, crisis, or public health exemption. The website also provides an EPA program contact to assist the State Lead Agencies with the application process.

Although OPP believes that emergency exemption applicants currently have reliable and useful resources for this information, EPA staff will evaluate how its web resources can be enhanced to respond to this recommendation.

Proposed Corrective Action and Timeframe for Completion: If, after evaluating our current web resources, OCSPP determines that enhancements to the Section 18 website are necessary, OCSPP will implement any needed web updates by December 2019.

Recommendation 6. Provide clear guidance to State Lead Agencies on how and when they can use efficacy data from other State Lead Agencies to satisfy the emergency exemption application criteria.

OCSPP Response: As a routine matter, state applications can readily address the expected efficacy of a proposed use, and data do not need to be state-specific.

The sole example cited by the OIG to support this recommendation represents an extremely rare situation. In this particular situation, the California Department of Pesticide Regulation (DPR) requested use of the same antibiotic materials as authorized under exemptions for use in Florida citrus (where widespread establishment of the disease has devastated commercial citrus). However, citrus greening had not (at the time) been detected in California's commercial citrus, with only very limited occurrence in residential trees in several areas of the state. To support their request, California cited data from Florida researchers that examined antibiotic use to improve health and production **of already-diseased trees.** In contrast to the Florida research and uses, California intended to make "prophylactic" treatments to healthy trees to protect them

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from infection. However, the Florida data did not, in fact, analyze or demonstrate the prophylactic effect on healthy trees that California was seeking. **In other words, the data submitted to support the emergency exemption in Florida represented very different conditions from those being experienced in California.**

Notwithstanding the challenges in trying to apply the Florida data to the circumstances in California, OCSPP worked collaboratively with California DPR to find a path forward for California growers to be able to use the requested antibiotics to meet their pest control needs. Ultimately, EPA authorized **quarantine** exemptions to California for the requested antibiotics. The uses allowed in California are for treatment of healthy trees in specified perimeters around positive detects of citrus greening, with the goal of preventing the spread, particularly into commercial citrus.

Proposed Corrective Action and Timeframe for Completion: OCSPP disagrees with this recommendation and is not providing a timeframe for completion.

Recommendation 7: Expand the data presented in the Office of Pesticide Programs Section 18 database by considering additional data points, such as application acreage requested, actual acreage applied and registration status of each exempted pesticide.

OCSPP Response: OCSPP agrees with OIG's recommendation and will consider additional data points, such as application acreage requested, decision documents, and registration status of each exempted pesticide, as OCSPP explores ways to improve the website database and its overall content.

Proposed Corrective Action and Timeframe for Completion: By December 2019, the Registration Division will make recommendations to the Director of the Office of Pesticide Programs for enhancing the Section 18 database. The recommendations will consider the additional data points suggested in Recommendation 7. By December 31, 2019, the Director of the Office of Pesticide Programs will provide a memorandum to the Assistant Administrator for the Office of Chemical Safety and Pollution Prevention with a plan for updating the Section 18 database addressing these recommendations.

Recommendation 8. Provide an annual update and information summary to State Lead Agencies to better inform them about any changes to the emergency exemption application and review process.

OCSPP Response: OCSPP agrees with OIG's recommendation and will explore how to provide periodic and useful program updates to applicants. To accomplish this, OCSPP will work with State Lead Agencies to identify the types of information they may find helpful for periodic updates.

Proposed Corrective Action and Timeframe for Completion: By December 2019, OCSPP will develop a strategy which details the activities that might be conducted to provide periodic and useful program updates to applicants.

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Appendix B

Distribution

The Administrator
Deputy Administrator
Chief of Staff
Chief of Operations
Special Advisor, Office of the Administrator
Assistant Administrator for Chemical Safety and Pollution Prevention
Agency Follow-Up Official (the CFO)
Agency Follow-Up Coordinator
General Counsel
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Associate Administrator for Public Affairs
Principal Deputy Assistant Administrator for Chemical Safety and Pollution Prevention
Deputy Assistant Administrator for Chemical Safety and Pollution Prevention
Director, Office of Continuous Improvement, Office of the Administrator
Director, Office of Pesticide Programs, Office of Chemical Safety and Pollution Prevention
Audit Follow-Up Coordinator, Office of the Administrator
Audit Follow-Up Coordinator, Office of Chemical Safety and Pollution Prevention
Audit Follow-Up Coordinator, Office of Pesticide Programs, Office of Chemical Safety and Pollution Prevention

EPAREF2656-000303

From:	Hill, Shaunta <Hill.Shaunta@epa.gov>
To:	Patel, Jean (CDC); Craig, Michael R (CDC); Harbottle, Heather; Gilbert, Jeffrey M; Wan, Ellen (CDC)
CC:	Jennings, Susan; Kough, John; Chandgoyal, Tara; Hicks, Karen; Blackwell, Ian
Sent:	4/19/2016 6:12:47 PM
Subject:	Final meeting minutes 2-10-16 CDC-EPA-FDA teleconference
Attachments:	Meeting minutes_02102016_EPA-CDC-FDA_Final_031616.pdf; Sec 3 grpfrt_tomato strep 152.pdf; Section 18 citrus 152 review_final.pdf

Hello everyone,
I just realized that I neglected to send the final meeting minutes to everyone concerning our Feb 2016 teleconference. Please see the final version which is attached. I am also including the final 152 reviews for the citrus section 18 (FL) and grapefruit/tomato section 3.

Thank you all for your inputs.

Regards,
****

Shaunta Hill-Hammond, Ph. D.
Acting Ombudsman
Antimicrobials Division, 7510P
Office of Pesticide Programs
U.S. Environmental Protection Agency
Washington, DC 20460
Tel: 703.347.8961

From:	Hill, Shaunta <Hill.Shaunta@epa.gov>
To:	Patel, Jean (CDC); Craig, Michael R (CDC); Harbottle, Heather; Gilbert, Jeffrey M; Wan, Ellen (CDC)
CC:	Jennings, Susan; Kough, John; Chandgoyal, Tara; Hicks, Karen; Blackwell, Ian
Sent:	4/19/2016 6:12:47 PM
Subject:	Final meeting minutes 2-10-16 CDC-EPA-FDA teleconference
Attachments:	Meeting minutes_02102016_EPA-CDC-FDA_Final_031616.pdf; Sec 3 grpfrt_tomato strep 152.pdf; Section 18 citrus 152 review_final.pdf

Hello everyone,
I just realized that I neglected to send the final meeting minutes to everyone concerning our Feb 2016 teleconference. Please see the final version which is attached. I am also including the final 152 reviews for the citrus section 18 (FL) and grapefruit/tomato section 3.

Thank you all for your inputs.

Regards,
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Shaunta Hill-Hammond, Ph. D.
Acting Ombudsman
Antimicrobials Division, 7510P
Office of Pesticide Programs
U.S. Environmental Protection Agency
Washington, DC 20460
Tel: 703.347.8961

From:	Hill, Shaunta <Hill.Shaunta@epa.gov>
To:	Patel, Jean (CDC); Craig, Michael R (CDC); Harbottle, Heather; Gilbert, Jeffrey M
CC:	Jennings, Susan; Kough, John; Chandgoyal, Tara; Hicks, Karen
Sent:	2/25/2016 6:37:32 PM
Subject:	Follow-up: Streptomycin and Oxytetracycline pesticide requests pending with EPA
Attachments:	Meeting minutes_02102016_EPA-CDC-FDA_antibiotics.docx; Mitigation Measures _HLB citrus FL.docx; Section 18 citrus 152 review.docx

Good Afternoon Everyone,
Thank you for participating in the teleconference on Feb 10, 2016. As promised, I am following-up with the group to share the draft meeting minutes. I would greatly appreciate your review of the minutes and any comments/corrections you find by 3/3/16.

I am also providing the 152 review for the proposed Florida – citrus Section 18 request. Based on the application and feedback during the teleconference, the team has assigned an overall risk estimate of "High".

As the Section 18 is a priority for the Agency, we would like to meet by teleconference to discuss proposed mitigation measures. A draft of the current proposal is included with the draft 152. If you could please share your availability for the following dates/times, that will help with our planning efforts on the Section 18.

The proposed meeting times are:

- Tuesday – March 8, 9 am
- Thursday - March 10, 1 pm
- Wednesday – March 16, 1 pm

Thank you and enjoy the rest of your day.

Regards,
****

Shaunta Hill-Hammond, Ph. D.
Plant Pathologist
U.S. EPA: Office of Chemical Safety and Pollution Prevention
Registration Division/Fungicide Branch (PYS)
1200 Pennsylvania Avenue, NW (7505P)
Washington, DC 20460

Tel: 703.347.8961 I Fax: 703.305.6920
E-mail: hill.shaunta@epa.gov

Jean – could you please forward the materials to Ellen.

From:	Jennings, Susan <Jennings.Susan@epa.gov>
To:	Carl Schultze; Julius Fajardo; Harbottle, Heather; Patel, Jean (CDC); Gilbert, Jeffrey M; Craig, Michael R (CDC); Rose Hammond
CC:	Conrath, Andrea B; Maignan, Tawanda; Johnson, Marion
Sent:	12/19/2016 3:39:39 PM
Subject:	FW: Antibiotic - Sec18 Protocols for Resistance Testing; also use and efficacy information
Importance:	High
Attachments:	_AgroSource 2017 THS18_Resistance Monitoring Protocol (v 2) (2).pdf; 12-5-16 recd from FDACS THS18 Monitoring Protocol -- for review.docx; NuFarm Antibiotic Resistance Monitoring Protocol - Oxytetracycline in Citrus Sec18.pdf

Hi All,

Attached are the protocols that we discussed last week. I apologize for not sending these out sooner. Tawanda or Andrea, cc:'d above, will contact you shortly about getting your feedback

Attachments are: (Andrea, if you want them to see any other materials, please forward. No one in the workgroup is cleared for CBI)

1. AgroSource protocol
2. Nufarm protocol
3. A draft rec'd from FDACS on 12-5-16 of an overall "generic" protocol they have developed for resistance monitoring.

Any questions or comments, please Respond All.

Thanks,

Susan.

From: Harbottle, Heather </O=FDA/OU=FIRST ADMINISTRATIVE GROUP/CN=RECIPIENTS /CN=HHARBOTT>
To: Conrath, Andrea B (Conrath.Andrea@epa.gov)
Sent: 1/3/2017 4:12:00 PM
Subject: FW: Antibiotic - Sec18 Protocols for Resistance Testing; also use and efficacy information
Importance: High
Attachments: _AgroSource 2017 THS18_Resistance Monitoring Protocol (v 2) (2).pdf; 12-5-16 recd from FDACS THS18 Monitoring Protocol -- for review.docx; NuFarm Antibiotic Resistance Monitoring Protocol - Oxytetracycline in Citrus Sec18.pdf

Hi Andrea,
Absolutely! These are the protocols, correct?

Also, B5
B5
B5 I think I mentioned it in an email to Susan just before the holiday. I'll set up a telecon or webex with anyone at EPA who would like to B5 Any ideas on who should be invited?

Thanks!
Heather

From: Jennings, Susan [mailto:Jennings.Susan@epa.gov]
Sent: Monday, December 19, 2016 10:40 AM
To: Carl Schultze; Julius Fajardo; Harbottle, Heather; Patel, Jean (CDC); Gilbert, Jeffrey M; Craig, Michael R (CDC); Rose Hammond
Cc: Conrath, Andrea B; Maignan, Tawanda; Johnson, Marion
Subject: FW: Antibiotic - Sec18 Protocols for Resistance Testing; also use and efficacy information
Importance: High

Hi All,

Attached are the protocols that we discussed last week. I apologize for not sending these out sooner. Tawanda or Andrea, cc:'d above, will contact you shortly about getting your feedback

Attachments are: (Andrea, if you want them to see any other materials, please forward. No one in the workgroup is cleared for CBI)
AgroSource protocol
Nufarm protocol
A draft rec'd from FDACS on 12-5-16 of an overall "generic" protocol they have developed for resistance monitoring.

Any questions or comments, please Respond All.

Thanks,

Susan.

From: Jennings, Susan <Jennings.Susan@epa.gov>
To: Harbottle, Heather; Gilbert, Jeffrey M; Julius Fajardo; Rose Hammond
CC: Johnson, Hope; Garvie, Heather; Patel, Jean (CDC); Craig, Michael R (CDC)
Sent: 8/1/2017 12:54:28 PM
Subject: FW: comments from CDC

Hello all,

Thanks for your comments. Below is what we've received from CDC.

Thanks to all,

Susan.

From: Patel, Jean (CDC/OID/NCEZID) [mailto:vzp4@cdc.gov]
Sent: Friday, July 28, 2017 11:35 AM
To: Johnson, Hope <Johnson.Hope@epa.gov>
Cc: Jennings, Susan <Jennings.Susan@epa.gov>; Craig, Michael R. (CDC/OID/NCEZID) <bez7@cdc.gov>
Subject: comments from CDC

Sorry for being a bit late.

Streptomycin & Tetracycline

B5

From: Johnson, Hope [mailto:Johnson.Hope@epa.gov]
Sent: Thursday, July 20, 2017 10:54 AM
To: Sow, Fatima <Sow.Fatima@epa.gov>; Jennings, Susan <Jennings.Susan@epa.gov>; Kough, John <Kough.John@epa.gov>; Collins, Samantha <collins.samantha@epa.gov>; Chandgoyal, Tara <Chandgoyal.Tara@epa.gov>; Garvie, Heather <Garvie.Heather@epa.gov>; Giles-Parker, Cynthia <Giles-

Parker.Cynthia@epa.gov>; Carl Schultze <Carl.P.Schulze@aphis.usda.gov>; Julius Fajardo <Julius.Fajardo@ARS.USDA.GOV>; Harbottle, Heather (FDA/CVM) <Heather.Harbottle@fda.hhs.gov>; Patel, Jean (CDC/OID/NCEZID) <vzp4@cdc.gov>; Gilbert, Jeffrey M (FDA/CVM) <Jeff.Gilbert@fda.hhs.gov>; Craig, Michael R. (CDC/OID/NCEZID) <bez7@cdc.gov>; Rose Hammond <Rose.Hammond@ARS.USDA.GOV>
Cc: Cook, Colwell <cook.colwell@epa.gov>; Britton, Cathryn <Britton.Cathryn@epa.gov>; Kaul, Monisha <Kaul.Monisha@epa.gov>
Subject: RE: Federal interagency Antibiotic Resistance Call

Thank you all again for your participation today on the call. Attached are all the Resistance Review documents for your review in one place. Our BEAD division is determining whether or not we can provide the draft Benefits documents as an FYI. The Benefits documents include discussion on efficacy and alternatives. We will forward those documents to you if we can as soon as possible.

We would appreciate any comments you have- please send as soon as possible and hopefully no later than COB Wednesday 7/26/2017.
Please send any comments to Susan Jennings and cc: myself (Hope Johnson) and Fatima Sow.

Again, please note that we are in the Risk Management stage of the review. In the coming few weeks, we will begin briefings for our Management along with drafting the Proposed Decision documents for each AI (active ingredient) in preparation for the Public Process. We hope to begin the Public Process by the beginning of October of this year. It will include a 30 day comment period and allows the public to look at all supporting documents associated with the Proposed Decision (Health Effects Division risk assessment, Environmental Fate and Effects Division risk assessment, Biological and Economic Analysis Division Benefits assessment, Resistance Review (former 152), proposed labels). The Proposed Decision will discuss any mitigation we are proposing for that specific AI's new use.

After the comment period has closed, the Agency responds to comments received and incorporates these responses along with any revisions to the Proposed Decision into a Final Decision document. This is then uploaded to the docket, the Registrations are signed, and the Final Rule is published establishing tolerances. We are striving to meet a January 2018 timeframe for the Final Decisions.

Please feel free to contact me if you have questions on the process.

Thank you,

Hope A. Johnson
Product Manager 21
U.S. Environmental Protection Agency
Office of Pesticide Programs
Registration Division
Fungicide Branch
Phone: 703-305-5410
Mail Code 7505P

From: Johnson, Hope
Sent: Thursday, July 20, 2017 8:18 AM
To: Sow, Fatima <Sow.Fatima@epa.gov>; Jennings, Susan <Jennings.Susan@epa.gov>; Kough, John <Kough.John@epa.gov>; Collins, Samantha <collins.samantha@epa.gov>; Chandgoyal, Tara <Chandgoyal.Tara@epa.gov>; Garvie, Heather <Garvie.Heather@epa.gov>; Giles-Parker, Cynthia <Giles-

Parker.Cynthia@epa.gov>; Carl Schultze <Carl.P.Schulze@aphis.usda.gov>; Julius Fajardo <Julius.Fajardo@ARS.USDA.GOV>;Heather.Harbottle@fda.hhs.gov; Jean Patel <vzp4@cdc.gov>;Jeff.Gilbert@fda.hhs.gov; Michael Craig <bez7@cdc.gov>; Rose Hammond <Rose.Hammond@ARS.USDA.GOV>
Cc: Cook, Colwell <cook.colwell@epa.gov>; Britton, Cathryn <Britton.Cathryn@epa.gov>
Subject: RE: Federal interagency Antibiotic Resistance Call

The original streptomycin grapefruit/tomato 152 review is attached here. Previously only the addendum was attached. This is the complete document .

Hope A. Johnson
Product Manager 21
U.S. Environmental Protection Agency
Office of Pesticide Programs
Registration Division
Fungicide Branch
Phone: 703-305-5410
Mail Code 7505P

From: Sow, Fatima
Sent: Wednesday, July 19, 2017 4:49 PM
To: Jennings, Susan <Jennings.Susan@epa.gov>; Kough, John <Kough.John@epa.gov>; Collins, Samantha <collins.samantha@epa.gov>; Chandgoyal, Tara <Chandgoyal.Tara@epa.gov>; Garvie, Heather <Garvie.Heather@epa.gov>; Johnson, Hope <Johnson.Hope@epa.gov>; Giles-Parker, Cynthia <Giles-Parker.Cynthia@epa.gov>; Carl Schultze <Carl.P.Schulze@aphis.usda.gov>; Julius Fajardo <Julius.Fajardo@ARS.USDA.GOV>;Heather.Harbottle@fda.hhs.gov; Jean Patel <vzp4@cdc.gov>;Jeff.Gilbert@fda.hhs.gov; Michael Craig <bez7@cdc.gov>; Rose Hammond <Rose.Hammond@ARS.USDA.GOV>
Subject: RE: Federal interagency Antibiotic Resistance Call

Documents to be discussed are attached.

-----Original Appointment-----
From: Jennings, Susan
Sent: Monday, June 19, 2017 10:19 AM
To: Jennings, Susan; Kough, John; Collins, Samantha; Chandgoyal, Tara; Garvie, Heather; Johnson, Hope; Giles-Parker, Cynthia; Carl Schultze; Julius Fajardo;Heather.Harbottle@fda.hhs.gov; Jean Patel;Jeff.Gilbert@fda.hhs.gov; Michael Craig; Rose Hammond
Cc: Sow, Fatima
Subject: Federal interagency Antibiotic Resistance Call
When: Thursday, July 20, 2017 8:00 AM-10:00 AM (UTC-05:00) Eastern Time (US & Canada).
Where: Conference call # 866-299-3188, code 7063558524

Documents to be discussed are attached to this invitation.

This is just a hold until we find a time that works for Federal Partners. Final meeting will be scheduled for 2 hours (but may be shorter).

From:	Hill, Shaunta <Hill.Shaunta@epa.gov>
To:	Harbottle, Heather
CC:	Gilbert, Jeffrey M
Sent:	2/10/2016 3:17:59 PM
Subject:	FW: EPA - Pending antibiotic request for Streptomycin, request for a teleconference
Attachments:	4. image2016-02-01-085505.pdf; 5. 080990-00003.20151123.revised Master Label.pdf; Meeting agenda.pdf

Hello Heather,
Hopefully it works this time…

Please see the following files which are attached.
-4. EPA review memo (image2016-02-01)
- 5. Proposed label (080990-00003.20151123. revised Master Label)
- Meeting Agenda

From: Hill, Shaunta
Sent: Wednesday, February 10, 2016 10:04 AM
To: 'Gilbert, Jeffrey M' <Jeff.Gilbert@fda.hhs.gov>; 'Harbottle, Heather' <Heather.Harbottle@fda.hhs.gov>
Subject: FW: EPA - Pending antibiotic request for Streptomycin, request for a teleconference

Heather –
There are 6 files attached to this message (including the agenda).

From: Hill, Shaunta
Sent: Wednesday, February 10, 2016 6:31 AM
To: Jennings, Susan <Jennings.Susan@epa.gov>
Cc:
Subject: EPA - Pending antibiotic request for Streptomycin, request for a teleconference

Good Morning Heather and Jeff,
Please see the attached agenda and support files for our teleconference Wednesday – Feb 10, 2016 at 11 am.
The conference line information is noted on the agenda.

**Due to the file sizes, two emails will be sent.*

If you would not mind, could you please provide contact information and title for both you and Jeff.
Thank you

From: Harbottle, Heather [mailto:Heather.Harbottle@fda.hhs.gov]
Sent: Tuesday, February 09, 2016 4:58 PM

To: Hill, Shaunta <Hill.Shaunta@epa.gov>; Jennings, Susan <Jennings.Susan@epa.gov>
Cc: Gilbert, Jeffrey M <Jeff.Gilbert@fda.hhs.gov>
Subject: RE: EPA - Pending antibiotic request for Streptomycin, request for a teleconference

Hi Shaunta,
We'll be happy to call in. Is there a call in number and agenda yet for the teleconference tomorrow at 11am?
Thanks!
Heather

From: Hill, Shaunta [mailto:Hill.Shaunta@epa.gov]
Sent: Monday, February 08, 2016 12:16 PM
To: Harbottle, Heather; Jennings, Susan
Cc: Gilbert, Jeffrey M
Subject: RE: EPA - Pending antibiotic request for Streptomycin, request for a teleconference

Hello Heather,
We did meet during the IR-4 meeting. Happy to hear that you and Jeff will be joining our discussion.
The meeting agenda will be finalized shortly and I will forward it along with several reference documents for our discussion.
In the meantime, I wanted to provide some background information on pesticide registrations.

The type of registrations permitted under FIFRA (i.e. Section 3 and Section 18) can be found here: http://www.epa.gov/pesticide-registration/types-registrations-under-fifra

Information on the general registration process can be found here: http://www.epa.gov/pesticide-registration/pesticide-registration-manual-chapter-1-overview-requirements-pesticide

I hope you find this initial information helpful.
If you have any questions, please let me know.

Regards,
****
Shaunta Hill-Hammond, Ph. D.
Plant Pathologist
U.S. EPA: Office of Chemical Safety and Pollution Prevention
Registration Division/Fungicide Branch (PYS)
1200 Pennsylvania Avenue, NW (7505P)
Washington, DC 20460

Tel: 703.347.8961 | Fax: 703.305.6920
E-mail: hill.shaunta@epa.gov
URL Address: www.epa.gov/pesticides

From: Harbottle, Heather [mailto:Heather.Harbottle@fda.hhs.gov]
Sent: Friday, February 05, 2016 8:35 AM
To: Hill, Shaunta <Hill.Shaunta@epa.gov>; Jennings, Susan <Jennings.Susan@epa.gov>
Cc: Gilbert, Jeffrey M <Jeff.Gilbert@fda.hhs.gov>
Subject: FW: EPA - Pending antibiotic request for Streptomycin, request for a teleconference
Importance: High

Good morning Ms. Hill and Ms. Jennings,

My name is Heather Harbottle and I believe we met during the IR-4 Bacterial Challenges Mini-Summit meeting "Understanding the ABCs (Awareness of Bacterial Challenges) with Antibiotics In Crops" in September of 2014. As you may remember, I delivered a presentation regarding FDA's use of GFI #152 due to our extensive use of this guidance assessing risk for the use of antimicrobials in food producing animals. I've been asked by Bill Flynn and my team leader, Dr. Jeff Gilbert, to get in touch with you regarding your email below. Dr. Gilbert and I would be happy to attend the teleconference on Wednesday, and provide any assistance with GFI #152 as it pertains to your application for streptomycin or any other antimicrobial.

Please let us know how we can be of help.

Best,
Heather Harbottle

From: Hill, Shaunta [mailto:Hill.Shaunta@epa.gov]
Sent: Thursday, February 04, 2016 9:59 AM
To: Flynn, William T
Cc: Jennings, Susan
Subject: EPA - Pending antibiotic request for Streptomycin, request for a teleconference

Hello Dr. William;

My name is Shaunta Hill and I am a Risk Assessor/Plant Pathologist with EPA's Office of Pesticide Programs – Registration Division.
I received your name from Dr. Jean Patel at CDC as a potential contact.

As EPA manages antibiotics for pesticidal use, we are interested in accessing the resistance risk potential along with human and environmental risks. We have previously worked with CDC and FDA (via David White) utilizing the FDA Guidance for Industry #152 for this purpose.

We have a number of applications currently pending and have scheduled a teleconference for **Wednesday Feb 10 at 11 am** to begin discussions.
I am hopefully that you are available to participate in this discussion as FDA input is valued.
The primary application for consideration next week is Streptomycin sulfate use on grapefruit and tomatoes via FIFRA Section 3 Registration.

If you are available, I can provide additional background information in addition to our meeting agenda.
Should you have any questions, please let us know. I have cc'ed on this communication

Susan Jennings, who serves as our Public Health Coordinator and is available to address questions on this meeting request as well.

Thank you for your time and I look forward to hearing from you.

Regards,
****

Shaunta Hill-Hammond, Ph. D.
Plant Pathologist
U.S. EPA: Office of Chemical Safety and Pollution Prevention
Registration Division/Fungicide Branch (PYS)
1200 Pennsylvania Avenue, NW (7505P)
Washington, DC 20460

Tel: 703.347.8961 | Fax: 703.305.6920
E-mail: hill.shaunta@epa.gov
URL Address: www.epa.gov/pesticides

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Fungicide/Bactericide
Agricultural Streptomycin

GROUP	25	FUNGICIDE

Active Ingredient:
Streptomycin Sulfate* 22.40%
Other Ingredients: 77.60%
100.00%
*Equivalent to 17% streptomycin

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(If you do not understand the label, find someone to explain it to you in detail.)

See Back Panel for Additional Precautionary Statements, First Aid and Directions for Use

EPA Reg. No. 80990-4

EPA Est. No. 39578-TX-1

Product Number 1004

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NET CONTENTS: 2 POUNDS

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FIRST AID

If On Skin or Clothing:	• Take off contaminated clothing. • Rinse skin immediately with plenty of water for 15-20 minutes. • Call a poison control center or doctor immediately for treatment advice.
If In Eyes:	• Hold eye open and rinse slowly and gently with water for 15-20 minutes. • Remove contact lenses, if present, after the first 5 minutes, then continue rinsing eye. • Call a poison control center or doctor immediately for treatment advice.

HOT LINE NUMBER

Have the product container or label with you when calling a poison control center or doctor or going for treatment. You may also contact InfoTrac at 1-800-535-5053 for emergency medical treatment information.

PRECAUTIONARY STATEMENTS
Hazards To Humans & Domestic Animals

CAUTION: Harmful if absorbed through skin. Prolonged or frequently repeated skin contact may cause allergic reactions in some individuals. Causes moderate eye irritation. Do not breathe dust or spray mist. This material is not to be used for medical, veterinary or human purposes.

Personal Protective Equipment (PPE):

Applicators and other handlers must wear:

- *long-sleeved shirt*
- long pants
- chemical-resistant gloves made of a waterproof material
- shoes plus socks
- MSHA/NIOSH approved dust/mist respirator with any R, P, or HE filter

Follow manufacturer's instructions for cleaning/maintaining PPE. If no such instructions for washables, use detergent and hot water. Keep and wash PPE separately from other laundry.

User Safety Recommendations:
Users should:

- Wash hands before eating, drinking, chewing gum, using tobacco or using the toilet.
- Remove clothing/PPE immediately if pesticide gets inside. Then wash thoroughly and put on clean clothing.
- Remove PPE immediately after handling this product. Wash the outside of gloves before removing. As soon as possible, wash thoroughly and change into clean clothing.

ENVIRONMENTAL HAZARDS

This product may be hazardous to aquatic plants. Do not apply directly to water, to areas where surface water is present or to intertidal areas below the mean high water mark. Do not contaminate water by cleaning of equipment or disposal of wastes.

DIRECTIONS FOR USE

It is a violation of Federal law to use this product in a manner inconsistent with its labeling. Do not apply this product by aircraft. Do not apply this product through any type of irrigation system. Do not apply this product in a way that will contact workers or other persons, either directly or through drift. Only protected handlers may be in the area during application. For any requirements specific to your State or Tribe, consult the agency responsible for pesticide regulation.

Application Restrictions: This product contains the antibiotic streptomycin. To reduce the development of drug-resistant bacteria and maintain the effectiveness of this and other antibacterial products, this product should be used only to treat or prevent infections that are proven or strongly suspected to be caused by bacteria. This material is not to be used for medical or veterinary purposes.

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AGRICULTURAL USE REQUIREMENTS

Use this product only in accordance with its labeling and with the Worker Protection Standard, 40 CFR part 170. This Standard contains requirements for the protection of agricultural workers on farms, forests, nurseries and greenhouses, and handlers of agricultural pesticides. It contains requirements for training, decontamination, notification and emergency assistance. It also contains specific instructions and exceptions pertaining to the statements on this label about personal protective equipment (PPE) and restricted entry interval. The requirements in this box apply to uses that are covered by the Worker Protection Standard.

Do not enter or allow worker entry into treated areas during the restricted-entry interval (REI) of 12 hours.

For early entry to treated areas that is permitted under the Worker Protection Standard and that involves contact with anything that has been treated, such as plants, soil or water, wear:

- Coveralls over long-sleeved shirt and long pants
- Chemical-resistant gloves made of a waterproof material
- Shoes plus socks

Resistance Management Statements FIREWALL™ 17 WP fungicide/bactericide contains a Group 25 fungicide/bactericide. Fungal isolates/bacterial strains with acquired resistance to Group 25 may eventually dominate the fungal/bacterial population if Group 25 fungicides/bactericides are used repeatedly in the same field or in successive years as the primary method of control for targeted species. This may result in partial or total loss of control of those species by **FIREWALL™ 17 WP** fungicide/bactericide or other Group 25 products.

To delay fungicide/bactericide resistance consider:

- Avoiding the consecutive use of **FIREWALL™ 17 WP** fungicide/bactericide or other target site of action Group 25 fungicides/bactericides that have a similar target site of action, on the same pathogens.
- Using tank-mixtures or premixes with fungicide/bactericides from different target site of action Groups as long as the involved products are all registered for the same use and are both effective at the tank mix or prepack rate on the pathogen(s) of concern.
- Basing fungicide/bactericide use on a comprehensive IPM program.
- Monitoring treated fungal/bacterial populations for loss of field efficacy.
- *Contacting your local extension specialist, certified crop advisors, and/or manufacturer for fungicide/bactericide* resistance management and/or IPM recommendations for specific crops and resistant pathogens.

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FIREWALL™ 17 WP Fungicide/Bactericide

Crop Use Directions - Vegetable Crops

Crop	Disease (*Pathogen*)	FireWall™ 17 WP Application Rate	Use Directions	Restrictions
Celery* (Florida area)	Bacterial Blight (*Pseudomonas cichorii*)	4 oz. per 25 gal. (0.056 lbs. a.i.) applied to 10,000 ft2	Seedlings in Greenhouse†: Apply first spray when seedlings are at 2-leaf stage, when first true leaves appear.	Minimum retreatment interval: 4 days. Maximum number of applications: 6
Peppers*	Bacterial Spot (*Xanthomonas campestris* pv *vesicatoria*)	4 oz. per 25 gal. (0.056 lbs. a.i.) applied to 10,000 ft2	Seedlings in Greenhouse†: Apply first spray when seedlings are at 2-leaf stage, when first true leaves appear.	Minimum retreatment interval: 4 days. Maximum number of applications: 6
Potatoes*	Soft Rot (*Erwinia carotovora* subsp. *atroseptica* Blackleg (*Erwinia carotovora* subsp. *carotovora*)	2 oz. per 25 gal. (0.028 lbs. a.i.) drench solution)	Pre-Plant: Soak cut seed pieces in solution for several *minutes; plant as usual.* NOTE: A suitable fungicide (such as Maxim® Potato Seed Protectant or Maxim ® MZ Potato Seed Protectant) should be used as an adjunct to this treatment for the control of fungal diseases associated with potato seed pieces.	Do not retreat seed.
Tomatoes*	Bacterial Spot (*Xanthomonas campestris* pv *vesicatoria*) Bacterial speck (*Pseudomonas syringae* pv tomato) Bacterial canker (*Clavibacter michiganensis* pv *michiganensis*)	Greenhouse†: 4 oz. per 25 gal. (0.056 lbs. a.i.) applied to 10,000 ft2	Seedlings in Greenhouse†: Apply first spray when seedlings are in the 2-leaf stage, when first true leaves appear.	Minimum retreatment interval: 4 days. Do not apply within 1 day of harvest or transplanting. Maximum number of applications: 4 Do not apply more than 16 oz. per 10,000 ft2, per season.
		Field: 1 lb. (0.22 lbs. a.i.)/A	Transplants in Field or Greenhouse†: Apply as a foliar spray to near runoff. Combine and/or rotate FireWall 17 WP applications with other products having different modes of action (e.g. *copper/mancozeb) for* resistance management.	Minimum retreatment interval: 7 days. Do not apply within 1 day of harvest. Maximum number of *applications: 4* Do not apply more than 4 lbs. per acre, per season.

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Crop Use Directions, Continued - Tree Fruit Crops

Crop	Disease (*Pathogen*)	FireWall™ 17 WP Application Rate	Use Directions	Restrictions
Apples*	Fire Blight (*Erwinia amylovora*)	1½ lbs. – 3 lbs. (0.34 lbs. – 0.67 lbs. a.i.) per acre per application	Begin spraying trees at 20%-30% bloom, according to risk potential based on fire blight forecasting model and advice from extension and/or professional crop advisor. For control of fire blight after hail/wind damage ("trauma blight"), spray as soon as possible after injury event but within 24 hours.	Do not apply within 50 days of harvest. Minimum retreatment interval: 3 days. Maximum number of applications: 9
Apples (California)	Fire Blight (*Erwinia amylovora*)	1.8 lbs. (28.8 oz.). (0.40 lbs. a.i.) per acre per application	Spray trees at full bloom. Apply at petal fall and late secondary bloom according to risk potential based on fire blight forecasting model and advice from extension and/or professional crop advisor. For control of fire blight after hail/wind damage ("trauma blight"), spray as soon as possible after injury event but within 24 hours.	Do not apply within 50 days of harvest. Minimum retreatment interval: 5 days. Maximum number of applications: 9
Pears*	Fire Blight (*Erwinia amylovora*)	1½ lbs. – 3 lbs. (0.34 lbs. – 0.67 lbs. a.i.) per acre per application	Begin spraying trees at 20%-30% bloom according to risk potential based on fire blight forecasting model and advice from extension and/or professional crop advisor. For control of fire blight after hail/wind damage ("trauma blight"), spray as soon as possible after injury event but within 24 hours.	Do not apply within 30 days of harvest. Minimum retreatment interval: 3 days. Maximum number of applications: 9
Pears (California)	Fire Blight (*Erwinia amylovora*)	1.8 lbs. (28.8 oz.). (0.40 lbs. a.i.) per acre per application	Spray trees at 10% bloom until all late bloom is over according to risk potential based on fire blight forecasting model and advice from extension and/or professional crop advisor. For control of fire blight after hail/wind damage ("trauma blight"), spray as soon as possible after injury event but within 24 hours.	Do not apply within 30 days of harvest. Minimum retreatment interval: 5 days. Maximum number of applications: 9

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Crop Use Directions, Continued - Tree Fruit Crops

Crop	Disease (*Pathogen*)	FireWall™ 17 WP Application Rate	Use Directions	Restrictions
Grapefruit (Florida Only)	Citrus Canker (*Xanthomonas citri* pv *citri*)	2 lbs. (0.44 lbs. a.i.) per acre per application	**Mature trees:** Apply as foliar spray to protect against bacterial canker. Combine and/or rotate FireWall applications with other products having different modes of action (e.g. copper) for resistance management.	Do not apply within 60 days of harvest. Minimum retreatment interval: 21 days. Do not apply more than 4 lbs. FireWall™ 17 WP per acre per season.
			Young trees: *Spray to near runoff* at the rate of 2 lbs. per 100 gallons, per acre.	*Do not exceed 2 lbs.* FireWall™ 17 WP per acre. Do not apply within 60 days of harvest (if applicable). Minimum retreatment interval: 21 days. *Do not apply more than 4* lbs. FireWall™ 17 WP per acre per season.

Crop Use Directions, Continued - Ornamentals

Crop	Disease (*Pathogen*)	FireWall™ 17 WP *Application Rate*	*Use Directions*	Restrictions
Chrysanthemums*	Bacterial Wilt (*Erwinia chrysanthemi*)	1 oz. per 25 gal. (0.014 lbs. a.i.) in drench solution	Soak plant cuttings in solution for 4 hours; plant as usual.	Do not retreat.
Dieffenbachia Cutting*	Bacterial Stem Rot (*Erwinia chrysanthemi*, *Erwinia carotovora* pv *carotovora*)	4 oz. per 25 gal. (0.056 lbs. a.i.) in drench solution	Soak cuttings in solution for 20 minutes. Plant cuttings in sterilized rooting medium.	Do not retreat.
		2 oz. per 25 gal. (*0.028 lbs. a.i.*) applied to 5,000 ft2	Apply as foliar application to check spread of stem rot in *stock plants.*	Minimum retreatment *interval 5 days. Maximum* number of applications 3
Philodendron*	Bacterial Leaf Rot (*Xanthomonas campestris*)	4 oz. per 25 gal. (0.056 lbs. a.i.) applied to 10,000 ft2	Apply as foliar application at first signs of water-soaked areas on leaf. If disease has spread, remove all rotted leaves from plant before spraying.	Minimum retreatment interval: 4 days. Maximum number of applications: 6

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Crop Use Directions, Continued – Ornamentals

Crop	Disease (*Pathogen*)	FireWall™ 17 WP Application Rate	Use Directions	Restrictions
Roses (New Jersey Area)*	Crown Gall (*Agrobacterium spp.*)	4 oz. per 25 gal. (0.056 lbs. a.i.) in drench solution	Remove infected plant. Cut out gall tissue. Soak the plant root system and cut surfaces of the infected area in solution for 15 minutes. Replant in soil free of the crown gall organism.	Do not retreat.
		1 oz. per 25 gal. (0.014 lbs. a.i.) applied to 3,000 ft^2	Use once as a watering solution. Follow with foliar sprays.	Minimum retreatment interval: 7 days. Maximum number of applications: 6.

Crop Use Directions, Continued - Home & Garden

Crop	Disease (*Pathogen*)	FireWall™ 17 WP Application Rate	Use Directions	Restrictions
Apple Trees, Pear Trees, Pyrancantha (Fire Thorn Bush) (CA)	Fire Blight (*Erwinia amylovora*) of the Rosaceae	2 oz. per 25 gal. (0.028 lbs. a.i.) applied to 3,000 ft^2	Apply as foliar sprays beginning at start of blossoming period. Continue spray applications during bloom period. Post bloom, continue to apply when weather conditions favor spread of fire blight.	Minimum retreatment interval during bloom: 3 days. Minimum retreatment post-bloom: 5 days. Do not apply after fruit is visible. Maximum number of applications: 6 Home & Garden users should use personal protective equipment (PPE) and observe restricted entry interval (12 hrs.).

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Crop Use Directions, Continued – Row Crops

Crop	Disease (*Pathogen*)	FireWall™ 17 WP Application Rate	Use Directions	Restrictions
Tobacco*	Wildfire and Blue Mold (*Peronospora tabacina*)	Before plants are set in the field: For preventative action: 2 oz./25 gal. (0.028 lbs. a.i.) applied to 5,000 ft.^{2} For curative action: 4 oz./25 gal. (0.056 lbs. a.i.) applied to 5,000 ft.^{2}	Apply first spray when plants are in the 2-leaf stage or about the size of a dime or when blue mold first appears in the area. Repeat application until plants are set in the field.	Minimum retreatment interval: 5 days. Maximum number of *applications: 4.* Additional protection may be obtained by spraying field plants.
		After plants are set in field: 1 lb. (0.22 lbs. a.i.)/A	In locations where wild fire mold has been a problem in recent years or where applications have been delayed until the disease appears, a foliar spray at the rate of 1 lb. per 100 gallons is recommended. Follow same restrictions as above.	Minimum retreatment interval: 7 *days.* Maximum number of applications: 6

* Except California
†Or similar type structure

Use of **FIREWALL™ 17 WP** fungicide/bactericide may cause phytotoxicity to the fruit and/or foliage of sensitive varieties of pears and apples.

Additional information regarding use of ***FIREWALL™ 17 WP*** *fungicide/bactericide may be obtained from your local* Agricultural Extension Agent or State Experimental Station.

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Pesticide Storage: Keep tightly closed and sealed. Store in a cool, dry place. Avoid any exposure to the atmosphere.
Pesticide Disposal: Wastes resulting from the use of this product may be disposed of on site or at an approved waste disposal facility.
Container Disposal: Non-refillable Container. Do not reuse or refill this container. Completely empty bag into application equipment. Then dispose of bag in a sanitary landfill, by incineration, or if allowed by State and local authorities, by burning. If burned, stay out of smoke.

EMERGENCY TELEPHONE NUMBER:
InfoTrac: 1-800-535-5053

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EPA – FDA – CDC Teleconference Discussion of pending agricultural antibiotic applications **Feb 10, 2016. 11 am**	**Teleconference Information:** **Dial:** **Code** B6

Meeting Lead: Shaunta Hill-Hammond EPA – OPP-RD (703-347-8961, hill.shaunta@epa.gov)
A list of participants will be provided with the MOU following the teleconference.

Agenda:

1. Introductions
2. Purpose of the meeting
3. Section 3 request: Streptomycin sulfate use on grapefruit and tomato (greenhouse and field)
   a. **Risk Management Summary:**

Target dates	
Last Science Due Date:	7/15/15
CDC/FDA teleconference	2/10/16
Public Participation Period:	3/24/16
PRIA Due Date:	5/16/16

   b. Relevant documents: files 1-5
   c. Grapefruit Considerations
      i. Currently approved via Section 18 (use granted 2013-2015)
      ii. One season of monitoring data available
   d. Tomato Considerations
      i. Current use is limited to greenhouse seedlings
      ii. No monitoring data available
      iii. No restrictions against treatment both in the greenhouse and field

TIME PERMITTING:

4. Section 18 request: Streptomycin sulfate and Oxytetracycline hydrochloride use on citrus-lemons, grapefruit and oranges (Florida limited)
   a. Relevant documents: files 6-8
   b. Considerations
      i. Streptomycin currently approved for Section 18 use on grapefruit.

Attachments:

1. Streptomycin monitoring protocol
2. Streptomycin monitoring report (2014 use season)
3. Applicant 152 document (49213202)
4. EPA review memo (image2016-02-01)
5. Proposed label (080990-00003.20151123. revised Master Label)
6. FL Citrus greening Section 18 petition
7. Applicant 152 – Streptomycin – citrus
8. Applicant 152 – Oxytetracycline hydrochloride –citrus

EPA – FDA – CDC Teleconference Discussion of pending agricultural antibiotic applications **Feb 10, 2016. 11 am**	**Teleconference Information:** **Dial:** **Code:** B6

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   c. Grapefruit Considerations
      i. Currently approved via Section 18 (use granted 2013-2015)
      ii. One season of monitoring data available
   d. Tomato Considerations
      i. Current use is limited to greenhouse seedlings
      ii. No monitoring data available
      iii. No restrictions against treatment both in the greenhouse and field

TIME PERMITTING:

4. Section 18 request: Streptomycin sulfate and Oxytetracycline hydrochloride use on citrus-lemons, grapefruit and oranges (Florida limited)
   a. Relevant documents: files 6-8
   b. Considerations
      i. Streptomycin currently approved for Section 18 use on grapefruit.

Attachments:

1. Streptomycin monitoring protocol
2. Streptomycin monitoring report (2014 use season)
3. Applicant 152 document (49213202)
4. EPA review memo (image2016-02-01)
5. Proposed label (080990-00003.20151123. revised Master Label)
6. FL Citrus greening Section 18 petition
7. Applicant 152 – Streptomycin – citrus
8. Applicant 152 – Oxytetracycline hydrochloride –citrus

From:	Harbottle, Heather </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=55429E94C1CE44C4B031B4CFEE99A90F-HHARBOTT>
To:	Jennings, Susan (Jennings.Susan@epa.gov)
Sent:	3/16/2018 2:59:39 PM
Subject:	FW: FDA Input on Tolerance Decisions for Oxytetracycline and Streptomycin - Revised FDA response
Attachments:	dietary exposure response tet strep final march 14.pdf

Hi Susan,
Did you see the attached edited letter that does not reference CDER at all? We are hoping that this will work for you now, as it is almost exactly the same letter from 2006.

Thanks,
Heather

From: Harbottle, Heather
Sent: Thursday, March 15, 2018 3:19 PM
To: 'Jennings, Susan' <Jennings.Susan@epa.gov>; Long, Charli <Charli.Long-Medrano@fda.hhs.gov>
Cc: Goodis, Michael <Goodis.Michael@epa.gov>; Gilbert, Jeffrey M <Jeff.Gilbert@fda.hhs.gov>; Giles-Parker, Cynthia <Giles-Parker.Cynthia@epa.gov>; Johnson, Hope <Johnson.Hope@epa.gov>
Subject: RE: FDA Input on Tolerance Decisions for Oxytetracycline and Streptomycin - Revised FDA response

Dear Dr. Jennings,
Per your February 27, 2018 request, we have attached an edited response to your request letter. We hope this letter satisfies your request, as it is modeled after our previous response to your request in 2006. Please feel free to contact us with any further questions.

B5

https://www.fda.gov/downloads/AnimalVeterinary/GuidanceComplianceEnforcement/GuidanceforIndustry/UCM124674.pdf

We look forward to collaborating with you in the future in this respect and regarding the risk for the development of antimicrobial resistance.

Best regards,
Heather Harbottle

Heather Harbottle, Ph.D.
Microbiologist
Microbial Food Safety Team
Division of Human Food Safety
Office of New Animal Drug Evaluation
Center for Veterinary Medicine, FDA
240-402-0791

From: Jennings, Susan [mailto:Jennings.Susan@epa.gov]
Sent: Tuesday, February 27, 2018 3:42 PM
To: Long, Charli <Charli.Long-Medrano@fda.hhs.gov>
Cc: Goodis, Michael <Goodis.Michael@epa.gov>; Gilbert, Jeffrey M <Jeff.Gilbert@fda.hhs.gov>; Harbottle, Heather <Heather.Harbottle@fda.hhs.gov>; Giles-Parker, Cynthia <Giles-Parker.Cynthia@epa.gov>; Johnson, Hope <Johnson.Hope@epa.gov>
Subject: FDA Input on Tolerance Decisions for Oxytetracycline and Streptomycin

Dr. Long:

Thank you for allowing Drs. Jeffrey Gilbert and Heather Harbottle to collaborate with us on our registrations for new uses for antibiotic pesticides. They have provided valuable input into our draft decisions and analyses and, along with our colleagues at CDC and USDA, helped EPA's decision be more robust and balanced.

While working on these decisions, our legal counsel has suggested that B5

B5

Again, thank you for your time and consideration, as well as your division's continued collaboration on antibiotic pesticide activities.

Susan Jennings
Senior Advisor for Public Health
Office of Pesticide Programs
(706) 355-8574 (office)
(703) 216-8627 (cell)

From: Jennings, Susan <Jennings.Susan@epa.gov>
To: Patel, Jean (CDC); Harbottle, Heather
CC: Julius Fajardo; Garvie, Heather; Johnson, Hope
Sent: 8/1/2017 12:56:51 PM
Subject: FW: Federal interagency Antibiotic Resistance Call
Attachments: Streptomycin 152 Firewall 50WP 07032017_JEF Comment.doc

Below are USDA's comments from Julius.

Thanks.

From: Fajardo, Julius [mailto:Julius.Fajardo@ARS.USDA.GOV]
Sent: Wednesday, July 26, 2017 3:34 PM
To: Jennings, Susan <Jennings.Susan@epa.gov>
Cc: Johnson, Hope <Johnson.Hope@epa.gov>; Sow, Fatima <Sow.Fatima@epa.gov>
Subject: RE: Federal interagency Antibiotic Resistance Call

Susan,
The process involved for these antibiotics is not a registration review, right?
Please find attached few comments of mine. My comments for streptomycin would be similar to the other two antibiotics.
Thanks and best regards,
Julius

From: Johnson, Hope [mailto:Johnson.Hope@epa.gov]
Sent: Thursday, July 20, 2017 3:09 PM
To: Sow, Fatima <Sow.Fatima@epa.gov>; Jennings, Susan <Jennings.Susan@epa.gov>; Kough, John <Kough.John@epa.gov>; Collins, Samantha <collins.samantha@epa.gov>; Chandgoyal, Tara <Chandgoyal.Tara@epa.gov>; Garvie, Heather <Garvie.Heather@epa.gov>; Giles-Parker, Cynthia <Giles-Parker.Cynthia@epa.gov>; Schulze, Carl P - APHIS <Carl.P.Schulze@aphis.usda.gov>; Fajardo, Julius <Julius.Fajardo@ARS.USDA.GOV>; Heather.Harbottle@fda.hhs.gov; Jean Patel <vzp4@cdc.gov>; Jeff.Gilbert@fda.hhs.gov; Michael Craig <bez7@cdc.gov>; Hammond, Rose <Rose.Hammond@ARS.USDA.GOV>
Cc: Cook, Colwell <cook.colwell@epa.gov>; Britton, Cathryn <Britton.Cathryn@epa.gov>; Kaul, Monisha <Kaul.Monisha@epa.gov>
Subject: RE: Federal interagency Antibiotic Resistance Call

Update: The draft Benefits reviews cannot be released at this time, however, they will be available to view during the public comment periods that are forthcoming.

Thank you,
Hope

Hope A. Johnson
Product Manager 21
U.S. Environmental Protection Agency
Office of Pesticide Programs
Registration Division
Fungicide Branch
Phone: 703-305-5410
Mail Code 7505P

From: Johnson, Hope
Sent: Thursday, July 20, 2017 10:53 AM

To: Sow, Fatima <Sow.Fatima@epa.gov>; Jennings, Susan <Jennings.Susan@epa.gov>; Kough, John <Kough.John@epa.gov>; Collins, Samantha <collins.samantha@epa.gov>; Chandgoyal, Tara <Chandgoyal.Tara@epa.gov>; Garvie, Heather <Garvie.Heather@epa.gov>; Giles-Parker, Cynthia <Giles-Parker.Cynthia@epa.gov>; 'Carl Schultze' <Carl.P.Schulze@aphis.usda.gov>; Julius Fajardo <Julius.Fajardo@ARS.USDA.GOV>; 'Heather.Harbottle@fda.hhs.gov' <Heather.Harbottle@fda.hhs.gov>; 'Jean Patel' <vzp4@cdc.gov>; 'Jeff.Gilbert@fda.hhs.gov' <Jeff.Gilbert@fda.hhs.gov>; 'Michael Craig' <bez7@cdc.gov>; 'Rose Hammond' <Rose.Hammond@ARS.USDA.GOV>
Cc: 'Cook, Colwell' <cook.colwell@epa.gov>; Britton, Cathryn <Britton.Cathryn@epa.gov>; Kaul, Monisha <Kaul.Monisha@epa.gov>
Subject: RE: Federal interagency Antibiotic Resistance Call

Thank you all again for your participation today on the call. Attached are all the Resistance Review documents for your review in one place. Our BEAD division is determining whether or not we can provide the draft Benefits documents as an FYI. The Benefits documents include discussion on efficacy and alternatives. We will forward those documents to you if we can as soon as possible.

We would appreciate any comments you have- please send as soon as possible and hopefully no later than COB Wednesday 7/26/2017.
Please send any comments to Susan Jennings and cc: myself (Hope Johnson) and Fatima Sow.

Again, please note that we are in the Risk Management stage of the review. In the coming few weeks, we will begin briefings for our Management along with drafting the Proposed Decision documents for each AI (active ingredient) in preparation for the Public Process. We hope to begin the Public Process by the beginning of October of this year. It will include a 30 day comment period and allows the public to look at all supporting documents associated with the Proposed Decision (Health Effects Division risk assessment, Environmental Fate and Effects Division risk assessment, Biological and Economic Analysis Division Benefits assessment, Resistance Review (former 152), proposed labels). The Proposed Decision will discuss any mitigation we are proposing for that specific AI's new use.

After the comment period has closed, the Agency responds to comments received and incorporates these responses along with any revisions to the Proposed Decision into a Final Decision document. This is then uploaded to the docket, the Registrations are signed, and the Final Rule is published establishing tolerances. We are striving to meet a January 2018 timeframe for the Final Decisions.

Please feel free to contact me if you have questions on the process.

Thank you,

Hope A. Johnson
Product Manager 21
U.S. Environmental Protection Agency
Office of Pesticide Programs
Registration Division
Fungicide Branch
Phone: 703-305-5410
Mail Code 7505P

From: Johnson, Hope
Sent: Thursday, July 20, 2017 8:18 AM
To: Sow, Fatima <Sow.Fatima@epa.gov>; Jennings, Susan <Jennings.Susan@epa.gov>; Kough, John <Kough.John@epa.gov>; Collins, Samantha <collins.samantha@epa.gov>; Chandgoyal, Tara <Chandgoyal.Tara@epa.gov>; Garvie, Heather <Garvie.Heather@epa.gov>; Giles-Parker, Cynthia <Giles-Parker.Cynthia@epa.gov>; Carl Schultze <Carl.P.Schulze@aphis.usda.gov>; Julius Fajardo <Julius.Fajardo@ARS.USDA.GOV>; Heather.Harbottle@fda.hhs.gov; Jean Patel <vzp4@cdc.gov>; Jeff.Gilbert@fda.hhs.gov; Michael Craig <bez7@cdc.gov>; Rose Hammond <Rose.Hammond@ARS.USDA.GOV>

Cc: Cook, Colwell <cook.colwell@epa.gov>; Britton, Cathryn <Britton.Cathryn@epa.gov>
Subject: RE: Federal interagency Antibiotic Resistance Call

The original streptomycin grapefruit/tomato 152 review is attached here. Previously only the addendum was attached. This is the complete document .

Hope A. Johnson
Product Manager 21
U.S. Environmental Protection Agency
Office of Pesticide Programs
Registration Division
Fungicide Branch
Phone: 703-305-5410
Mail Code 7505P

From: Sow, Fatima
Sent: Wednesday, July 19, 2017 4:49 PM
To: Jennings, Susan <Jennings.Susan@epa.gov>; Kough, John <Kough.John@epa.gov>; Collins, Samantha <collins.samantha@epa.gov>; Chandgoyal, Tara <Chandgoyal.Tara@epa.gov>; Garvie, Heather <Garvie.Heather@epa.gov>; Johnson, Hope <Johnson.Hope@epa.gov>; Giles-Parker, Cynthia <Giles-Parker.Cynthia@epa.gov>; Carl Schultze <Carl.P.Schulze@aphis.usda.gov>; Julius Fajardo <Julius.Fajardo@ARS.USDA.GOV>; Heather.Harbottle@fda.hhs.gov; Jean Patel <vzp4@cdc.gov>; Jeff.Gilbert@fda.hhs.gov; Michael Craig <bez7@cdc.gov>; Rose Hammond <Rose.Hammond@ARS.USDA.GOV>
Subject: RE: Federal interagency Antibiotic Resistance Call

Documents to be discussed are attached.

-----Original Appointment-----
From: Jennings, Susan
Sent: Monday, June 19, 2017 10:19 AM
To: Jennings, Susan; Kough, John; Collins, Samantha; Chandgoyal, Tara; Garvie, Heather; Johnson, Hope; Giles-Parker, Cynthia; Carl Schultze; Julius Fajardo; Heather.Harbottle@fda.hhs.gov; Jean Patel; Jeff.Gilbert@fda.hhs.gov; Michael Craig; Rose Hammond
Cc: Sow, Fatima
Subject: Federal interagency Antibiotic Resistance Call
When: Thursday, July 20, 2017 8:00 AM-10:00 AM (UTC-05:00) Eastern Time (US & Canada).
Where: Conference call # 866-299-3188, code 7063558524

Documents to be discussed are attached to this invitation.

This is just a hold until we find a time that works for Federal Partners. Final meeting will be scheduled for 2 hours (but may be shorter).

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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

MEMORANDUM

SUBJECT: Review of Arysta Life Science's Analysis of Kasugamycin's Safety with Regard to Its Microbiological Effect on Bacteria of Human Health Concern (FDA/CVM Guidance to Industry #152)

FROM: Samantha Collins, Microbiologist
Product Science Branch
Antimicrobials Division (7510P)

Samantha Collins 9/28/2017

John L. Kough, Ph.D., Biologist
Microbial Pesticides Branch, Biopesticides and Pollution Prevention Division (7511P)

John L. Kough 9/28/20817

TO: Heather Garvie
Product Team 21
Registration Division (RD, 7505P)

ACTION REQUESTED: To review information related to the potential of kasugamycin's agricultural use to select for bacteria of human health concern with enhanced resistance to clinical antibiotics. This analysis is adapted from the Food and Drug Administration's Center for Veterinary Medicine's Guidance to Industry #152 which was designed to address the microbial resistance associated with new animal drug uses. Potential exposure from both consuming treated foods and to workers during application and post-application farm activities are also considered.

DATA REVIEW RECORD

Active Ingredient:	Kasugamycin
Product Name:	Kasumin 2L
Company Name:	Arysta LifeScience North America LLC
Title of Report:	Kasugamycin: Benefits Overview and Resistance Potential Evaluation (per FDA Guidance Document 152)
Authors:	Dave G. Bolin, Ph.D.

EPAREF2656-000346

Date: October 6, 2015
Laboratory Project ID: RG092815
MRID: 499461-05

BACKGROUND: In 2010, Arysta Life Science of North America petitioned EPA (the Agency) for Section 3 registration of the aminoglycoside antibiotic kasugamycin for control of bacterial diseases on tomatoes, peppers, walnuts and pome fruits (apples and pears). Arysta had petitioned for and received an import tolerance at 0.04 ppm for kasugamycin on Crop Group 8 (Fruiting Vegetables except cucurbits) in 2005. An analysis following FDA's guidance to industry #152 was completed in 2013 with a consideration of uses on pome fruits, walnuts, tomatoes and peppers. In 2014 the Agency granted a registration for kasugamycin and approved a tolerance for kasugamycin residues less than 0.20 ppm resulting from use on pome fruits crop group 11-10 to control fire blight (*Erwinia amylovora*) (CFR 180.614). This decision was based in part on the field monitoring data provided from trials in Michigan apples. In order to expand the uses for the current section 3 registration, Arysta was asked to provide field monitoring data on the presence of kasugamycin resistant bacteria in the requested crops and a revised analysis of the microbiological effects on bacteria of human health concern associated with the proposed expanded uses. The current updated #152 is intended to address the issues related to the expanded uses of kasugamycin for walnut and cherries subgroup 12-12A. Monitoring data for the kasugamycin resistant microflora of leaves and soil within the dripline cherry and walnut trees was provided (MRID 49946102 and 499460101, respectively) but not reviewed in this memorandum.

DISCUSSION: The qualitative risk assessment as described in the FDA's 152 guidance to industry, with modifications from PRN 2001-5 appropriate to managing resistance in agricultural chemicals, consists of a release assessment, and exposure assessment and a consequence assessment. These three elements provide the information to make an overall qualitative risk estimate. The release assessment considers the probability that resistant bacteria are present on food commodities as a result of antibiotic use on crops. In the case of an agricultural use of an antibiotic on a food crop, the primary expression of this resistance would be a failure of the antibiotic to control the intended disease or the appearance of antibiotic resistance in epiphytic or soil bacteria. Either of these scenarios could indicate an increase in the likelihood of antibiotic resistance transfer to microbes of human health concern and require a closer examination of the resistance trait to determine its mobility among bacterial populations.

The exposure assessment considers two routes of exposure: 1) the probability that humans would ingest or be exposed to bacteria from the treated food commodity; and 2) the probability that workers would be exposed to the antibiotic and resistance could develop in bacteria of human concern on their bodies. In the case of an agricultural use antibiotic, the incidence of foodborne illness associated with consumption of the crop would provide the background for the exposure scenarios. Another consideration would be increasing exposure to bacteria of human health concern through the use of improperly treated animal manures. The consequence assessment considers the probability that the exposure to resistant bacteria could result in an adverse health consequence. Any change in the incidence of foodborne disease found with consumption of the treated crop or an

increased failure to treat human disease related to ingesting the crop would be cogent for the consequence assessment.

Given the importance of antibiotics to control bacterial diseases in humans, domestic animals and plants, it is essential that procedures to lessen the likelihood that antibiotic use in crops leads to selection for resistant bacterial populations be adopted. The guidance given in PRN 2001-5 outline general considerations for prudent agricultural use including the avoidance of single chemistry for control, rotating control measures over the season, employing tank mixes to reduce resistance development of the sprays used, and basing control strategies on integrated pest management programs. An important first step in any resistance control scheme is to monitor for loss of field efficacy and confirm its source. EPA assumes that loss of field efficacy for the targeted bacterium, while not the sole indication of antibiotic resistance of importance to bacteria of human health concern, is an important sign that continued agricultural use could affect clinical medicine.

The adaptation of the FDA's 152 Guidance to Industry for the assessment of agricultural use of antibiotics is useful in providing consistent public health goals for deploying antibiotics outside clinical medicine. The 152 guidance is circumspect for adaptation to agricultural antibiotic uses due to certain dissimilarities to the animal husbandry uses. Selection for resistance to kasugamycin in phytopathogens and environmental bacteria will occur with its broader adoption as a control measure for bacterial plant diseases. Definitive knowledge on the connection between kasugamycin resistance and possible cross resistance to clinically important antibiotics is lacking. However, field monitoring data provided by Arysta indicates that co-selection was not apparent for resistance to a group of 5 antibiotics (cefotaxime, ampicillin, tetracycline, gentamicin and streptomycin) used in clinical medicine that CDC and FDA suggested be screened.

SUMMARY OF DATA SUBMITTED: Arysta provided a summary of the benefits of the use of kasugamycin along with the 152 analysis. The benefits information is not reviewed in this memorandum. The submission is divided into four sections that correlate with the format proposed by the 152 Guidance to Industry: 1) The Release Assessment which covers antibiotic product characterization information, use pattern and a discussion of what is known for target susceptibility, spectrum of activity, resistance mechanisms and selection pressure. 2) The Exposure Assessment which examines the human exposure to food-borne bacteria by way of the treated crop. 3) The Consequence Assessment which relates the foregoing information to the loss of efficacy of antibiotics for human clinical use. 4) The Risk Estimation integrates the release, exposure and consequence findings with an overall estimate of risk (ranked low, medium or high); associated with the proposed antibiotic use. Most of the differences between the animal uses and the agricultural uses relate to the lack of pharmacodynamics of antibiotics for crop use, the lower likelihood of direct contamination of food crops by bacteria of human health concern and the much broader exposure of sprayed antibiotics in agriculture compared to injected or orally consumed antibiotics in animal husbandry. These differences will be reiterated in the individual section discussions.

RELEASE ASSESSMENT

The boundaries of the release assessment relate to the proposed use pattern on apple and pear,

cherry subgroup 12-12A and walnut. The acres treated were estimated for each crop with apple and pear being 365,000 acres to control fire blight; 115,000 acres of cherries for bacterial canker and 300,000 acres of walnut for bacterial blight. Arysta asserts that the original request for 170,00 acres of peppers and tomatoes is similar to the current request of 115,000 acres of cherries. Arysta suggests the prior "low" release assessment rating is conservative for the added cherry subgroup 12-12A use. These numbers represent an upper limit of 100% of the crop treated with kasugamycin. The usage may vary annually according to disease pressure driven by weather and could be expected to be lower.

The proposed label for apples and pears allows a maximum of 4 applications per year with a 30-day pre-harvest interval. Four applications per year with a 100-day pre-harvest interval are proposed for walnuts. The application technology for these uses is by conventional ground application which would most likely be air-blast sprayers for orchard trees. The directions for use indicate that this product should be used when weather conditions favor disease development.

The conditions favoring disease development vary with each host-pathogen combination. For fire blight, the disease is first found in blossoms in the spring and is favored when temperatures are around 80°F with heavy rain, dew and mists. The bacterium prefers flowers and succulent fast growing tissues (emerging leaves and expanding stems). Secondary infections can continue throughout the growing season but new infections are reduced in the presence of dry and warm weather. Economic damage is due to fruit loss, tree disfigurement and mortality. Walnut blight is favored by free moisture and is not as affected by temperature as fire blight. The bacterium is harbored in dormant buds and infected twigs and primary infection occurs as buds break and catkins emerge. The economic damage results from nut infection and quality loss. In cherries, the incidence of canker and blossom blast disease shows a similar relation to free moisture but is also associated with frost damage. Computer assisted disease forecasting systems are available for both fire blight of pome fruit and bacterial blight of walnut but no similar system exists for the bacterial canker and blossom blast diseases of cherry.

Kasugamycin is in the aminoglycoside class of antibiotics but differs from other clinically important members in the class. Kasugamycin acts against protein synthesis by inhibiting the formation of the initiation complex of typical or canonical mRNA with 30S ribosomal subunits. Several classes of organisms can also translate mRNA without this canonical leader by binding 70S ribosomal subunits directly therefore resistance to kasugamycin can occur in some populations at a rather high frequency. Clinically important aminoglycosides also act on protein synthesis but act further in the process at the level of miscoding of the mRNA within the 70S complex. A possible mechanism for cross resistance with both kasugamycin and the other clinically important aminoglycosides has not been reported. Data provided by the company as part of the field monitoring reports indicates that kasugamycin resistance has no relation to the frequency of resistance to 5 clinically important antibiotics.

The spectrum of activity for kasugamycin is gram negative bacteria and a limited number of fungi. Although kasugamycin is used in Japan for control of rice blast (*Pyricularia oryzae*), there are currently no fungal label claims or requests for including control of any fungal diseases in this

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submission. In 2013 Arysta presented results from screening kasugamycin for activity against a set of clinically important bacteria and the related activity levels for the other clinically important aminoglycosides. The levels reported for kasugamycin to have activity against clinically important bacteria were typically 2 orders of magnitude higher than that reported for the other aminoglycosides and kasugamycin is said by Arysta to be not effective at practical use levels against clinically important bacteria. The bacterial species tested were *Micrococcus luteus, Bacillus subtilis, B. anthracis, Corynebacterium bovis, Escherichia coli, Shigella dynsenteriae, Salmonella typhi, Pseudomonas aeruginosa, P. fluorescens, P. maltophila* and *Yersina entercolitica*. As previously mentioned, kasugamycin showed no activity against the gram positive bacteria *Micrococcus luteus, Bacillus subtilis,* and *B. anthracis.* The results were from a paper by T. Tamamura and K. Sato in the Japanese Journal of Antibiotics 52:57-67 (1999).

To address the cross resistance to other aminoglycoside antibiotics, Arysta presented data on the sensitivity of target plant pathogenic bacteria *Xanthomonas campestris* and *Pseudomonas syringae*. These strains were selected for kasugamycin resistance in the laboratory then examined for sensitivity to streptomycin and kanamycin. The kasugamycin resistant strains showed similar levels of sensitivity to streptomycin and kanamycin as that of the kasugamycin sensitive strains. This is purported to indicate a lack of cross resistance to other aminoglycosides when kasugamycin resistance is found. The field monitoring data confirm these 2013 results as well as address the lack of cross-resistance to the five selected clinically important antibiotics. The clinical antibiotics were cefotaxime, ampicillin, tetracycline, gentamicin and streptomycin.

The pharmacodynamics and pharmacokinetics of kasugamycin were not discussed for the plant uses. Since there is little indication that externally applied antibiotics are taken up and distributed within plants, the endpoint of pharmacodynamics and pharmacokinetics is not relevant. The most analogous endpoint would be environmental persistence of the antibiotic. There was a claim by Arysta that kasugamycin has a half-life in aerobic soil of about 40 days. The current EFED assessment indicates that kasugamycin half-lives in various natural environments range from 5.7 days to 12.3 days in field conditions and 17.4 to 45 days in lake water or lake or river water and sediments. The longest half lives in a natural environment were in anaerobic environments of 105 days in an anaerobic aquatic environment and 147 days in an anaerobic paddy soil environment. The resistance mechanisms were not discussed but it is known that kasugamycin resistance can be selected in the laboratory and that, in some cases, this resistance is due to structural changes in the 16S ribosomal subunit (R.A. Zimmerman *et al.*, 1973). In *Escherichia coli*, this type of resistance is due to an enzyme with ribosome methylation activity. The rate of this mutation to kasugamycin resistance and its occurrence in target plant pathogenic bacteria are not known.

The baseline level of resistance to kasugamycin in environmental bacteria and tracking the effect of kasugamycin treatments on the frequency of resistance to clinically important classes of antibiotics in these environmental isolates was provided in the 2 field monitoring studies mentioned previously. The clinical antibiotics were cefotaxime, ampicillin, tetracycline, gentamicin and streptomycin. The studies looked at bacterial populations in both kasugamycin treated and untreated cherry and walnut orchards. Bacterial populations of the walnut and cherry leaf and the soil environment under the trees were examined in both kasugamycin treatment situations. The

results are similar to those reported for the apple orchard environments. The level of resistance to the surveyed clinical antibiotics was low in populations of epiphytic bacteria recovered from leaves. Higher frequencies of resistance to the surveyed antibiotics and greater species diversity of bacterial populations were found in soil samples. The percentage of bacteria resistant to the surveyed antibiotics was always higher in soil populations of bacteria compared to foliar isolates. The data from the surveys did not reveal any significantly enhanced selection for resistance to the surveyed antibiotics related to the kasugamycin treatment.

PARAMETER	COMMENT	RELEASE RATING
Mechanism of activity	Different site from other aminoglycosides; low likelihood to have cross resistance for other antibiotics.	Low
Spectrum of activity	Gram negatives; less effective against human pathogenic species.	Low
Resistance mechanism	Ribosomal methylating enzyme reported; others possible.	Medium
Selection pressure	Wide use likely to create significant selection pressure	Medium
Resistance transfer	No data available; likely to be easily transferred since related to enzyme activity, not ribosomal structural sequence.	Low

The release assessment rating for the proposed uses would be expected to be "low" based on the limited information available for kasugamycin. Since there is no definitive data to cite for the resistance transfer endpoint, this would be an area for further examination and a possible monitoring endpoint for the expanded uses.

EXPOSURE ASSESSMENT

The adaptation of the FDA's 152 guidance from the veterinary to the agricultural scenario has two aspects that greatly complicate the exposure assessment. The animal drug use, administered directly to animals in medicated feeds or by injection, has much less environmental exposure compared to agricultural sprays of antibiotics. The animal use is more likely to have direct effects on potential antibiotic resistance in human pathogens due to the presence of bacteria of human health concern in the intestinal flora of treated animals. The intestinal tract of treated animals also provides high density, homogenous bacterial populations for genetic interactions with consistent temperatures and environmental conditions. The agricultural use has a much greater environmental exposure due to the application by air blast or other spray technologies.

The agricultural use, however, has much greater environmental exposure and worker exposure due to the application by air blast or other spray technologies. The agricultural use exposes more different types of bacteria to selection for antibiotic resistance but has an unknown impact on bacteria of human health concern. Although bacteria of human health concern are a relatively

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minor component of the general environment (unless improperly handled animal manures are used in treated fields); they are very likely to be found in or on workers who could be exposed to the antibiotic from dermal, incidental oral or inhalation exposure.

The human health concern comes mostly from contamination of food crops with bacteria of human health concern and the transfer of resistance traits from environmental strains to these microbes of human health concern. A link between kasugamycin resistance and resistance to clinically important antibiotics (especially other aminoglycosides) is not suggested by the submitted field monitoring results. However, quantifying the potential for any resistance traits to move from environmental bacteria into clinically important bacteria has not been established.

The current exposure assessment is based on information about walnuts and cherries alone. Since the proposed use expands to walnut and cherry subgroup 12-12A growing areas, the amount of the food commodity being consumed will be higher. For the uses on walnuts and cherries subgroup 12-12A, the amount of food commodity being consumed is "medium". The level of food commodity contamination for all the crops on the proposed section 3 label is low but variable. The reports of walnut and cherry subgroup 12-12A being implicated in food poisoning incidents is "low". This would yield a rating of "low" for the exposure assessment.

CONSEQUENCE ASSESSMENT

The ranking for the consequence assessment under the 152 guidance differs from the previous "high", "medium" and "low" to be expressed as "important", "highly important" and "critical". The consequence assessment is "important". "Important" is the lowest risk ranking for FDA's 152 consequence assessment. This low risk rating is due to the submitted data from the field monitoring data on cherries and walnuts showing no change in resistance frequency to other aminoglycosides in the presence of kasugamycin resistance in tested bacteria. This can also be supported by the difference in sensitivity to kasugamycin for plant pathogenic bacteria compared to clinically important species. There are currently no clinical uses for kasugamycin. This assessment may change to "highly important" or "critical" if it is found that kasugamycin resistance, when it develops, can provide cross resistance to clinically important aminoglycosides. The data to establish or refute this supposition is not available. It is unlikely there is cross resistance at the current time due to kasugamycin's activity at a different binding site in bacterial protein translation and the results submitted by Arysta for field trails in cherries and walnuts.

Currently, the kasugamycin section 3 registration is for pome fruit. The new request expands the use to include cherry subgroup 12-12A and walnut so the exposure, and consequently, the selection pressure for resistance, will expand but probably not more than was estimated in 2013.

OVERALL QUALITATIVE RISK ESTIMATION

The risk estimation integrates the three previous assessments to provide an overall rating. There are certain uncertainties associated with these assessments. For the release assessment, it was noted that information is lacking on kasugamycin susceptibility for the range of bacteria associated with

food borne incidents in the crops proposed to be treated. Field monitoring data for cherries and walnuts suggests kasugamycin does not co-select for resistance to other clinical antibiotics. For the exposure assessment, data on the actual level of contamination with bacteria of human concern on the food commodities proposed for use is not available. For the consequence assessment, it is clear that there are currently no clinical uses for kasugamycin but if the agricultural use did co-select for resistance to other clinically important antibiotics, the rating could change.

Given the "low" release, "low" exposure and "important" consequence ratings, the overall qualitative risk estimation would be "low" for the use in cherry subgroup 12-12A and walnuts. This finding may change after more closely considering the monitoring results and additional information.

REFERENCES

Tamamura, T. and Sato, K. (1999) Comparative studies on in vitro activities of kasugamycin and clinically used aminoglycoside antibiotics, Japanese Journal of Antibiotics 52:57-67.

Zimmermann, R.A., Ikeya, Y. and P.F. Sparling (1973) Alteration of Ribosomal Protein S4 by Mutation Linked to Kasugamycin Resistance in *Escherichia coli*, Proceedings of the National Academies of Science 70:71-75.

EPAREF2656-000353

From: Jennings, Susan <Jennings.Susan@epa.gov>
To: Harbottle, Heather; Gilbert, Jeffrey M
Sent: 7/6/2017 12:41:12 PM
Subject: FW: Trying to schedule the July interagency (time sensitive)

Heather,

Are you in this week? I need to schedule this today and I'm getting out of offices back from Jeff's email.

If I don't hear from either of you, I will just grab two times and you can pick.

Hope you enjoyed your time off.

Thanks,

Susan.

From: Jennings, Susan
Sent: Wednesday, July 05, 2017 9:55 AM
To: Kough, John <Kough.John@epa.gov>; Collins, Samantha <collins.samantha@epa.gov>; Chandgoyal, Tara <Chandgoyal.Tara@epa.gov>; Carl Schultze <Carl.P.Schulze@aphis.usda.gov>; Fajardo, Julius <Julius.Fajardo@ARS.USDA.GOV>; Heather.Harbottle@fda.hhs.gov; Jean Patel <vzp4@cdc.gov>; Jeff.Gilbert@fda.hhs.gov; Michael Craig <bez7@cdc.gov>; Rose Hammond <Rose.Hammond@ARS.USDA.GOV>
Cc: Giles-Parker, Cynthia <Giles-Parker.Cynthia@epa.gov>; Garvie, Heather <Garvie.Heather@epa.gov>; Johnson, Hope <Johnson.Hope@epa.gov>
Subject: Trying to schedule the July interagency (time sensitive)

Hello all,

Because of various scheduling conflicts, I am going to try again to schedule our interagency meeting to discuss the EPA assessments for streptomycin, kasugamycin, and oxytetracycline.

The only times that I could find are:

Tuesday morning, July 18 from
9 to 11
10 to 12
11 to 1

Wednesday morning, July 19, from:
9 to 11
10 to 12
11 – 1

Thursday, July 20, from 8-10.

I would really appreciate everyone's help in trying to make one of these times work for everyone.

If you each could fill respond to this email asap, I would be very appreciative.

Thanks,

Susan.

Susan Jennings
Senior Advisor for Public Health
Office of Pesticide Programs
(706) 355-8574 (office)
(703) 216-8627 (cell)

From: Jennings, Susan <Jennings.Susan@epa.gov>
To: Carl Schultze; Julius Fajardo; Harbottle, Heather; Patel, Jean (CDC); Gilbert, Jeffrey M; Craig, Michael R (CDC); Rose Hammond
Sent: 3/19/2018 3:55:02 PM
Subject: Meeting?

Hi all,

We are about to start working on the registration review of streptomycin and oxytetracycline. As you may recall from our earlier meeting, this process is a review of existing labels and uses. Some uses that we've discussed include homeowner uses and application by air.

I will be travelling to DC the week of May 7th and was hoping that we might be able to have a face-to-face meeting on the 9th or 10th, at least for those of you who are in town? Maybe a half-day or a bit longer? We haven't met for a while and it would be a good chance to regroup and rethink our approach to these compounds, especially in light of what we have learned from the recent new uses.

Please let me know if you think you will be available.

Thanks,

Susan.

Susan Jennings
Senior Advisor for Public Health
Office of Pesticide Programs
(706) 355-8574 (office)
(703) 216-8627 (cell)

From: Johnson, Hope <Johnson.Hope@epa.gov>
To: Harbottle, Heather
Sent: 8/2/2017 3:16:04 PM
Subject: RE: AR Comments - Oxytetracycline

Thank you Heather!

Hope A. Johnson
Product Manager 21
U.S. Environmental Protection Agency
Office of Pesticide Programs
Registration Division
Fungicide Branch
Phone: 703-305-5410
Mail Code 7505P

From: Harbottle, Heather [mailto:Heather.Harbottle@fda.hhs.gov]
Sent: Wednesday, August 02, 2017 11:05 AM
To: Jennings, Susan <Jennings.Susan@epa.gov>; Patel, Jean (CDC) <vzp4@cdc.gov>; Julius Fajardo <Julius.Fajardo@ARS.USDA.GOV>
Cc: Johnson, Hope <Johnson.Hope@epa.gov>; Garvie, Heather <Garvie.Heather@epa.gov>
Subject: RE: AR Comments - Oxytetracycline

Hi everyone,
As promised, our comments on the oxytetracycline assessment. Our comments are similar. We don't have any additional comments for the kasugamycin assessment.

Comments on Oxytetracycline 152 17WP 07032017

B5

B5

Thanks again for giving us the opportunity to comment. Please let us know if you have any questions or further discussion is needed.

Best,
Heather

From: Jennings, Susan [mailto:Jennings.Susan@epa.gov]
Sent: Tuesday, August 01, 2017 8:59 AM
To: Patel, Jean (CDC); Julius Fajardo
Cc: Harbottle, Heather; Johnson, Hope; Garvie, Heather
Subject: FW: AR Comments - Streptomycin

And from FDA.

After you've read each other's comments, if anyone would like to hold another conference call to discuss, please let me know.

Thanks,

Susan.

From: Harbottle, Heather [mailto:Heather.Harbottle@fda.hhs.gov]
Sent: Monday, July 31, 2017 5:51 PM
To: Jennings, Susan <Jennings.Susan@epa.gov>; Gilbert, Jeffrey M <Jeff.Gilbert@fda.hhs.gov>
Cc: Johnson, Hope <Johnson.Hope@epa.gov>; Garvie, Heather <Garvie.Heather@epa.gov>
Subject: AR Comments - Streptomycin

Hi Susan and all,
Please find below our comments on the Streptomycin application and the addendum summarizing the CDC MIC data. I'll get back to you with comments on the tetracycline and kasugamycin application by Weds/Thurs. Although, unless something jumps out at us regarding the kasugamycin application, B5

B5

Comments for Streptomycin 152 Firewall 50WP 07032017 Document and the Addendum summarizing CDC MIC data on streptomycin:

B5

B5

Thank you for giving us the opportunity to comment on these assessments. I will send our comments on oxytetracycline (and kasugamycin, if any) on Weds/Thurs at the latest.

Let us know if you have questions!

Best,
Heather

From: Jennings, Susan [mailto:Jennings.Susan@epa.gov]
Sent: Monday, July 31, 2017 11:33 AM
To: Harbottle, Heather; Gilbert, Jeffrey M
Cc: Johnson, Hope; Garvie, Heather
Subject: RE: AR Comments

Ok. thanks.

From: Harbottle, Heather [mailto:Heather.Harbottle@fda.hhs.gov]
Sent: Monday, July 31, 2017 11:31 AM
To: Jennings, Susan <Jennings.Susan@epa.gov>; Gilbert, Jeffrey M <Jeff.Gilbert@fda.hhs.gov>
Subject: RE: AR Comments

Hi Susan,
I'll look them over today and get back to you asap. We do have some comments.
Thanks!
Heather

From: Jennings, Susan [mailto:Jennings.Susan@epa.gov]
Sent: Monday, July 31, 2017 11:29 AM
To: Harbottle, Heather; Gilbert, Jeffrey M

Subject: AR Comments

Hi,

Did you have any comments on the antibiotic assessments from EPA? Or are you OK with them?

Thanks,

Susan.

From: Jennings, Susan <Jennings.Susan@epa.gov>
To: Craig, Michael R (CDC); Harbottle, Heather; Patel, Jean (CDC); Carl Schultze; Julius Fajardo; Gilbert, Jeffrey M; Rose Hammond; Avery, Lacey (CDC*)
Sent: 1/17/2017 1:40:56 PM
Subject: RE: detailed outline attached for joint statement
Attachments: detailed outline 1-17-17.docx

Attached is the detailed draft outline with FDA and CDC comments incorporated. B5

B5

If all are ok, the B5

Thanks,

Susan.

From: Craig, Michael R. (CDC/OID/NCEZID) [mailto:bez7@cdc.gov]
Sent: Monday, January 16, 2017 10:08 PM
To: Harbottle, Heather (FDA/CVM) <Heather.Harbottle@fda.hhs.gov>; Patel, Jean (CDC/OID/NCEZID) <vzp4@cdc.gov>; Jennings, Susan <Jennings.Susan@epa.gov>; Carl Schultze <Carl.P.Schulze@aphis.usda.gov>; Julius Fajardo <Julius.Fajardo@ARS.USDA.GOV>; Gilbert, Jeffrey M (FDA/CVM) <Jeff.Gilbert@fda.hhs.gov>; Rose Hammond <Rose.Hammond@ARS.USDA.GOV>; Avery, Lacey (CDC/OID/NCEZID) (CTR) <xmh2@cdc.gov>
Subject: RE: detailed outline attached for joint statement

Should CDC start working on a draft based on this version?

Thanks,
MC

From: Harbottle, Heather (FDA/CVM)
Sent: Wednesday, January 11, 2017 2:10 PM
To: Patel, Jean (CDC/OID/NCEZID) <vzp4@cdc.gov>; Jennings, Susan <Jennings.Susan@epa.gov>; Carl Schultze <Carl.P.Schulze@aphis.usda.gov>; Julius Fajardo <Julius.Fajardo@ARS.USDA.GOV>; Gilbert, Jeffrey M (FDA/CVM) <Jeff.Gilbert@fda.hhs.gov>; Craig, Michael R. (CDC/OID/NCEZID) <bez7@cdc.gov>; Rose Hammond <Rose.Hammond@ARS.USDA.GOV>; Avery, Lacey (CDC/OID/NCEZID) (CTR) <xmh2@cdc.gov>
Subject: FW: detailed outline attached for joint statement

Hi Susan, Jean, and all,
Some of our top folks at FDA commented on the joint statement outline, on top of Jean's comments. They further suggested to maximize the document's impact, it will be important to provide concrete next steps.

Thanks for considering these comments and suggestions.
Best,
Heather

From: Patel, Jean (CDC/OID/NCEZID) <vzp4@cdc.gov>
To: Jennings, Susan; Carl Schultze; Julius Fajardo; Harbottle, Heather; Gilbert, Jeffrey M; Craig, Michael R (CDC); Rose Hammond; Avery, Lacey (CDC*)
Sent: 12/30/2016 2:20:47 PM
Subject: RE: detailed outline attached for joint statement
Attachments: detailed outline 12 14 16CDCedits.docx

Susan

Attached is a version with some suggestions from CDC. The revisions address comments I have included in the document. B5

B5

Thanks for considering these suggestions.

Jean

From: Jennings, Susan [mailto:Jennings.Susan@epa.gov]
Sent: Friday, December 16, 2016 9:14 AM
To: Carl Schultze <Carl.P.Schulze@aphis.usda.gov>; Julius Fajardo <Julius.Fajardo@ARS.USDA.GOV>; Harbottle, Heather (FDA/CVM) <Heather.Harbottle@fda.hhs.gov>; Patel, Jean (CDC/OID/NCEZID) <vzp4@cdc.gov>; Gilbert, Jeffrey M (FDA/CVM) <Jeff.Gilbert@fda.hhs.gov>; Craig, Michael R. (CDC/OID /NCEZID) <bez7@cdc.gov>; Rose Hammond <Rose.Hammond@ARS.USDA.GOV>
Subject: detailed outline attached for joint statement

Hi all,

Attached is the detailed outline that we discussed on Wednesday. If you could all read through it and send comments back, using REPLY ALL, that would be great.

Our goal was to have this finalized by early next week.

Thanks,

Susan.

From:	Hammond, Rose <Rose.Hammond@ARS.USDA.GOV>
To:	Jennings, Susan; Craig, Michael R (CDC); Harbottle, Heather; Patel, Jean (CDC); Schulze, Carl P - APHIS; Fajardo, Julius; Gilbert, Jeffrey M; Avery, Lacey (CDC*)
Sent:	1/17/2017 1:54:51 PM
Subject:	RE: detailed outline attached for joint statement
Attachments:	detailed outline 1-17-17 rwh.docx

Just some thoughts.

Rose

Dr. Rosemarie W. Hammond, Research Plant Pathologist
USDA ARS NEA BARC Molecular Plant Pathology Laboratory
Building 004 Room 214 BARC-West
10300 Baltimore Avenue
Beltsville, MD 20705
(P) 301-504-5203 (Fax) 301-504-5449
rose.hammond@ars.usda.gov

From: Jennings, Susan [mailto:Jennings.Susan@epa.gov]
Sent: Tuesday, January 17, 2017 8:41 AM
To: Craig, Michael R. (CDC/OID/NCEZID); Harbottle, Heather (FDA/CVM); Patel, Jean (CDC/OID/NCEZID); Schulze, Carl P - APHIS; Fajardo, Julius; Gilbert, Jeffrey M (FDA/CVM); Hammond, Rose; Avery, Lacey (CDC/OID/NCEZID) (CTR)
Subject: RE: detailed outline attached for joint statement

Attached is the detailed draft outline with FDA and CDC comments incorporated. I did a small amount of rewording for a couple of the FDA sentences, but not enough to change the meaning. Please let me know if any of you have any additional comments.

If all are ok, the CDC can start working on a draft of this version.

Thanks,

Susan.

From: Craig, Michael R. (CDC/OID/NCEZID) [mailto:bez7@cdc.gov]
Sent: Monday, January 16, 2017 10:08 PM
To: Harbottle, Heather (FDA/CVM) <Heather.Harbottle@fda.hhs.gov>; Patel, Jean (CDC/OID/NCEZID) <vzp4@cdc.gov>; Jennings, Susan <Jennings.Susan@epa.gov>; Carl Schultze <Carl.P.Schulze@aphis.usda.gov>; Julius Fajardo <Julius.Fajardo@ARS.USDA.GOV>; Gilbert, Jeffrey M (FDA/CVM) <Jeff.Gilbert@fda.hhs.gov>; Rose Hammond <Rose.Hammond@ARS.USDA.GOV>; Avery, Lacey (CDC/OID/NCEZID) (CTR) <xmh2@cdc.gov>
Subject: RE: detailed outline attached for joint statement

Should CDC start working on a draft based on this version?

Thanks,
MC

From: Harbottle, Heather (FDA/CVM)
Sent: Wednesday, January 11, 2017 2:10 PM
To: Patel, Jean (CDC/OID/NCEZID) <vzp4@cdc.gov>; Jennings, Susan <Jennings.Susan@epa.gov>; Carl Schultze <Carl.P.Schulze@aphis.usda.gov>; Julius Fajardo <Julius.Fajardo@ARS.USDA.GOV>; Gilbert, Jeffrey M (FDA/CVM) <Jeff.Gilbert@fda.hhs.gov>; Craig, Michael R. (CDC/OID/NCEZID) <bez7@cdc.gov>; Rose Hammond <Rose.Hammond@ARS.USDA.GOV>; Avery, Lacey (CDC/OID/NCEZID) (CTR) <xmh2@cdc.gov>

Subject: FW: detailed outline attached for joint statement

Hi Susan, Jean, and all,

B5

Thanks for considering these comments and suggestions.
Best,
Heather

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From: Harbottle, Heather </O=FDA/OU=FIRST ADMINISTRATIVE GROUP/CN=RECIPIENTS /CN=HHARBOTT>
To: Jennings, Susan; Gilbert, Jeffrey M
Sent: 10/13/2017 1:16:59 PM
Subject: RE: Draft Decision Document Interagency discussion

Hi Susan,
You are good to go to use the language included below from FDA in your draft document. Good luck and let us know if you need anything.
Best,
Heather

From: Jennings, Susan [mailto:Jennings.Susan@epa.gov]
Sent: Wednesday, October 11, 2017 8:11 AM
To: Harbottle, Heather <Heather.Harbottle@fda.hhs.gov>; Gilbert, Jeffrey M <Jeff.Gilbert@fda.hhs.gov>
Subject: RE: Draft Decision Document Interagency discussion

The whole document is 20 pages or so.

From: Harbottle, Heather [mailto:Heather.Harbottle@fda.hhs.gov]
Sent: Tuesday, October 10, 2017 6:15 PM
To: Jennings, Susan <Jennings.Susan@epa.gov>; Gilbert, Jeffrey M <Jeff.Gilbert@fda.hhs.gov>
Subject: RE: Draft Decision Document Interagency discussion

Hi Susan,
We'll get back to you asap. When is your deadline? B5
B5
Thanks!
Heather

From: Jennings, Susan [mailto:Jennings.Susan@epa.gov]
Sent: Tuesday, October 10, 2017 9:49 AM
To: Patel, Jean (CDC) <vzp4@cdc.gov>; Harbottle, Heather <Heather.Harbottle@fda.hhs.gov>; Gilbert, Jeffrey M <Jeff.Gilbert@fda.hhs.gov>; Rose Hammond <Rose.Hammond@ARS.USDA.GOV>; Julius Fajardo <Julius.Fajardo@ARS.USDA.GOV>
Cc: Garvie, Heather <Garvie.Heather@epa.gov>; Johnson, Hope <Johnson.Hope@epa.gov>
Subject: Draft Decision Document Interagency discussion

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Could each of you please read through this and let me know if there are any issues? I want to stick as closely to web language as possible since we don't have time for interagency concurrence.

Thanks,

Susan.

==========

Other agencies in the federal government (CDC, FDA, USDA) are aware of the potential for resistance to develop from the use of antibiotics in agriculture and have been working within their areas of expertise to address the problem. CDC cites "Improving Antibiotic Prescribing/Stewardship" as one of its Four Core Actions to Fight Resistance. CDC believes antibiotic stewardship is the "commitment to always use antibiotics appropriately and safely -- only when they are needed to treat disease, and to choose the right antibiotics and to administer them in the right way in every case." For more on CDC's views, see https://www.cdc.gov/drugresistance/about.html/.

FDA is committed to further advancing antimicrobial stewardship by focusing on the following key initiatives: (1) aligning antimicrobial drug products with the principles of antimicrobial stewardship in veterinary settings; (2) supporting efforts to foster stewardship of antimicrobials in veterinary settings; and (3) assessing the impact of strategies intended to curb the emergence of antimicrobial resistance associated with the use of antimicrobial drugs in veterinary settings. For more on FDA's views, see https://www.fda.gov/AnimalVeterinary/SafetyHealth/AntimicrobialResistance/JudiciousUseofAntimicrobials/ucm535158.htm]

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EPA believes that the management of pesticide resistance development is an important part of sustainable pest management and, in conjunction with alternative pest management strategies and IPM programs, can make significant contributions to reducing risks to humans and the environment. In support of these goals, EPA is assessing the potential development of antibiotic resistance as an adverse effect under FIFRA.

==========

From: Jennings, Susan <Jennings.Susan@epa.gov>
To: Harbottle, Heather; Gilbert, Jeffrey M
Sent: 10/11/2017 12:09:49 PM
Subject: RE: Draft Decision Document Interagency discussion

A response to a petition for approval/registration of new uses of oxytetracycline. We'll be issuing it shortly.

I'm really just looking to make sure that your web language is still current (I quoted from the web to make sure we don't need concurrence).

Please let me know if you have any more questions.

Thanks,

Susan.

From: Harbottle, Heather [mailto:Heather.Harbottle@fda.hhs.gov]
Sent: Tuesday, October 10, 2017 6:15 PM
To: Jennings, Susan <Jennings.Susan@epa.gov>; Gilbert, Jeffrey M <Jeff.Gilbert@fda.hhs.gov>
Subject: RE: Draft Decision Document Interagency discussion

Hi Susan,
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B5
Thanks!
Heather

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To: Patel, Jean (CDC) <vzp4@cdc.gov>; Harbottle, Heather <Heather.Harbottle@fda.hhs.gov>; Gilbert, Jeffrey M <Jeff.Gilbert@fda.hhs.gov>; Rose Hammond <Rose.Hammond@ARS.USDA.GOV>; Julius Fajardo <Julius.Fajardo@ARS.USDA.GOV>
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Susan.

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its Four Core Actions to Fight Resistance. CDC believes antibiotic stewardship is the "commitment to always use antibiotics appropriately and safely -- only when they are needed to treat disease, and to choose the right antibiotics and to administer them in the right way in every case." For more on CDC's views, see https://www.cdc.gov/drugresistance/about.html/.

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==========

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B5
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Sent: Tuesday, October 10, 2017 9:49 AM
To: Patel, Jean (CDC) <vzp4@cdc.gov>; Harbottle, Heather <Heather.Harbottle@fda.hhs.gov>; Gilbert, Jeffrey M <Jeff.Gilbert@fda.hhs.gov>; Rose Hammond <Rose.Hammond@ARS.USDA.GOV>; Julius Fajardo <Julius.Fajardo@ARS.USDA.GOV>
Cc: Garvie, Heather <Garvie.Heather@epa.gov>; Johnson, Hope <Johnson.Hope@epa.gov>
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Susan.

==========

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==========

From: Hill, Shaunta <Hill.Shaunta@epa.gov>
To: Harbottle, Heather
Sent: 2/10/2016 2:56:22 PM
Subject: RE: EPA - Pending antibiotic request for Streptomycin, request for a teleconference

Thank you Heather.

From: Harbottle, Heather [mailto:Heather.Harbottle@fda.hhs.gov]
Sent: Wednesday, February 10, 2016 8:40 AM
To: Hill, Shaunta <Hill.Shaunta@epa.gov>; Jennings, Susan <Jennings.Susan@epa.gov>
Cc: Gilbert, Jeffrey M <Jeff.Gilbert@fda.hhs.gov>
Subject: RE: EPA - Pending antibiotic request for Streptomycin, request for a teleconference

Good morning Shaunta,
Thank you for the information. Contact information for Jeff and me are provided below. Talk to you at 11am.
Thanks!
Heather

Jeff Gilbert, Ph.D.
Team Leader
Microbial Food Safety Team
Office of New Animal Drug Evaluation
Center for Veterinary Medicine
FDA
Jeff.gilbert@fda.hhs.gov
240-402-0706

Heather Harbottle, Ph.D.
Microbiologist
Microbial Food Safety Team
Office of New Animal Drug Evaluation
Center for Veterinary Medicine
FDA
Heather.harbottle@fda.hhs.gov
240-402-0791

From: Hill, Shaunta [mailto:Hill.Shaunta@epa.gov]
Sent: Wednesday, February 10, 2016 6:34 AM
To: Harbottle, Heather; Jennings, Susan
Cc: Gilbert, Jeffrey M
Subject: EPA - Pending antibiotic request for Streptomycin, request for a teleconference

Good Morning Heather and Jeff,
Please see the attached agenda and support files for our teleconference Wednesday – Feb 10, 2016 at 11 am.
The conference line information is noted on the agenda.

*Due to the file sizes, two emails will be sent.

If you would not mind, could you please provide contact information and title for both you and Jeff.
Thank you

From: Harbottle, Heather [mailto:Heather.Harbottle@fda.hhs.gov]
Sent: Tuesday, February 09, 2016 4:58 PM
To: Hill, Shaunta <Hill.Shaunta@epa.gov>; Jennings, Susan <Jennings.Susan@epa.gov>
Cc: Gilbert, Jeffrey M <Jeff.Gilbert@fda.hhs.gov>
Subject: RE: EPA - Pending antibiotic request for Streptomycin, request for a teleconference

Hi Shaunta,
We'll be happy to call in. Is there a call in number and agenda yet for the teleconference tomorrow at 11am?
Thanks!
Heather

From: Hill, Shaunta [mailto:Hill.Shaunta@epa.gov]
Sent: Monday, February 08, 2016 12:16 PM
To: Harbottle, Heather; Jennings, Susan
Cc: Gilbert, Jeffrey M
Subject: RE: EPA - Pending antibiotic request for Streptomycin, request for a teleconference

Hello Heather,
We did meet during the IR-4 meeting. Happy to hear that you and Jeff will be joining our discussion.
The meeting agenda will be finalized shortly and I will forward it along with several reference documents for our discussion.
In the meantime, I wanted to provide some background information on pesticide registrations.

The type of registrations permitted under FIFRA (i.e. Section 3 and Section 18) can be found here: http://www.epa.gov/pesticide-registration/types-registrations-under-fifra

Information on the general registration process can be found here: http://www.epa.gov/pesticide-registration/pesticide-registration-manual-chapter-1-overview-requirements-pesticide

I hope you find this initial information helpful.
If you have any questions, please let me know.

Regards,
****
Shaunta Hill-Hammond, Ph. D.
Plant Pathologist
U.S. EPA: Office of Chemical Safety and Pollution Prevention
Registration Division/Fungicide Branch (PYS)
1200 Pennsylvania Avenue, NW (7505P)
Washington, DC 20460

Tel: 703.347.8961 | Fax: 703.305.6920
E-mail: hill.shaunta@epa.gov
URL Address: www.epa.gov/pesticides

From: Harbottle, Heather [mailto:Heather.Harbottle@fda.hhs.gov]
Sent: Friday, February 05, 2016 8:35 AM
To: Hill, Shaunta <Hill.Shaunta@epa.gov>; Jennings, Susan <Jennings.Susan@epa.gov>
Cc: Gilbert, Jeffrey M <Jeff.Gilbert@fda.hhs.gov>
Subject: FW: EPA - Pending antibiotic request for Streptomycin, request for a teleconference
Importance: High

Good morning Ms. Hill and Ms. Jennings,

My name is Heather Harbottle and I believe we met during the IR-4 Bacterial Challenges Mini-Summit meeting "Understanding the ABCs (Awareness of Bacterial Challenges) with Antibiotics In Crops" in September of 2014. As you may remember, I delivered a presentation regarding FDA's use of GFI #152 due to our extensive use of this guidance assessing risk for the use of antimicrobials in food producing animals. I've been asked by Bill Flynn and my team leader, Dr. Jeff Gilbert, to get in touch with you regarding your email below. Dr. Gilbert and I would be happy to attend the teleconference on Wednesday, and provide any assistance with GFI #152 as it pertains to your application for streptomycin or any other antimicrobial.

Please let us know how we can be of help.

Best,
Heather Harbottle

From: Hill, Shaunta [mailto:Hill.Shaunta@epa.gov]
Sent: Thursday, February 04, 2016 9:59 AM
To: Flynn, William T
Cc: Jennings, Susan
Subject: EPA - Pending antibiotic request for Streptomycin, request for a teleconference

Hello Dr. William;

My name is Shaunta Hill and I am a Risk Assessor/Plant Pathologist with EPA's Office of Pesticide Programs – Registration Division.
I received your name from Dr. Jean Patel at CDC as a potential contact.

As EPA manages antibiotics for pesticidal use, we are interested in accessing the resistance risk potential along with human and environmental risks. We have previously worked with CDC and FDA (via David White) utilizing the FDA Guidance for Industry #152 for this purpose.

We have a number of applications currently pending and have scheduled a teleconference

for **Wednesday Feb 10 at 11 am** to begin discussions.
I am hopefully that you are available to participate in this discussion as FDA input is valued.
The primary application for consideration next week is Streptomycin sulfate use on grapefruit and tomatoes via FIFRA Section 3 Registration.

If you are available, I can provide additional background information in addition to our meeting agenda.
Should you have any questions, please let us know. I have cc'ed on this communication Susan Jennings, who serves as our Public Health Coordinator and is available to address questions on this meeting request as well.

Thank you for your time and I look forward to hearing from you.

Regards,
****

Shaunta Hill-Hammond, Ph. D.
Plant Pathologist
U.S. EPA: Office of Chemical Safety and Pollution Prevention
Registration Division/Fungicide Branch (PYS)
1200 Pennsylvania Avenue, NW (7505P)
Washington, DC 20460

Tel: 703.347.8961 | Fax: 703.305.6920
E-mail: hill.shaunta@epa.gov
URL Address: www.epa.gov/pesticides

From: Hill, Shaunta <Hill.Shaunta@epa.gov>
To: Harbottle, Heather; Jennings, Susan
CC: Gilbert, Jeffrey M
Sent: 2/10/2016 3:02:12 PM
Subject: RE: EPA - Pending antibiotic request for Streptomycin, request for a teleconference

Hi Heather,
I will resend the emails.

From: Harbottle, Heather [mailto:Heather.Harbottle@fda.hhs.gov]
Sent: Wednesday, February 10, 2016 9:47 AM
To: Hill, Shaunta <Hill.Shaunta@epa.gov>; Jennings, Susan <Jennings.Susan@epa.gov>
Cc: Gilbert, Jeffrey M <Jeff.Gilbert@fda.hhs.gov>
Subject: RE: EPA - Pending antibiotic request for Streptomycin, request for a teleconference

Hi Shaunta,
We received 6 attachments in the 2 emails. I don't see an agenda attached to either email containing the call-in information?
Thanks!
Heather

From: Hill, Shaunta [mailto:Hill.Shaunta@epa.gov]
Sent: Wednesday, February 10, 2016 6:34 AM
To: Harbottle, Heather; Jennings, Susan
Cc: Gilbert, Jeffrey M
Subject: EPA - Pending antibiotic request for Streptomycin, request for a teleconference

This is the second email for Wednesday's teleconference.
If you have any questions / trouble with the files, please let me know.
Thank you

Regards,
****
Shaunta Hill-Hammond, Ph. D.
Plant Pathologist
U.S. EPA: Office of Chemical Safety and Pollution Prevention
Registration Division/Fungicide Branch (PYS)
1200 Pennsylvania Avenue, NW (7505P)
Washington, DC 20460

Tel: 703.347.8961 | Fax: 703.305.6920
E-mail: hill.shaunta@epa.gov
URL Address: www.epa.gov/pesticides

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Sent: Tuesday, February 09, 2016 4:58 PM
To: Hill, Shaunta <Hill.Shaunta@epa.gov>; Jennings, Susan <Jennings.Susan@epa.gov>
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Subject: RE: EPA - Pending antibiotic request for Streptomycin, request for a teleconference

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Plant Pathologist
U.S. EPA: Office of Chemical Safety and Pollution Prevention
Registration Division/Fungicide Branch (PYS)
1200 Pennsylvania Avenue, NW (7505P)
Washington, DC 20460

Tel: 703.347.8961 | Fax: 703.305.6920
E-mail: hill.shaunta@epa.gov
URL Address: www.epa.gov/pesticides

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Cc: Gilbert, Jeffrey M <Jeff.Gilbert@fda.hhs.gov>
Subject: FW: EPA - Pending antibiotic request for Streptomycin, request for a teleconference
Importance: High

Good morning Ms. Hill and Ms. Jennings,

My name is Heather Harbottle and I believe we met during the IR-4 Bacterial Challenges Mini-Summit meeting "Understanding the ABCs (Awareness of Bacterial Challenges) with Antibiotics In Crops" in September of 2014. As you may remember, I delivered a presentation regarding FDA's use of GFI #152 due to our extensive use of this guidance assessing risk for the use of antimicrobials in food producing animals. I've been asked by Bill Flynn and my team leader, Dr. Jeff Gilbert, to get in touch with you regarding your email below. Dr. Gilbert and I would be happy to attend the teleconference on Wednesday, and provide any assistance with GFI #152 as it pertains to your application for streptomycin or any other antimicrobial.

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Best,
Heather Harbottle

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Cc: Jennings, Susan
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I received your name from Dr. Jean Patel at CDC as a potential contact.

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I am hopefully that you are available to participate in this discussion as FDA input is valued.
The primary application for consideration next week is Streptomycin sulfate use on grapefruit and tomatoes via FIFRA Section 3 Registration.

If you are available, I can provide additional background information in addition to our meeting agenda.

Should you have any questions, please let us know. I have cc'ed on this communication Susan Jennings, who serves as our Public Health Coordinator and is available to address questions on this meeting request as well.

Thank you for your time and I look forward to hearing from you.

Regards,
****

Shaunta Hill-Hammond, Ph. D.
Plant Pathologist
U.S. EPA: Office of Chemical Safety and Pollution Prevention
Registration Division/Fungicide Branch (PYS)
1200 Pennsylvania Avenue, NW (7505P)
Washington, DC 20460

Tel: 703.347.8961 | Fax: 703.305.6920
E-mail: hill.shaunta@epa.gov
URL Address: www.epa.gov/pesticides

From: Harbottle, Heather </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=55429E94C1CE44C4B031B4CFEE99A90F-HHARBOTT>
To: Jennings, Susan
Sent: 3/13/2018 8:31:35 PM
Subject: RE: EPA Request

Ok great, hopefully that will do it!

Best,
Heather

From: Jennings, Susan [mailto:Jennings.Susan@epa.gov]
Sent: Tuesday, March 13, 2018 4:29 PM
To: Harbottle, Heather <Heather.Harbottle@fda.hhs.gov>
Subject: RE: EPA Request

That's what I meant by adequately protective. Basically, if the pesticide residues are negligible when compared to residues from the livestock use, then they will be even more negligible (if there is such a thing) when compared with the therapeutic use. I made this argument and haven't heard anything back, so I suspect the lawyer is checking with her supervisors. Hopefully, we're good to go.

Thanks,

Susan.

From: Harbottle, Heather [mailto:Heather.Harbottle@fda.hhs.gov]
Sent: Tuesday, March 13, 2018 4:04 PM
To: Jennings, Susan <Jennings.Susan@epa.gov>
Subject: RE: EPA Request

Ok, do let me know if you hear from either of them, and I'll do the same. I have a meeting with some of our policy people in management tomorrow, to see if there's something else we can do for you.

B5

Heather

From: Jennings, Susan [mailto:Jennings.Susan@epa.gov]
Sent: Tuesday, March 13, 2018 3:51 PM
To: Harbottle, Heather <Heather.Harbottle@fda.hhs.gov>
Subject: RE: EPA Request

No, I'm just waiting to hear back. I am making an argument that it's adequately protective and if we go that way we are done.

Thanks for your help and I'll let you know if I hear anything.

Susan.

From: Harbottle, Heather [mailto:Heather.Harbottle@fda.hhs.gov]
Sent: Tuesday, March 13, 2018 3:11 PM
To: Jennings, Susan <Jennings.Susan@epa.gov>
Subject: RE: EPA Request

Hi Susan,
Just checking in with you – have you had any response from Mike at CFSAN or Ed from CDER? I have not heard from either.

Thanks,
Heather

From: Jennings, Susan [mailto:Jennings.Susan@epa.gov]
Sent: Monday, March 12, 2018 6:56 AM
To: Harbottle, Heather <Heather.Harbottle@fda.hhs.gov>; Cox, Edward M <Edward.Cox@fda.hhs.gov>
Subject: RE: EPA Request

Ok. Thanks. Once we figure out what we're doing, I'll let you know.

Thanks,

Susan.

Susan Jennings
Senior Advisor for Public Health
Office of Pesticide Programs
(706) 355-8574 (office)
B6 (cell)

From: Harbottle, Heather [mailto:Heather.Harbottle@fda.hhs.gov]
Sent: Friday, March 09, 2018 5:10 PM
To: Jennings, Susan <Jennings.Susan@epa.gov>; Cox, Edward M <Edward.Cox@fda.hhs.gov>
Subject: RE: EPA Request

Ed seems to be an authoritative figure over there, so you might want to give him a try. The person you talked to might not have had the authority to figure it out. I am seeing his phone number as 301-796-1300 and email is Edward.cox@fda.hhs.gov.

I too haven't heard back from Mike, will let you know if I do.

Thanks,
Heather

From: Jennings, Susan [mailto:Jennings.Susan@epa.gov]
Sent: Friday, March 09, 2018 5:05 PM
To: Harbottle, Heather <Heather.Harbottle@fda.hhs.gov>
Cc: Gilbert, Jeffrey M <Jeff.Gilbert@fda.hhs.gov>
Subject: RE: EPA Request

Thank you. I never spoke to Ed Cox, but was referred to someone else. I'd appreciate any direction that you could provide. I sent it to Mike, but haven't heard anything back. I suspect he hasn't read it yet.

Thanks and have a good weekend,

Susan.

From: Harbottle, Heather [mailto:Heather.Harbottle@fda.hhs.gov]
Sent: Friday, March 09, 2018 4:25 PM
To: Jennings, Susan <Jennings.Susan@epa.gov>
Cc: Gilbert, Jeffrey M <Jeff.Gilbert@fda.hhs.gov>
Subject: FW: EPA Request

Hi Susan,

I'm trying to get a name for you at CDER, but in the meantime, perhaps these folks at CFSAN (email below) would be appropriate/helpful. I'll let you know when I hear something back from them, or if I hit a dead end there.

Also, it looks to me from the FDA organizational chart that Ed Cox is the Office Director (above Division director here at FDA) of the Office of Antimicrobial Products. So the only people above him would be the Office of New Drugs director (vacant in this ORG chart) and Deputy Office director Peter Stein and Chief of Staff Peter Frey.

https://www.fda.gov/AboutFDA/CentersOffices/OrganizationCharts/ucm350931.htm

Jeff also suggests B5

B5

Best,
Heather

From: Harbottle, Heather
Sent: Friday, March 09, 2018 4:10 PM
To: Shah, Romina <Romina.Shah@fda.hhs.gov>
Cc: Dinovi, Michael J <Michael.Dinovi@fda.hhs.gov>; Gilbert, Jeffrey M <jeff.gilbert@fda.hhs.gov>
Subject: EPA Request -Any idea who evaluates dietary exposure of antimicrobial residues from fruits and vegetables?

Thanks Romina! Hi Mike!

EPA is re-registering (also known as re-approving) the use of two antibiotics (oxytetracycline and streptomycin) as pesticides on fruits and vegetables. B5

B5

B5

B5

B5

They are under a tight deadline so I apologize for asking you to consider this when you have time, and let us know if this is something CFSAN would do, or if it really lands in CDER's lap. The contacts we have spoken to at CDER don't seem to think it is their territory.

Thanks again and feel free to give me a call/email if you have further clarifying questions.

Best,
Heather Harbottle
240-402-0791

From: Shah, Romina
Sent: Friday, March 09, 2018 3:52 PM
To: Harbottle, Heather <Heather.Harbottle@fda.hhs.gov>
Cc: Dinovi, Michael J <Michael.Dinovi@fda.hhs.gov>
Subject: RE: Any idea who evaluates dietary exposure of antimicrobial residues from fruits and vegetables?

Hi H, I'm sending your email to Mike, he's the CFSAN expert for dietary exposure. RS

From: Harbottle, Heather
Sent: Friday, March 9, 2018 3:40 PM
To: Shah, Romina <Romina.Shah@fda.hhs.gov>
Subject: Any idea who evaluates dietary exposure of antimicrobial residues from fruits and vegetables?

Hey Romina,
EPA is asking for a contact for people who evaluate dietary exposure of humans from antimicrobial residues on fruits and vegetables. Do you know if CFSAN does that? And who might be the person we can contact?

Thanks!
Heather

Heather Harbottle, Ph.D.
Microbiologist
Microbial Food Safety Team
Division of Human Food Safety
Office of New Animal Drug Evaluation
Center for Veterinary Medicine, FDA
240-402-0791

From: Harbottle, Heather </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=55429E94C1CE44C4B031B4CFEE99A90F-HHARBOTT>
To: Jennings, Susan
CC: Gilbert, Jeffrey M
Sent: 3/14/2018 7:06:17 PM
Subject: RE: EPA Request

Hi Susan,
I just called and left you a message on your voicemail. B5

B5

The letter would be identical B5

B5

If it will give you what you need, let us know if you need it before Monday. As I said I can get it signed Monday without issue as the Office director on Monday will have participated in this discussion and agreed. If you need it before Monday, that is likely doable but I'll need to have another meeting with the Office Director who is in office until Friday. J

Best,
Heather

From: Jennings, Susan [mailto:Jennings.Susan@epa.gov]
Sent: Tuesday, March 13, 2018 4:29 PM
To: Harbottle, Heather <Heather.Harbottle@fda.hhs.gov>
Subject: RE: EPA Request

That's what I meant by adequately protective. Basically,

B5

B5

Thanks,

Susan.

From: Harbottle, Heather [mailto:Heather.Harbottle@fda.hhs.gov]
Sent: Tuesday, March 13, 2018 4:04 PM
To: Jennings, Susan <Jennings.Susan@epa.gov>
Subject: RE: EPA Request

Ok, do let me know if you hear from either of them, and I'll do the same. I have a meeting with some of our policy people in management tomorrow, to see if there's something else we can do for you.

B5

Heather

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Sent: Tuesday, March 13, 2018 3:51 PM
To: Harbottle, Heather <Heather.Harbottle@fda.hhs.gov>
Subject: RE: EPA Request

No, I'm just waiting to hear back. **B5**
B5

Thanks for your help and I'll let you know if I hear anything.

Susan.

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Subject: RE: EPA Request

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Thanks,
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Sent: Monday, March 12, 2018 6:56 AM
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Subject: RE: EPA Request

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Thanks,

Susan.

Susan Jennings
Senior Advisor for Public Health
Office of Pesticide Programs
(706) 355-8574 (office)
(703) 216-8627 (cell)

From: Harbottle, Heather [mailto:Heather.Harbottle@fda.hhs.gov]
Sent: Friday, March 09, 2018 5:10 PM
To: Jennings, Susan <Jennings.Susan@epa.gov>; Cox, Edward M <Edward.Cox@fda.hhs.gov>
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To: Harbottle, Heather <Heather.Harbottle@fda.hhs.gov>
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Thanks and have a good weekend,

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B6

B5

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B5

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Sent: Friday, March 9, 2018 3:40 PM

To: Shah, Romina <Romina.Shah@fda.hhs.gov>
Subject: Any idea who evaluates dietary exposure of antimicrobial residues from fruits and vegetables?

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EPA is asking for a contact for people who evaluate dietary exposure of humans from antimicrobial residues on fruits and vegetables. Do you know if CFSAN does that? And who might be the person we can contact?

Thanks!
Heather

Heather Harbottle, Ph.D.
Microbiologist
Microbial Food Safety Team
Division of Human Food Safety
Office of New Animal Drug Evaluation
Center for Veterinary Medicine, FDA
240-402-0791

From: Jennings, Susan <Jennings.Susan@epa.gov>
To: Harbottle, Heather; Cox, Edward M
CC: Friedlander, Lynn G; Gilbert, Jeffrey M
Sent: 2/2/2018 2:25:23 PM
Subject: RE: EPA request re: antimicrobials in humans

Thanks, you too.

From: Harbottle, Heather [mailto:Heather.Harbottle@fda.hhs.gov]
Sent: Friday, February 02, 2018 9:13 AM
To: Jennings, Susan <Jennings.Susan@epa.gov>; Cox, Edward M <Edward.Cox@fda.hhs.gov>
Cc: Friedlander, Lynn G <Lynn.Friedlander@fda.hhs.gov>; Gilbert, Jeffrey M <Jeff.Gilbert@fda.hhs.gov>
Subject: RE: EPA request re: antimicrobials in humans

Hi Susan,
Lynn Friedlander works in CVM, in my division. B5

B5

If you are looking for residue exposure in the agricultural crops listed in the registrations, I'm not sure who in our Center for Food Safety and Applied Nutrition may work on that.

Have a good weekend,
Heather

From: Jennings, Susan [mailto:Jennings.Susan@epa.gov]
Sent: Friday, February 02, 2018 8:58 AM
To: Cox, Edward M <Edward.Cox@fda.hhs.gov>; Harbottle, Heather <Heather.Harbottle@fda.hhs.gov>
Subject: RE: EPA request re: antimicrobials in humans

Thanks.

B5

Two other people provided Lynn Friedlander as a name to contact. Once we've ironed out exactly what we're looking for (likely early next week) I'll contact both of you and we can work from there.

Thanks in advance for your help on this issue,

Susan.

Susan Jennings
Senior Advisor for Public Health
Office of Pesticide Programs
(706) 355-8574 (office)
(703) 216-8627 (cell)

From: Cox, Edward M [mailto:Edward.Cox@fda.hhs.gov]
Sent: Thursday, February 01, 2018 4:36 PM
To: Jennings, Susan <Jennings.Susan@epa.gov>; Harbottle, Heather <Heather.Harbottle@fda.hhs.gov>

Subject: RE: EPA request re: antimicrobials in humans

Hi Susan and Heather,

Thanks for your e-mails. I read through and took a quick look at the letter. I couldn't tell exactly what's needed here and it sounds like maybe you are still working to figure that out. We may be able to contribute depending on the assessment needed.

B5

If you need us, just let me know.

Thanks.
-Ed

From: Jennings, Susan [mailto:Jennings.Susan@epa.gov]
Sent: Thursday, February 01, 2018 2:35 PM
To: Harbottle, Heather <Heather.Harbottle@fda.hhs.gov>; Cox, Edward M <Edward.Cox@fda.hhs.gov>
Subject: RE: EPA request re: antimicrobials in humans

Thanks, Heather.

B5

Because of the tight timeframes, I am hoping to identify the right contact now so that we can move more quickly when needed.

Thank you for your help,

Susan.

Susan Jennings
Senior Advisor for Public Health
Office of Pesticide Programs
(706) 355-8574 (office)
(703) 216-8627 (cell)

From: Harbottle, Heather [mailto:Heather.Harbottle@fda.hhs.gov]
Sent: Thursday, February 01, 2018 2:14 PM
To: Cox, Edward M <Edward.Cox@fda.hhs.gov>; Jennings, Susan <Jennings.Susan@epa.gov>
Subject: EPA request re: antimicrobials in humans

Good afternoon Dr. Cox,
Susan Jennings from EPA has been leading a working group with regard to the registration of antimicrobials in agricultural crops (CVM has been consulting) and is looking for a contact at FDA who works with antimicrobial approvals for humans. B5

B5 I suggested she contact your group in hopes that someone there is the correct person and if not, you may know who would be the best person for her to contact.

Thanks for your help.

Best,

Heather Harbottle, Ph.D.
Microbiologist
Microbial Food Safety Team
Division of Human Food Safety
Office of New Animal Drug Evaluation
Center for Veterinary Medicine, FDA
240-402-0791

From: Harbottle, Heather </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=55429E94C1CE44C4B031B4CFEE99A90F-HHARBOTT>
To: Jennings, Susan; Cox, Edward M
CC: Friedlander, Lynn G; Gilbert, Jeffrey M
Sent: 2/2/2018 2:12:59 PM
Subject: RE: EPA request re: antimicrobials in humans

Hi Susan,
Lynn Friedlander works in CVM, in my division. B5

B5

If you are looking for residue exposure in the agricultural crops listed in the registrations, I'm not sure who in our Center for Food Safety and Applied Nutrition may work on that.

Have a good weekend,
Heather

From: Jennings, Susan [mailto:Jennings.Susan@epa.gov]
Sent: Friday, February 02, 2018 8:58 AM
To: Cox, Edward M <Edward.Cox@fda.hhs.gov>; Harbottle, Heather <Heather.Harbottle@fda.hhs.gov>
Subject: RE: EPA request re: antimicrobials in humans

Thanks.

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Two other people provided Lynn Friedlander as a name to contact. Once we've ironed out exactly what we're looking for (likely early next week) I'll contact both of you and we can work from there.

Thanks in advance for your help on this issue,

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Microbiologist
Microbial Food Safety Team
Division of Human Food Safety
Office of New Animal Drug Evaluation
Center for Veterinary Medicine, FDA
240-402-0791

From: Jennings, Susan <Jennings.Susan@epa.gov>
To: Cox, Edward M; Harbottle, Heather
Sent: 2/2/2018 1:57:46 PM
Subject: RE: EPA request re: antimicrobials in humans

Thanks.

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Sent: Thursday, February 01, 2018 4:36 PM
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Microbiologist
Microbial Food Safety Team
Division of Human Food Safety
Office of New Animal Drug Evaluation
Center for Veterinary Medicine, FDA
240-402-0791

From: Jennings, Susan <Jennings.Susan@epa.gov>
To: Harbottle, Heather; Cox, Edward M
Sent: 2/1/2018 7:35:13 PM
Subject: RE: EPA request re: antimicrobials in humans
Attachments: 2006 EPA FDA aggregate oxytet letter.pdf

Thanks, Heather.

B5

Because of the tight timeframes, I am hoping to identify the right contact now so that we can move more quickly when needed.

Thank you for your help,

Susan.

Susan Jennings
Senior Advisor for Public Health
Office of Pesticide Programs
(706) 355-8574 (office)
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Microbiologist
Microbial Food Safety Team
Division of Human Food Safety
Office of New Animal Drug Evaluation
Center for Veterinary Medicine, FDA

From: Gilbert, Jeffrey M </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=80308E6A2328498ABB1E3BF85E99784C-JGILBERT>
To: Harbottle, Heather; Jennings, Susan
Sent: 2/2/2018 2:15:59 PM
Subject: RE: EPA request re: antimicrobials in humans

I discussed with Lynn – she may give you a call, Susan. B5

B5 Stay tuned.....

From: Harbottle, Heather
Sent: Friday, February 02, 2018 9:13 AM
To: Jennings, Susan <Jennings.Susan@epa.gov>; Cox, Edward M <Edward.Cox@fda.hhs.gov>
Cc: Friedlander, Lynn G <Lynn.Friedlander@fda.hhs.gov>; Gilbert, Jeffrey M <Jeff.Gilbert@fda.hhs.gov>
Subject: RE: EPA request re: antimicrobials in humans

Hi Susan,
Lynn Friedlander works in CVM, in my division. We estimate the acceptable daily intake for antimicrobial residues in animal tissues, and Lynn's group sets tolerances in that context. We only deal with edible animal tissues, so I'm not sure that Lynn is the person you may need. I've copied her on this email as well as Jeff.

If you are looking for residue exposure in the agricultural crops listed in the registrations, I'm not sure who in our Center for Food Safety and Applied Nutrition may work on that.

Have a good weekend,
Heather

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Thanks for your help.

Best,

Heather Harbottle, Ph.D.
Microbiologist
Microbial Food Safety Team
Division of Human Food Safety
Office of New Animal Drug Evaluation
Center for Veterinary Medicine, FDA
240-402-0791

From: Jennings, Susan <Jennings.Susan@epa.gov>
To: Harbottle, Heather
CC: Gilbert, Jeffrey M
Sent: 3/16/2018 3:24:33 PM
Subject: RE: FDA Input on Tolerance Decisions for Oxytetracycline and Streptomycin - Revised FDA response

That's ok. Thanks for trying. Ed responded and I'll be getting back to him shortly.

From: Harbottle, Heather [mailto:Heather.Harbottle@fda.hhs.gov]
Sent: Friday, March 16, 2018 11:08 AM
To: Jennings, Susan <Jennings.Susan@epa.gov>
Cc: Gilbert, Jeffrey M <Jeff.Gilbert@fda.hhs.gov>
Subject: RE: FDA Input on Tolerance Decisions for Oxytetracycline and Streptomycin - Revised FDA response

Oh no! B5

B5

Has anyone responded from Ed's group?

Sorry Susan, B5

Best,
Heather

From: Jennings, Susan [mailto:Jennings.Susan@epa.gov]
Sent: Friday, March 16, 2018 11:02 AM
To: Harbottle, Heather <Heather.Harbottle@fda.hhs.gov>
Subject: RE: FDA Input on Tolerance Decisions for Oxytetracycline and Streptomycin - Revised FDA response

Yes, but the times are changing and it won't work.

Thanks for trying.

From: Harbottle, Heather [mailto:Heather.Harbottle@fda.hhs.gov]
Sent: Friday, March 16, 2018 11:00 AM
To: Jennings, Susan <Jennings.Susan@epa.gov>
Subject: FW: FDA Input on Tolerance Decisions for Oxytetracycline and Streptomycin - Revised FDA response

Hi Susan,
Did you see the attached edited letter that does not reference CDER at all? We are hoping that this will work for you now, B5

Thanks,
Heather

From: Harbottle, Heather
Sent: Thursday, March 15, 2018 3:19 PM

To: 'Jennings, Susan' <Jennings.Susan@epa.gov>; Long, Charli <Charli.Long-Medrano@fda.hhs.gov>
Cc: Goodis, Michael <Goodis.Michael@epa.gov>; Gilbert, Jeffrey M <Jeff.Gilbert@fda.hhs.gov>; Giles-Parker, Cynthia <Giles-Parker.Cynthia@epa.gov>; Johnson, Hope <Johnson.Hope@epa.gov>
Subject: RE: FDA Input on Tolerance Decisions for Oxytetracycline and Streptomycin - Revised FDA response

Dear Dr. Jennings,
Per your February 27, 2018 request, we have attached an edited response to your request letter. We hope this letter satisfies your request, B5 Please feel free to contact us with any further questions.

B5

https://www.fda.gov/downloads/AnimalVeterinary/GuidanceComplianceEnforcement/GuidanceforIndustry/UCM124674.pdf

We look forward to collaborating with you in the future in this respect and regarding the risk for the development of antimicrobial resistance.

Best regards,
Heather Harbottle

Heather Harbottle, Ph.D.
Microbiologist
Microbial Food Safety Team
Division of Human Food Safety
Office of New Animal Drug Evaluation
Center for Veterinary Medicine, FDA
240-402-0791

From: Jennings, Susan [mailto:Jennings.Susan@epa.gov]
Sent: Tuesday, February 27, 2018 3:42 PM
To: Long, Charli <Charli.Long-Medrano@fda.hhs.gov>
Cc: Goodis, Michael <Goodis.Michael@epa.gov>; Gilbert, Jeffrey M <Jeff.Gilbert@fda.hhs.gov>; Harbottle, Heather <Heather.Harbottle@fda.hhs.gov>; Giles-Parker, Cynthia <Giles-Parker.Cynthia@epa.gov>; Johnson, Hope <Johnson.Hope@epa.gov>
Subject: FDA Input on Tolerance Decisions for Oxytetracycline and Streptomycin

Dr. Long:

Thank you for allowing Drs. Jeffrey Gilbert and Heather Harbottle to collaborate with us on our registrations for new uses for antibiotic pesticides. They have provided valuable input into our draft decisions and analyses and, along with our colleagues at CDC and USDA, helped EPA's decision be more robust and balanced.

While working on these decisions, our legal counsel has suggested B5
B5
B5 EPA is required by the Federal Food, Drug and Cosmetic Act to consider this information when establishing tolerances on agricultural

commodities. The attached letter, signed by Michael Goodis (Director, Registration Division) provides more information and serves as the official request. If it all possible, we would appreciate receiving a response to this letter by March 7, 2018. If this is not possible, please let us know so that we can readjust our schedules accordingly.

Again, thank you for your time and consideration, as well as your division's continued collaboration on antibiotic pesticide activities.

Susan Jennings
Senior Advisor for Public Health
Office of Pesticide Programs
(706) 355-8574 (office)
(703) 216-8627 (cell)

From: Jennings, Susan <Jennings.Susan@epa.gov>
To: Harbottle, Heather
Sent: 3/9/2018 8:25:24 PM
Subject: RE: FDA Input on Tolerance Decisions for Oxytetracycline and Streptomycin

Can you call me? 706-425-9595. Thanks.

From: Harbottle, Heather [mailto:Heather.Harbottle@fda.hhs.gov]
Sent: Friday, March 09, 2018 3:17 PM
To: Jennings, Susan <Jennings.Susan@epa.gov>; Long, Charli <Charli.Long-Medrano@fda.hhs.gov>
Cc: Goodis, Michael <Goodis.Michael@epa.gov>; Gilbert, Jeffrey M <Jeff.Gilbert@fda.hhs.gov>; Giles-Parker, Cynthia <Giles-Parker.Cynthia@epa.gov>; Johnson, Hope <Johnson.Hope@epa.gov>; Luddy, Elizabeth A <Elizabeth.Luddy@fda.hhs.gov>
Subject: RE: FDA Input on Tolerance Decisions for Oxytetracycline and Streptomycin

Happy Friday Susan and all,
We have attached the signed letter of input you requested. Let us know if you need anything further!

Have a great weekend!

Best,
Heather

From: Jennings, Susan [mailto:Jennings.Susan@epa.gov]
Sent: Tuesday, February 27, 2018 3:42 PM
To: Long, Charli <Charli.Long-Medrano@fda.hhs.gov>
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Susan Jennings
Senior Advisor for Public Health

Office of Pesticide Programs
(706) 355-8574 (office)
(703) 216-8627 (cell)

From:	Johnson, Hope <Johnson.Hope@epa.gov>
To:	Sow, Fatima; Jennings, Susan; Kough, John; Collins, Samantha; Chandgoyal, Tara; Garvie, Heather; Giles-Parker, Cynthia; Carl Schultze; Julius Fajardo; Harbottle, Heather; Patel, Jean (CDC); Gilbert, Jeffrey M; Craig, Michael R (CDC); Rose Hammond
CC:	Cook, Colwell; Britton, Cathryn
Sent:	7/20/2017 12:18:01 PM
Subject:	RE: Federal interagency Antibiotic Resistance Call
Attachments:	Sec 3 grpfrt_tomato strep 152.pdf

The original streptomycin grapefruit/tomato 152 review is attached here. Previously only the addendum was attached. This is the complete document .

Hope A. Johnson
Product Manager 21
U.S. Environmental Protection Agency
Office of Pesticide Programs
Registration Division
Fungicide Branch
Phone: 703-305-5410
Mail Code 7505P

From: Sow, Fatima
Sent: Wednesday, July 19, 2017 4:49 PM
To: Jennings, Susan <Jennings.Susan@epa.gov>; Kough, John <Kough.John@epa.gov>; Collins, Samantha <collins.samantha@epa.gov>; Chandgoyal, Tara <Chandgoyal.Tara@epa.gov>; Garvie, Heather <Garvie.Heather@epa.gov>; Johnson, Hope <Johnson.Hope@epa.gov>; Giles-Parker, Cynthia <Giles-Parker.Cynthia@epa.gov>; Carl Schultze <Carl.P.Schulze@aphis.usda.gov>; Julius Fajardo <Julius.Fajardo@ARS.USDA.GOV>; Heather.Harbottle@fda.hhs.gov; Jean Patel <vzp4@cdc.gov>; Jeff.Gilbert@fda.hhs.gov; Michael Craig <bez7@cdc.gov>; Rose Hammond <Rose.Hammond@ARS.USDA.GOV>
Subject: RE: Federal interagency Antibiotic Resistance Call

Documents to be discussed are attached.

-----Original Appointment-----
From: Jennings, Susan
Sent: Monday, June 19, 2017 10:19 AM
To: Jennings, Susan; Kough, John; Collins, Samantha; Chandgoyal, Tara; Garvie, Heather; Johnson, Hope; Giles-Parker, Cynthia; Carl Schultze; Julius Fajardo; Heather.Harbottle@fda.hhs.gov; Jean Patel; Jeff.Gilbert@fda.hhs.gov; Michael Craig; Rose Hammond
Cc: Sow, Fatima
Subject: Federal interagency Antibiotic Resistance Call
When: Thursday, July 20, 2017 8:00 AM-10:00 AM (UTC-05:00) Eastern Time (US & Canada).
Where: Conference call # 8 B6

Documents to be discussed are attached to this invitation.

This is just a hold until we find a time that works for Federal Partners. Final meeting will be scheduled for 2 hours (but may be shorter).

From: Sow, Fatima <Sow.Fatima@epa.gov>
To: Jennings, Susan; Kough, John; Collins, Samantha; Chandgoyal, Tara; Garvie, Heather; Johnson, Hope; Giles-Parker, Cynthia; Carl Schultze; Julius Fajardo; Harbottle, Heather; Patel, Jean (CDC); Gilbert, Jeffrey M; Craig, Michael R (CDC); Rose Hammond
Sent: 7/19/2017 8:49:07 PM
Subject: RE: Federal interagency Antibiotic Resistance Call
Attachments: addendum to strep 152 grapefrt tomato.doc; Kasugamin Arysta 152 -07-03-2017.docx; Oxytetracycline 152 Fireline 17WP 07032017.doc; Streptomycin 152 Firewall 50WP 07032017 .doc

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From: Hill, Shaunta <Hill.Shaunta@epa.gov>
To: Harbottle, Heather; Patel, Jean (CDC); Craig, Michael R (CDC); Gilbert, Jeffrey M
Sent: 3/1/2016 9:21:57 PM
Subject: RE: Follow-up: Streptomycin and Oxytetracycline pesticide requests pending with EPA

Hello everyone,

That comment is relative to EPA's request for a written position from CDC and FDA that we could share with management.

I believe B5

B5

As time would be needed to provide such a memo, we would appreciate concurrence on the meeting minutes. (Assuming we have captured the thoughts/concerns correctly).

Notes from the meeting:

B5

B5 2. FDA's position to encourage judicious use of the antibiotics; 3. Increased detection of resistance mediated plasmids; etc.

Please let me know if you have additional questions.

Regards,
****

Shaunta Hill-Hammond, Ph. D.
Plant Pathologist
U.S. EPA: Office of Chemical Safety and Pollution Prevention
Registration Division/Fungicide Branch (PYS)
1200 Pennsylvania Avenue, NW (7505P)
Washington, DC 20460

Tel: 703.347.8961 | Fax: 703.305.6920
E-mail: hill.shaunta@epa.gov

From: Harbottle, Heather [mailto:Heather.Harbottle@fda.hhs.gov]
Sent: Tuesday, March 01, 2016 10:40 AM
To: Hill, Shaunta <Hill.Shaunta@epa.gov>; Patel, Jean (CDC) <vzp4@cdc.gov>; Craig, Michael R (CDC) <bez7@cdc.gov>; Gilbert, Jeffrey M <Jeff.Gilbert@fda.hhs.gov>
Subject: RE: Follow-up: Streptomycin and Oxytetracycline pesticide requests pending with EPA

Good Morning Shaunta, Jean, and Michael,

I've been reading over the minutes that Shaunta sent out and making comments to send back for inclusion. I noticed that there's a line item for FDA and CDC and wondered if I could get some clarification.

"CDC and FDA jointly will provide:

1. Position statement on the use of streptomycin as a pesticide"

Could you please clarify what you'd like us to send? Jean, Michael, have you yet addressed this?

Thanks,
Heather

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Sent: Thursday, February 25, 2016 1:38 PM
To: Patel, Jean (CDC); Craig, Michael R (CDC); Harbottle, Heather; Gilbert, Jeffrey M
Cc: Jennings, Susan; Kough, John; Chandgoyal, Tara; Hicks, Karen
Subject: Follow-up: Streptomycin and Oxytetracycline pesticide requests pending with EPA

Good Afternoon Everyone,
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B5

The proposed meeting times are:

- Tuesday – March 8, 9 am
- Thursday - March 10, 1 pm
- Wednesday – March 16, 1 pm

Thank you and enjoy the rest of your day.

Regards,
****

Shaunta Hill-Hammond, Ph. D.
Plant Pathologist
U.S. EPA: Office of Chemical Safety and Pollution Prevention
Registration Division/Fungicide Branch (PYS)
1200 Pennsylvania Avenue, NW (7505P)
Washington, DC 20460

Tel: 703.347.8961 | Fax: 703.305.6920

E-mail: hill.shaunta@epa.gov

Jean – could you please forward the materials to Ellen.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

DRAFT
MEMORANDUM **March 3, 2016**

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EPAREF2656-000412

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EPAREF2656-000413

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EPAREF2656-000414

Document properties

Author: cgrable
Company: EPA
Template: Normal.dotm
Page count: 2
Paragraph count: 85
Line count: 169
Word count: 1046
Character count (spaces excluded): 6088
Character count (spaces included): 7147

Document Comments
Total Comments: 6

Author: Harbottle, Heather
Date: 3/3/2016 10:20:00 AM
Initial: HH

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Author: Harbottle, Heather
Date: 3/3/2016 10:32:00 AM
Initial: HH

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Author: Harbottle, Heather
Date: 3/3/2016 10:29:00 AM
Initial: HH

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Author: Harbottle, Heather
Date: 3/3/2016 10:23:00 AM
Initial: HH
Range: Same comment at HH1
Scope: tetracyclines

Author: Harbottle, Heather
Date: 3/3/2016 10:32:00 AM
Initial: HH
Range: Same comment as HH2
Scope: acre

Author: Harbottle, Heather
Date: 3/3/2016 10:32:00 AM
Initial: HH
Range: Same comment as HH3
Scope: development

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

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MEMORANDUM **DRAFT March 3, 2016**

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EPAREF2656-000418

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EPAREF2656-000419

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EPAREF2656-000420

Document properties

Author: Hill, Shaunta
Company: US FDA
Template: Normal.dotm
Page count: 3
Paragraph count: 54
Line count: 168
Word count: 1230
Character count (spaces excluded): 7487
Character count (spaces included): 8767

Document Comments
Total Comments: 8

Author: Harbottle, Heather
Date: 3/3/2016 10:03:00 AM
Initial: HH

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Scope: interval

Author: Harbottle, Heather
Date: 3/3/2016 10:04:00 AM
Initial: HH

B5

Scope: 534

Author: Harbottle, Heather
Date: 3/3/2016 10:09:00 AM
Initial: HH

B5

Author: Harbottle, Heather
Date: 3/3/2016 10:14:00 AM
Initial: HH

B5

Scope: populations

Author: Harbottle, Heather
Date: 3/3/2016 10:15:00 AM
Initial: HH

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Scope: be

Author: Harbottle, Heather
Date: 3/3/2016 10:16:00 AM
Initial: HH

B5

Scope: species

Author: Harbottle, Heather
Date: 3/3/2016 10:16:00 AM
Initial: HH

B5

Author: Harbottle, Heather
Date: 3/3/2016 11:15:00 AM

Initial: HH

B5

Scope: populations

From: Hill, Shaunta <Hill.Shaunta@epa.gov>
To: Patel, Jean (CDC); Harbottle, Heather; Craig, Michael R (CDC); Gilbert, Jeffrey M
Sent: 3/2/2016 5:14:23 PM
Subject: RE: Follow-up: Streptomycin and Oxytetracycline pesticide requests pending with EPA

Hello Jean,
Your comments by Monday morning will be fine.
Thank you
-Shaunta

From: Patel, Jean (CDC/OID/NCEZID) [mailto:vzp4@cdc.gov]
Sent: Wednesday, March 02, 2016 12:11 PM
To: Hill, Shaunta <Hill.Shaunta@epa.gov>; Harbottle, Heather (FDA/CVM) <Heather.Harbottle@fda.hhs.gov>; Craig, Michael R. (CDC/OID/NCEZID) <bez7@cdc.gov>; Gilbert, Jeffrey M (FDA/CVM) <Jeff.Gilbert@fda.hhs.gov>
Subject: RE: Follow-up: Streptomycin and Oxytetracycline pesticide requests pending with EPA

Shaunta

Could I please send comments/edits on the notes by Monday, March 6th. I will send in the am.

Also, March 16th works best for me. I think for Michael as well, but will let him respond if not.

Thanks,

Jean

From: Hill, Shaunta [mailto:Hill.Shaunta@epa.gov]
Sent: Tuesday, March 01, 2016 4:22 PM
To: Harbottle, Heather (FDA/CVM) <Heather.Harbottle@fda.hhs.gov>; Patel, Jean (CDC/OID/NCEZID) <vzp4@cdc.gov>; Craig, Michael R. (CDC/OID/NCEZID) <bez7@cdc.gov>; Gilbert, Jeffrey M (FDA/CVM) <Jeff.Gilbert@fda.hhs.gov>
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B5

B5 ; 2. FDA's position to encourage judicious use of the antibiotics; 3. Increased detection of resistance mediated plasmids; etc.

Please let me know if you have additional questions.

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Tel: 703.347.8961 | Fax: 703.305.6920
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To: Hill, Shaunta
CC: Gilbert, Jeffrey M
Sent: 3/3/2016 7:03:04 PM
Subject: RE: Follow-up: Streptomycin and Oxytetracycline pesticide requests pending with EPA
Attachments: Meeting minutes_02102016_EPA-CDC-FDA_antibiotics.docx; Mitigation Measures _HLB citrus FL hh comments.docx; Section 18 citrus 152 review hh comments.docx

Thanks Shaunta!

I'll work with Jeff and our management toward an official statement from FDA for you. You did capture the sentiment below in your "notes from the meeting" section.

I have attached my notes on the telecom minutes, with which we concur. One major area that needed clarification was our concern for the potential for impact on the human intestinal flora. Do we have any idea if

B5

Please do email me with any questions or concerns. I have also attached your 152 assessment document and mitigations document with a few comments.

Thanks!
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Tel: 703.347.8961 1 Fax: 703.305.6920
E-mail: hill.shaunta@epa.gov

Jean – could you please forward the materials to Ellen.

From: Kough, John <Kough.John@epa.gov>
To: Harbottle, Heather
Sent: 3/7/2017 12:10:56 PM
Subject: RE: Initiation of a research project to address some data gaps

Heather,

I just want to confirm that I am interested in helping with the research project looking at use of agricultural antibiotics and selection pressures that presents. I know that Susan Jennings has already indicated our interest and just wanted to inform you directly. Look forward to more information and providing any feedback you may need.

John Kough
Senior Scientist
Biopesticides and Pollution Prevention Division
Office of Pesticide Programs
703-308-8267

From: Harbottle, Heather [mailto:Heather.Harbottle@fda.hhs.gov]
Sent: Thursday, March 02, 2017 12:07 PM
To: Conrath, Andrea B <Conrath.Andrea@epa.gov>; Maignan, Tawanda <Maignan.Tawanda@epa.gov>; Kough, John <Kough.John@epa.gov>; Jennings, Susan <Jennings.Susan@epa.gov>; Johnson, Marion <Johnson.Marion@epa.gov>; Chandgoyal, Tara <Chandgoyal.Tara@epa.gov>; Rose Hammond <Rose.Hammond@ARS.USDA.GOV>; Gilbert, Jeffrey M <Jeff.Gilbert@fda.hhs.gov>; Craig, Michael R (CDC) <bez7@cdc.gov>; Patel, Jean (CDC) <vzp4@cdc.gov>; Julius Fajardo <Julius.Fajardo@ARS.USDA.GOV>; Carl Schultze <Carl.P.Schulze@aphis.usda.gov>
Cc: Rosenblatt, Daniel <Rosenblatt.Dan@epa.gov>; Foley, Steven <Steven.Foley@fda.hhs.gov>
Subject: Initiation of a research project to address some data gaps

Hello everyone and Happy March,
I apologize for copying everyone on this email but thought that it would be the best way to identify the most appropriate individuals to participate/advise on the planning of a research project that may begin to fill some of the data gaps we identified in our meetings regarding the potential for antimicrobial resistance development (or current state of that resistance) in bacterial groups exposed to antimicrobials during plant agricultural treatments (citrus, apple, etc).

B5

Best,
Heather

From: Conrath, Andrea B [mailto:Conrath.Andrea@epa.gov]
Sent: Wednesday, January 11, 2017 6:57 PM
To: Maignan, Tawanda; Kough, John; Jennings, Susan; Johnson, Marion; Chandgoyal, Tara; Rose Hammond; Gilbert,

Jeffrey M; Craig, Michael R (CDC); Patel, Jean (CDC); Harbottle, Heather; Julius Fajardo; Carl Schultze
Cc: Rosenblatt, Daniel
Subject: RE: Resistance Monitoring Protocols from FL - Discussion
Importance: High

Hello all –

Thank you again for your participation in our discussion today. It was very helpful and informative!

I have attached my meeting notes of what was discussed. However, I may have missed, mis-stated, or misunderstood some of the discussion so I'd greatly appreciate you giving these a quick look and getting back to me with any additional comments or corrections.

In particular, I'd appreciate those from outside of EPA commenting on the last paragraph, on a discussion we had after the call ended about concentrations to be used for plating samples.

For your reference, I also attached the points for discussion from the meeting.

Our management is particularly interested in what transpired, so I'd appreciate your input at your earliest convenience (and more importantly, while it's still fresh in your minds!)

Thanks again, I look forward to hearing from you!

Andrea

new sig new cube no jpg

From: Harbottle, Heather </O=FDA/OU=FIRST ADMINISTRATIVE GROUP/CN=RECIPIENTS /CN=HHARBOTT>
To: Kough, John; Jennings, Susan (Jennings.Susan@epa.gov); Conrath, Andrea B (Conrath.Andrea@epa.gov)
CC: Foley, Steven
Sent: 3/7/2017 2:52:33 PM
Subject: RE: Initiation of a research project to address some data gaps

Thanks John, Susan, and Andrea! I've gotten some feedback from all 4 agencies so I'll try to set up a meeting for next week or soon after. Feel free to add in any other folks you'd like to have input. I'll send out some potential dates today or tomorrow.

Thanks,
Heather

From: Kough, John [mailto:Kough.John@epa.gov]
Sent: Tuesday, March 07, 2017 7:11 AM
To: Harbottle, Heather
Subject: RE: Initiation of a research project to address some data gaps

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B5

B5

I'd like to set up a telecom with interested parties from this group with Dr. Foley to begin the discussion and define project objectives. Please let me know if you or any of your colleagues would be the most appropriate folks to join the discussion/form a collaboration.

Best,
Heather

From: Conrath, Andrea B [mailto:Conrath.Andrea@epa.gov]
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To: Maignan, Tawanda; Kough, John; Jennings, Susan; Johnson, Marion; Chandgoyal, Tara; Rose Hammond; Gilbert, Jeffrey M; Craig, Michael R (CDC); Patel, Jean (CDC); Harbottle, Heather; Julius Fajardo; Carl Schultze
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Andrea

new sig new cube no jpg

From: Manupella, Matthew <Manupella.Matthew@epa.gov>
To: Jennings, Susan; Carl Schultze; Julius Fajardo; Harbottle, Heather; Patel, Jean (CDC); Gilbert, Jeffrey M; Craig, Michael R (CDC); Rose Hammond; Zinn, Nicole; Costello, Kevin; Garvie, Heather; Johnson, Hope; Collins, Samantha; Kaul, Monisha; Kough, John; Chandgoyal, Tara
CC: Giles-Parker, Cynthia; Cook, Colwell; Adeeb, Shanta; Smith, Charles; Sow, Fatima
Sent: 5/10/2018 12:34:39 PM
Subject: RE: Interagency Meeting on Antibiotic Resistance and Pesticides
Attachments: Antibiotics in Registration Review for Federal Parteners May 9.docx

Sorry this is a little last minute, but I've attached a summary for the registration review discussion.

I will bring copies.

Thanks,
Matt

-----Original Appointment-----
From: Jennings, Susan
Sent: Wednesday, May 9, 2018 6:05 PM
To: Jennings, Susan; Carl Schultze; Julius Fajardo; Heather.Harbottle@fda.hhs.gov; Jean Patel; Jeff.Gilbert@fda.hhs.gov; Michael Craig; Rose Hammond; Manupella, Matthew; Zinn, Nicole; Costello, Kevin; Garvie, Heather; Johnson, Hope; Collins, Samantha; Kaul, Monisha; Kough, John; Chandgoyal, Tara
Cc: Giles-Parker, Cynthia; Cook, Colwell; Adeeb, Shanta; Smith, Charles; Sow, Fatima
Subject: Interagency Meeting on Antibiotic Resistance and Pesticides
When: Thursday, May 10, 2018 9:30 AM-12:30 PM (UTC-05:00) Eastern Time (US & Canada).
Where: DCRoomPYS8100/Potomac-Yard-One

Having received no comments on the agenda, I guess it's ok. So for tomorrow, our agenda will be:

9:30	Update from CDC, FDA and USDA
10:00	Update from the Vancouver meeting (CDC)
10:20	Registration update on Registrations (RD)
10:40	Uses for Registration Review (PRD)
10:55	AR Reports, what changes in Registration Review in ARRT assessments (John Kough)
11:20	Mitigation options for Registration Review (PRD)
11:50	Next Steps (are we all ok w/ tabling the joint statement?)

#209

Guidance for Industry

The Judicious Use of Medically Important Antimicrobial Drugs in Food-Producing Animals

Submit comments on this guidance at any time. Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Room 1061, Rockville, MD 20852. Submit electronic comments on the guidance at http://www.regulations.gov. All written comments should be identified with the Docket No. FDA-2010-D-0094.

For further information regarding this document, contact William T. Flynn, Center for Veterinary Medicine (HFV-1), Food and Drug Administration, 7519 Standish Place, Rockville, MD 20855, 240-276-9084. E-mail: william.flynn@fda.hhs.gov.

Additional copies of this guidance document may be requested from the Communications Staff (HFV-12), Center for Veterinary Medicine, Food and Drug Administration, 7519 Standish Place, Rockville, MD 20855, and may be viewed on the Internet at either http://www.fda.gov/AnimalVeterinary/GuidanceComplianceEnforcement/GuidanceforIndustry/default.htm or http://www.regulations.gov.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Veterinary Medicine
April 13, 2012

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III. Key Reports and Peer-Reviewed Scientific Literature on the Issue 5

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VIII. Conclusion 22

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EPAREF2656-000436

The Judicious Use of Medically Important Antimicrobial Drugs in Food-Producing Animals

This guidance represents the Food and Drug Administration's (FDA) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the FDA staff responsible for implementing this guidance. If you cannot identify the appropriate FDA staff, call the number listed on the previous page of this guidance.

I. Executive Summary

Antimicrobial drugs have been widely used in human and veterinary medicine for more than 50 years, with tremendous benefits to both human and animal health. The development of resistance to this important class of drugs, and the resulting loss of their effectiveness as antimicrobial therapies, poses a serious public health threat. Misuse and overuse of antimicrobial drugs creates selective evolutionary pressure that enables antimicrobial resistant bacteria to increase in numbers more rapidly than antimicrobial susceptible bacteria and thus increases the opportunity for individuals to become infected by resistant bacteria. Because antimicrobial drug use contributes to the emergence of drug resistant organisms, these important drugs must be used judiciously in both animal and human medicine to slow the development of resistance. Efforts have been made to promote the judicious use of these drugs in humans (see http://www.cdc.gov/getsmart/index.html) as well as in animals (see http://www.avma.org/issues/default.asp). Using these drugs judiciously means that unnecessary or inappropriate use should be avoided. The focus of this document is on the use of medically important antimicrobial drugs[1] in food-producing animals. Based on a consideration of the available scientific information, FDA is providing a framework for the voluntary adoption of practices to ensure the appropriate or judicious use of medically important antimicrobial drugs in food-producing animals. This framework includes the principles of phasing in such measures as 1) limiting medically important antimicrobial drugs to uses in food-producing animals that are considered necessary for assuring animal health; and 2) limiting such drugs to uses in food-producing animals that include veterinary oversight or consultation. Developing strategies for reducing antimicrobial resistance is critically important for protecting both public and animal health. Collaboration involving the public, the public health, animal health, and animal agriculture communities on the development and implementation of such strategies is needed to assure that the public health is protected while also assuring that such strategies are feasible and that the health needs of animals are addressed.

[1] The term "medically important antimicrobial drugs" generally refers to antimicrobial drugs that are important for therapeutic use in humans.

EPAREF2656-000437

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word "should" in Agency guidances means that something is suggested or recommended, but not required.

II. Introduction

Antimicrobial resistance[2], and the resulting failure of antimicrobial therapies in humans, is a mounting public health problem of global significance. This phenomenon is driven by many factors including the use of antimicrobial drugs in both humans and animals. In regard to animal use, this document addresses the use of medically important antimicrobial drugs in food-producing animals for production or growth-enhancing purposes. These uses, referred to as production[3] uses throughout this document, are typically administered through the feed or water on a herd- or flock-wide basis and are approved for such uses as increasing rate of weight gain or improving feed efficiency. Unlike other uses of these drugs in animals (e.g., for the treatment, control, and prevention of disease), these "production uses" are not intended to manage a specific disease that may be ongoing or at risk of occurring, but rather are expressly indicated and used for the purpose of enhancing the production of animal-derived products (e.g., increasing rate of weight gain or improving feed efficiency). This document summarizes some of the key reports and scientific literature related to the use of antimicrobial drugs in animal agriculture and outlines FDA's current thinking on strategies for assuring that medically important antimicrobial drugs are used judiciously in food-producing animals in order to help minimize antimicrobial resistance development. In finalizing this guidance, FDA has considered comments that were submitted to the docket, and other relevant information. If you have additional relevant information, please submit it to the docket at any time. We are particularly interested in any new information regarding the use of medically important antimicrobials in food-producing animals and its impact on the development of drug-resistant bacteria.

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[2] The term "antimicrobial" refers broadly to drugs with activity against a variety of microorganisms including bacteria, viruses, fungi, and parasites. Antimicrobial drugs that have specific activity against bacteria are referred to as antibacterial or antibiotic drugs. However, the broader term "antimicrobial," commonly used in reference to drugs with activity against bacteria, is used in this document interchangeably with the terms antibacterial or antibiotic. Antimicrobial resistance is the ability of bacteria or other microbes to resist the effects of a drug. Antimicrobial resistance, as it relates to bacterial organisms, occurs when bacteria change in some way that reduces or eliminates the effectiveness of drugs, chemicals, or other agents designed to treat bacterial infections.

[3] Production uses are also referred to as "nontherapeutic" or "subtherapeutic" uses, terms that we believe lack sufficient clarity.

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III. Key Reports and Peer-Reviewed Scientific Literature on the Issue

Questions regarding the use of antimicrobial drugs in food-producing animals have been raised and debated for many years. A variety of recognized international, governmental, and professional organizations have studied the issue. We have briefly summarized below the findings and recommendations from some of the notable reports that have addressed this issue over the past 40 years. These reports provide context to FDA's current thinking on this issue, and highlight the longstanding concerns that have been the subject of discussion in the scientific community as a whole.

We have also provided a list below of some of the more recent primary scientific literature that FDA has considered. This is not intended to represent an exhaustive summary of the scientific literature, but rather to highlight some of the more recent scientific research related to the use of antimicrobial drugs in animal agriculture and the impact of such use on antimicrobial resistance. We acknowledge that a significant body of scientific information exists, including some information that may present equivocal findings or contrary views.

Unless otherwise indicated, the page numbers cited in this section refer to the relevant page numbers in the referenced report. A complete list of the reports summarized in this section is provided at Section IX of this document.

Reports Prepared by Various International, Governmental, and Professional Organizations

1969 Report of the Joint Committee on the Use of Antibiotics in Animal Husbandry and Veterinary Medicine

In July 1968, a Joint Committee was established in the United Kingdom to obtain information regarding the use of antibiotics in animal husbandry and veterinary medicine, particularly with respect to antibiotic resistance. This report, often referred to as the "Swann Report," was presented to Parliament in November 1969 by the Secretary of State for Social Services, the Secretary of State for Scotland, the Minister of Agriculture, Fisheries and Food, and the Secretary of State for Wales. The report concluded that the administration of antimicrobials to food-producing animals, particularly at subtherapeutic levels, poses a hazard to human and animal health.

The report stated, "It is clear that there has been a dramatic increase over the years in the numbers of strains of enteric bacteria of animal origin which show resistance to one or more antibiotics. Further, these resistant strains are able to transmit this resistance to other bacteria. This resistance has resulted from the use of antibiotics for growth promotion and other purposes in farm livestock" (*Ref. 1,* p. 60). The report also noted, "There is ample and incontrovertible evidence to show that man may commonly ingest enteric bacteria of animal origin" (*Ref. 1,* p. 60).

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The report provided a number of recommendations including that only antimicrobials which "have little or no application as therapeutic agents in man or animals and will not impair the efficacy of a prescribed therapeutic drug or drugs through the development of resistant strains of organisms" should be used without prescription in animal feed (*Ref. 1*, p. 61). Furthermore, the report concluded that antimicrobials used for therapeutic purposes in food-producing animals should remain available but only under veterinary supervision.

1970 FDA Task Force Report, "The Use of Antibiotics in Animal Feed"

In April 1970, FDA established a task force of scientists to undertake a comprehensive review of the use of antibiotics in animal feed *(Ref. 2)*. The task force included ten specialists on infectious diseases and animal science from FDA, the National Institutes of Health, the U.S. Department of Agriculture, and the Centers for Disease Control and Prevention, as well as five consultants from universities and industry.

This task force acknowledged that the understanding at the time it conducted its study was that the use of antimicrobials in food-producing animals, especially in subtherapeutic amounts, was associated with the development of resistant bacteria, and that treated animals might serve as a reservoir of antimicrobial-resistant pathogens that could produce human disease.

The recommendations of the Task Force included that antimicrobial drugs used in human clinical medicine that failed to meet certain guidelines established by the Task Force should be prohibited from growth promotion and any subtherapeutic use in food-producing animals by certain dates. Furthermore, those antimicrobials that failed to meet the guidelines should be limited to short-term therapeutic use and use only by a veterinarian or on a veterinarian's prescription.

As a consequence of the 1970 Task Force report, requirements for data to address microbiological safety concerns for subtherapeutic uses of antimicrobials in food-producing animals were outlined in the Code of Federal Regulations (21 CFR 558.15). Sponsors of antibiotic products administered in animal feed for subtherapeutic purposes were required to submit study results demonstrating that their product did not promote bacterial drug resistance. Depending on the class of drug, sponsors were required to submit all information to the agency on the impact of their drug on enteric salmonella in treated animals by specific dates.

1980 National Academy of Sciences Report, "The Effects on Human Health of Subtherapeutic Use of Antimicrobial Drugs in Animal Feeds"

In 1977, FDA proposed to withdraw the new animal drug approvals for subtherapeutic uses of penicillin and tetracyclines in animal feed on the ground that evidence showed that these drugs, when used for such purposes in animal feed, had not been shown to be safe. These two drugs were chosen because of their importance in human medicine. The proposal was criticized because, at that time, there was not adequate epidemiological evidence (or only just-emerging evidence) to show that drug-resistant

bacteria of animal origin were commonly transmitted to humans and caused serious illness. Subsequently, Congress directed FDA to conduct further studies related to the use of antimicrobials in animal feed and to hold in abeyance the implementation of the proposed antimicrobial withdrawal actions pending the outcome of these studies.

In accordance with Congress' directive to conduct further studies, FDA contracted with the National Academy of Science to conduct a study of the safety issues related to the use of antimicrobials in animal feed. In particular, FDA asked the National Academy of Science to: 1) study the human health effects of the subtherapeutic use of penicillin and tetracycline in animal feed; 2) review and analyze published and unpublished data relevant to assessing human health consequences of such use; 3) assess the scientific feasibility of additional epidemiological studies; and (4) make recommendations about additional research needed.

The National Academy of Sciences issued a study report in 1980. The study report concluded that a very limited amount of epidemiological research had been completed on either the subtherapeutic or therapeutic use of antimicrobials in animal feed. According to the study report, much of the information available on the subject involved "poorly controlled studies of small numbers of subjects for brief periods" (*Ref. 3*, p. 52). Based on a consideration of available evidence, the report concluded that existing data could neither prove nor disprove the postulated hazards to human health from subtherapeutic antimicrobial use in animal feed. However, the report cautioned that "The lack of data linking human illness with subtherapeutic levels of antimicrobials must not be equated with proof that the proposed hazards do not exist. The research necessary to establish and measure a definitive risk has not been conducted and, indeed, may not be possible" (*Ref. 3*, p. 53).

<u>1984 Seattle-King County Study: "Surveillance of the Flow of Salmonella and Campylobacter in a Community"</u>

As noted above, Congress directed FDA to hold in abeyance any implementation of the proposed withdrawal of new animal drug approvals for the subtherapeutic uses of penicillin and tetracyclines in animal feed, pending completion of additional studies related to the use of antimicrobials in animal feed. Therefore, in addition to the National Academy of Sciences study described above, the FDA also contracted with the Seattle-King County Health Department to complete a study intended to provide additional information regarding potential public health concerns regarding the use of antimicrobial drugs in animal feed. Under the contract, the Communicable Disease Control Section of the Seattle-King County Health Department was tasked with studying the relationship between the occurrence of Salmonella spp. (*Salmonella*) and Campylobacter jejuni (*C. jejuni*) in foods of animal origin and the occurrence of human illness caused by those two organisms. These two organisms, *Salmonella* and *C. jejuni*, were chosen to serve as models to estimate the flow of potentially pathogenic bacteria from animals to man through the food chain. The study involved a two-pronged surveillance system that included sampling of retail meats over a 20 month period and simultaneous investigation of *Salmonella* and *C. jejuni* enteritis cases in humans. Bacterial isolates from food and human cases were subjected to

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antibiotic susceptibility testing, plasmid analysis, and serotyping. In 1984, the Seattle-King County Health Department prepared a report summarizing the results of the study. The 1984 study report found that *C. jejuni* was a more common cause of enteritis than *Salmonella*. Also, it concluded that *C. jejuni* "does appear to flow from chickens to man via consumption of poultry products" (*Ref. 4*, p. 3). The report stated, "isolates from human cases and those from retail poultry had similar antibiotic susceptibility patterns, including prevalence of 29.7% and 32.8%, respectively, for tetracycline resistance, which was found to be plasmid-mediated" (*Ref. 4*, p. 3).

1988 Institute of Medicine (IOM) Report: "Human Health Risks with the Subtherapeutic Use of Penicillin or Tetracyclines in Animal Feed"

In 1987, FDA asked the IOM to conduct an independent review of the human health risks associated with the subtherapeutic use of penicillin and tetracycline in animal feed. IOM established a committee and directed it to perform "a quantitative risk assessment" of these human health consequences and to "assess the adequacy of the existing human health data and use such data to arrive at an estimate of risk" (*Ref. 5*, p. iii). If quantification of human health risks was not possible due to inadequate data, the Committee was to evaluate the scientific information that had become available since the 1980 National Academy of Science report cited above.

The Committee developed a risk-analysis model, using data only on *Salmonella* infections that resulted in human death. However, the Committee was unable to find a substantial body of direct evidence demonstrating that the subtherapeutic use of penicillin or tetracycline in animal feed posed a human health hazard. Nonetheless, the Committee's 1988 report found a considerable body of indirect evidence implicating both subtherapeutic and therapeutic use of antimicrobials as a potential human health hazard. The Committee also strongly recommended further study of the issue.

1997 World Health Organization (WHO) Report, "The Medical Impact of Antimicrobial Use in Food Animals"

In October 1997, the WHO convened a meeting of experts to examine the question of whether the use of antimicrobials in livestock production, including through use in animal feed, contributes to the escalation of antimicrobial resistance in humans. The findings of the meeting, which were summarized in a report, included the conclusion that all uses of antimicrobials lead to the selection of resistant forms of bacteria. Furthermore, the report stated that "low-level, long-term exposure to antimicrobials may have greater selective potential than short-term, full-dose therapeutic use" (*Ref. 6*, p. 5). The report found that the selection of resistant bacteria has adverse consequences for preventing and treating disease in humans, animals, and plants.

The WHO expert committee recommended that the use of antimicrobial drugs for growth promotion in animals be terminated if these drugs are also prescribed for use as anti-infective agents in human medicine or if they are known to induce cross-resistance to antimicrobials used for human medical therapy. The Committee also recommended the

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development of a systematic approach towards replacing growth-promoting antimicrobials with safer non-antimicrobial alternatives. The expert committee called for enhanced monitoring of resistance among isolates of enteric bacteria from food animals and food of animal origin. In addition, the Committee recommended managing risk at the primary production level through measures that promote the prudent use of antimicrobials, including enforcement of relevant laws pertaining to antimicrobial use, education for prescribers and producers, and requiring that use of antimicrobials for treatment of infections in animals be prescribed by veterinarians.

1999 National Research Council (NRC) Report: "The Use of Drugs in Food Animals – Benefits and Risks"

The Panel on Animal Health, Food Safety, and Public Health, jointly sponsored by the NRC's Board on Agriculture and IOM's Food and Nutrition Board, initiated a project to review the issues and relevant information regarding the use of drugs in food-producing animals and to make recommendations about such use. The panel convened the Committee on Drug Use in Food Animals to examine the benefits and risks associated with drug use in food-producing animals and to prepare a report and make recommendations.

The Committee's 1999 report included a review of the issues related to antibiotic use in food-producing animals and provided a number of recommendations. The report recommended establishing national databases to support scientific process and policy development for the approval and use of antibiotics in food-producing animals. The report also recommended that FDA use interdisciplinary panels of experts so that "further development and use of antibiotics in both human and animal medicine have oversight by an interdisciplinary panel of experts composed of representatives of the veterinary and animal health industry, the human medicine community, consumer advocacy groups, the animal production industry, and the regulatory agencies" (*Ref. 7*, p. 11).

1999 United States Government Accountability Office (GAO) Report – "Food Safety: The Agricultural Use of Antibiotics and Its Implications for Human Health"

In response to a request from Congress, the GAO initiated a study in May 1998 to examine: "1) how antibiotics are used in agriculture and the implications of that use for human health; 2) federal roles and responsibilities for overseeing the use of antibiotics in agriculture; and 3) issues surrounding the debate over whether to further regulate or restrict the use of antibiotics in agriculture" (*Ref. 8*, p. 1).

In its study report, dated April 1999, GAO concluded that although research has linked the use of antibiotics in agriculture to the emergence of resistant foodborne pathogens, "there are no current comprehensive estimates of the extent to which antibiotic-resistance strains have resulted in illness and deaths" (*Ref. 8*, p. 1). GAO concluded that the debate over whether antibiotic use should be restricted in agriculture centers on the risk antibiotics pose to human health relative to their benefits to agriculture. The GAO report recommended that "the departments of Agriculture and Health and Human Services work

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together to develop and implement a plan with specific goals, time frames and resources needed for determining the safe use of antibiotics in agriculture."

1999 European Commission Report, "Opinion of the Scientific Steering Committee on Antimicrobial Resistance"

Due to the public and animal health concerns associated with the increasing rate of antimicrobial resistance development, the European Commission, Directorate-General XXIV, asked that organization's Scientific Steering Committee to "scientifically evaluate the current position regarding the prevalence and development of antimicrobial resistance, examine its implications for human and animal health, particularly with regard to the development and management of infections" (*Ref. 9*, p. 7).

The Committee's report concluded that actions should be taken promptly to reduce the overall use of antimicrobials. Four primary recommendations were forwarded: (1) antimicrobial drugs should be used prudently; (2) infections should be prevented and resistant organisms contained; (3) research for new modalities of prevention and treatment of infections should be undertaken; and (4) the effects of such interventions should be monitored and evaluated.

2000 World Health Organization (WHO) Expert Consultation: "WHO Global Principles for the Containment of Antimicrobial Resistance in Animals Intended for Food"

The Food and Agriculture Organization of the United Nations (FAO) and the World Organization for Animal Health (OIE) participated in the June 2000 WHO expert consultation, the purpose of which was to develop global principles for minimizing the negative public health impact associated with the use of antimicrobial agents in food-producing animals while providing for their safe and effective use in veterinary medicine *(Ref. 10)*.

The principles were part of a comprehensive WHO global strategy for the containment of antimicrobial resistance and provided a framework of recommendations to reduce the overuse and misuse of antimicrobials in food-producing animals for the protection of human health. The principles strengthened and endorsed earlier WHO recommendations such as the need to terminate the use of antimicrobial growth promoters pending comprehensive human health safety evaluations, the need to ensure that all antimicrobials for animal use are only supplied through authorized outlets (e.g., by veterinary prescription), and the need to establish surveillance systems on antimicrobial drug consumption.

2003 Report, "Joint FAO/OIE/WHO Expert Workshop on Non-Human Antimicrobial Usage and Antimicrobial Resistance: Scientific assessment"

In December 2003, the Food and Agriculture Organization of the United Nations (FAO), the World Organization for Animal Health (OIE), and the World Health Organization (WHO) convened a workshop to "perform a scientific assessment of the antimicrobial resistance risks arising from non-human usage of antimicrobials and to

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formulate recommendations and options for future risk management actions to be considered by the Codex Alimentarius Commission (Codex) and OIE" (*Ref. 11*, p. 1).

The expert panel's findings from the workshop were documented in a report which contained a number of conclusions, including: 1) "there is clear evidence of adverse human health consequences due to resistant organisms resulting from non-human usage of antimicrobials;" 2) "the amount and pattern of non-human usage of antimicrobials impact the occurrence of resistant bacteria in animals and on food commodities and thereby human exposure to these resistant bacteria;" 3) "the foodborne route is the major transmission pathway for resistant bacteria and resistance genes from food animals to humans, but other routes of transmission exist;" and 4) the "consequences of antimicrobial resistance are particularly severe when pathogens are resistant to antimicrobials critically important in humans" (*Ref. 11*, p. 1).

The expert panel recommended that WHO appoint a group of experts to define which antimicrobials are considered critically important in humans. In addition, the panel commented on the need to further develop risk assessment approaches that adequately address the broad range of potential human health impacts and encouraged OIE to continue its work on risk analysis in coordination with FAO and WHO. Finally, the panel recommended that Codex collaborate with OIE to define a more efficient risk management system for addressing the risks.

2003 Institute of Medicine (IOM) Report, "Microbial Threats to Health: Emergence, Detection and Response"

The Committee on Emerging Microbial Threats to Health in the 21st Century was charged by the IOM to "review the current state of knowledge on the emergence of infectious diseases; assess the capacity of the United States to detect and respond to microbial threats to public health; and identify potential challenges and opportunities for public health actions, both global and domestic, to strengthen capabilities in prevention, detection, and response" (*Ref. 12*, p. 3).

The Committee's report discussed thirteen factors[4] that account for the emergence of new or enhanced microbial threats. The report noted "the convergence of any number of factors can create an environment where infectious diseases can emerge…" (*Ref. 12*, p. 4). In addition, the Committee provided a number of recommended actions for responding to the increasing infectious disease rates prompted by these emergence factors. One of the recommendations was to "more finely target the use of antimicrobials" including expanding efforts to decrease the inappropriate use of antimicrobials in human medicine (*Ref. 12*, p. 6). In addition, the committee recommended that "FDA ban the use of

[4] The thirteen factors included 1) microbial adaptation and change, 2) human vulnerability, 3) climate and weather, 4) changing ecosystems, 5) economic development and land use, 6) human demographics and behavior, 7) technology and industry, 8) international travel and commerce, 9) breakdown of public health measures, 10) poverty and social inequality, 11) war and famine, 12) lack of political will, and 13) intent to harm.

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antimicrobials for growth promotion in animals if those classes of antimicrobials are also used in humans" (*Ref. 12*, p. 15).

2004 Report, "Second Joint FAO/OIE/WHO Expert Workshop on Non-Human Antimicrobial Usage and Antimicrobial Resistance: Management Options"

As summarized above, a preliminary scientific assessment of the antimicrobial resistance risks arising from non-human usage of antimicrobials was conducted by the first Joint Expert Workshop on Non-Human Antimicrobial Usage in December 2003 in Geneva *(Ref. 13)*. The outcome of the first workshop, plus other relevant information, formed the basis for consideration by this second workshop. The report of this second workshop included suggestions to Codex, FAO, WHO, and OIE for moving forward on the issue.

Some of the key conclusions and recommendations in the report included: 1) the risks associated with non-human antimicrobial use and antimicrobial resistance should be part of human safety assessments for regulatory decisions relating to veterinary antimicrobials, 2) the concept of "critically-important" classes of antimicrobials for humans should be developed by WHO, 3) good agricultural practices can reduce the necessity for antimicrobials, 4) there is a need for capacity building and networking to help implement antimicrobial resistance surveillance systems in various countries, and 5) a Codex/OIE Task Force should be established to develop risk management options for antimicrobial resistance related to non-human use of antimicrobials.

2004 United States Government Accountability Office (GAO) Report – "Antibiotic Resistance: Federal Agencies Need to Better Focus Efforts to Address Risks to Humans from Antibiotic Use in Animals"

In response to a request from Congress, GAO initiated a study in May 2003 to "examine 1) scientific evidence on the transference of antibiotic resistance from animals to humans and extent of potential harm to human health, 2) agencies' efforts to assess and address these risks, 3) the types of data needed to support research on these risks and extent to which the agencies collect these data, 4) use of antibiotics in animals in the United States compared with its key agricultural trading partners and competitors, and 5) information on how use has affected trade" (*Ref. 14*, p. 3).

In its study report, dated April 2004, GAO concluded that antibiotic-resistant bacteria have been transferred from animals to humans. GAO also stated that many of the studies reviewed as part of GAO's research found that this transference from animals to humans poses significant risks for human health. According to GAO's findings, studies have shown two types of evidence related to the transfer of antibiotic-resistant bacteria from animals to humans. First, some studies have provided evidence of associations between changes in antibiotic use in animals and resistance to antibiotics in human bacteria. For example, researchers have found that antibiotic-resistant *Escherichia coli* (*E. coli*) and *Campylobacter* increased in humans as use of the antibiotics increased in animals.

Second, GAO concluded that studies that have examined the genetic makeup of the bacteria have provided stronger scientific evidence that antibiotic-resistant *Campylobacter*

and *Salmonella* bacteria are transferred from animals to humans. In those studies, strains of antibiotic-resistant bacteria infecting humans were indistinguishable from those found in animals, leading researchers to conclude that the animals were the source of human infection.

The GAO report noted that researchers disagree about the extent of the human health risk caused by this transference. According to the report, "many researchers contend that antibiotic use in animals poses significant risk for human health." The GAO report also noted that "a small number of studies contend that the health risks of the transference are minimal" (*Ref. 14*, p. 23).

GAO recommended that "the Commissioner of FDA expedite FDA's risk assessments of the antibiotics used in animals that the agency has identified as critically important to human health to determine if action is necessary to restrict or prohibit animal uses in order to safeguard human health" (*Ref. 14*, p. 48). GAO also recommended that the Secretaries of Agriculture and of Health and Human Services "jointly develop and implement a plan for collecting data on antibiotic use in animals..." (*Ref. 14*, p. 48).

The Department of Health and Human Services (HHS) reviewed and subsequently responded to the 2004 GAO Report on Antibiotic Resistance. In its response, HHS cited 11 additional supporting studies not included in the GAO report (See End Note)[i], and provided the following comments:

"The draft report presents or refers to significant and growing evidence demonstrating the human health consequences of drug resistant infections related to antibiotic use in agriculture." "These [11 additional] studies, along with those cited in the GAO report, all demonstrate a relationship between the use of antimicrobials in food-producing animals, antibiotic resistance in humans, and adverse human health consequences as a result. We believe that there is a preponderance of evidence that the use of antimicrobials in food-producing animals has adverse human consequences." "There is little evidence to the contrary."

<u>2005 Codex Alimentarius Commission (Codex), "Code of Practice to Minimize and Contain Antimicrobial Resistance" (Code of Practice)</u>

The Code of Practice provides guidance for the responsible and prudent use of antimicrobials in food-producing animals *(Ref. 15)*. Its objectives are to minimize adverse impacts on public health associated with the use of antimicrobial drugs in food-producing animals.

The Code of Practice makes a number of recommendations regarding the responsible use of antimicrobials in food-producing animals. For example, the document recommends that responsible use 1) should be controlled by the veterinary profession or other parties with the requisite expertise, and 2) does not include the use for growth promotion of veterinary antimicrobial drugs that belong to or are able to cause cross-resistance to classes

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of antimicrobial agents used in humans (or submitted for approval for use in humans) in the absence of an appropriate risk analysis.

2006 Antimicrobial Resistance: Implications for the Food System, Comprehensive Reviews in Food Science and Food Safety

This report was conducted under the auspices of the Institute of Food Technologists and the IFT foundation *(Ref. 16)*. The panelists found the extent to which antibiotic use in food animals produces clinically important antibiotic resistant infections in humans is unknown. However, they do state in their recommendations that "In veterinary medicine and production agriculture implementation of various management strategies (such as responsible use guidelines, quality assurance programs, and antibiotic alternatives), coupled with government regulations, should decrease opportunities for the selection of antibiotic resistant microorganisms." Specifically, they stated "Always practice prudent use of antimicrobials to limit resistance selection and to maintain maximal benefit of antimicrobials in the future."

2009 American Academy of Microbiology. Antibiotic Resistance: An Ecological Perspective on an Old Problem

This report emphasizes the ecological fact that antibiotic resistance is a natural phenomenon that cannot be eliminated *(Ref. 17)*. The practical approach is to find effective ways to cope with antibiotic resistant bacteria harmful to humans and animals and to control the development of new types of resistance. Controlling antibiotic-resistant bacteria and subsequent infections requires vigilance on many fronts. The prudent and responsible use of antibiotics and the elimination of unnecessary use (e.g., viral infections; unnecessary, prolonged treatment) are noted as mandatory steps to an appropriate public health strategy to limit infections by resistant organisms.

2011 WHO Report: Tackling antibiotic resistance from a food safety perspective in Europe

This report follows a long series of WHO reports addressing antibiotic resistance in the food chain *(Ref. 18)*. The WHO continues to highlight the urgent need for action in remediating antibiotic resistance through a holistic, intersectoral, and multifaceted approach that includes all efforts to reduce unnecessary use of antibiotics, including those uses in food production. Specific regulatory strategies include: 1) eliminating the use of antibiotics as growth promoters in food animals; 2) requiring that antibiotics be administered to animals only when prescribed by a veterinarian; and 3) requiring the antibiotics identified as critically important in human medicine - especially fluoroquinolones and third- and fourth-generation cephalosporins - only be used in food animals when their use is justified.

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Brief Summary of Recent Peer-Reviewed Scientific Literature

2008. Applied and Environmental Microbiology. Longitudinal study of antimicrobial resistance among *Escherichia coli* isolates from integrated multisite cohorts of humans and swine. Alali et al.

This study longitudinally examined the relationship between antimicrobial resistant *E. coli* from human wastewater and swine fecal samples and several risk factors including host species, production type, vocation (e.g., slaughter plant workers), and season. Authors reported that the higher levels of *E. coli* resistance in swine isolates as compared with human isolates was likely associated with either the past or current use of injectable antimicrobial agents (e.g., ceftiofur sodium) or the use of antimicrobial agents in feed (e.g., chlortetracycline) or water. Furthermore, slaughter plant workers were shown to be at higher risk of carrying multidrug-resistant *E. coli* than non-swine workers.

2008. Applied and Environmental Microbiology. Diversity and distribution of commensal fecal *Escherichia coli* bacteria in beef cattle administered selected subtherapeutic antimicrobials in a feedlot setting. Sharma et al.

This study investigated the influence of administration of chlortetracycline alone or in combination with sulfamethazine on the development of resistance, dissemination of defined strain types, and prevalence of resistance determinants in feedlot cattle *(Ref. 20)*. Shedding of tetracycline-resistant *E. coli* was higher in animals receiving both treatments. While tetracycline resistance was detected in cattle with no prior antimicrobial exposure, shedding of tetracycline-resistant *E. coli* was higher in animals subjected to either of the two treatments.

2008. Applied and Environmental Microbiology. Effect of subtherapeutic administration of antibiotics on the prevalence of antibiotic-resistant *Escherichia coli* bacteria in feedlot cattle. Alexander et al.

This study involved the collection of 3,300 fecal samples over a 314-day period from 300 feedlot steers receiving subtherapeutic levels of antibiotics *(Ref. 21)*. Study findings indicated that administration of tetracycline in combination with sulfamethazine clearly increased the prevalence of tetracycline- and ampicillin-resistant *E. coli* in cattle and the numbers of resistant *E. coli* organisms shed.

2009. American Journal of Veterinary Research. A metagenomic approach for determining prevalence of tetracycline resistance genes in the fecal flora of conventionally raised feedlot steers and feedlot steers raised without antimicrobials. Harvey et al.

This study compared the prevalence of tetracycline-resistance genes in the fecal flora of conventionally raised feedlot steers and feedlot steers raised without antimicrobials *(Ref. 22)*. Authors observed that the percentage of fecal samples with 11 tetracycline resistance genes was significantly higher for fecal samples from conventionally raised cattle (35/61 [57%]) than for fecal samples from antimicrobial-free cattle (16/61 [26%]).

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2009. Foodborne Pathogens and Disease. Association between tetracycline consumption and tetracycline resistance in *Escherichia coli* from healthy Danish slaughter pigs. Vieira et al.

The objective of this Danish study was to investigate the association between tetracycline-resistant *Escherichia coli* isolates from the intestinal tract of healthy pigs and patterns of tetracycline consumption in the herds of origin, together with other risk factors *(Ref. 23)*. The study showed that the larger the time since the last administration of tetracycline, the lower the likelihood of isolating a resistant *E. coli* .

2009. Preventive Veterinary Medicine. Associations between reported on-farm antimicrobial use practices and observed antimicrobial resistance in generic fecal *Escherichia coli* isolated from Alberta finishing swine farms. Varga et al.

This study used statistical models to evaluate the associations between various antimicrobial use practices and resistance to antimicrobials among generic fecal Escherichia coli isolated from Alberta finishing swine *(Ref. 24)*. In-feed antimicrobial use was significantly associated with an increased risk of resistance to ampicillin, chloramphenicol, streptomycin, and sulfisoxazole in *E. coli* isolates. Chlortetracycline use in grower rations was associated with ampicillin and tetracycline resistance.

2010. International Journal of Food Microbiology. Farm-to-fork characterization of *Escherichia coli* associated with feedlot cattle with a known history of antimicrobial use. Alexander et al.

This study investigated antimicrobial-resistant *Escherichia coli* isolated from cattle fed diets containing chlortetracycline plus sulfamethazine (AS700) *(Ref. 25)*. Compared to the control, in which no feed antibiotics were administered, the prevalence of ampicillin-resistant and tetracycline-resistant *E. coli* was three- and four-fold greater in feces from treated animals respectively, but was similar between treatments for animal hide samples.

2011. Environmental Health Perspectives. Lower prevalence of antibiotic-resistant Enterococci on U.S. conventional poultry farms that transitioned to organic practices. Sapkota et al.

This study compared antimicrobial resistance in enterococci recovered from conventional poultry farms using antibiotics with farms that transitioned to antibiotic-free production practices and had just received organic certification *(Ref. 26)*. Over 40% of *Enterococcus faecalis* isolates from conventional poultry houses were multidrug resistant, compared with 10% of isolates from newly organic poultry houses. In addition, 84% of *Enterococcus faecium* isolates from conventional poultry houses were multidrug resistant, compared with 17% of isolates from newly organic poultry houses.

2011. Foodborne Pathogens and Disease. Association between antimicrobial resistance in *Escherichia coli* isolates from food animals and blood stream isolates from humans in Europe: an ecological study. Vieira et al.

The authors analyzed the correlation between the prevalence of antimicrobial resistance in *E. coli* isolates from blood stream infections in humans and in *E. coli* isolates from poultry, pigs, and cattle in 11 countries between 2005 and 2008 *(Ref. 27)*. Resistance against multiple drugs in *E. coli* isolates from food animals (especially poultry and pigs) was highly correlated with resistance in isolates from humans.

2011. BMC Microbiology. Distribution and characterization of ampicillin- and tetracycline-resistant *Escherichia coli* from feedlot cattle fed subtherapeutic antimicrobials. Mirzaagha et al.

Authors characterized *E. coli* isolates recovered from cattle that either received no dietary antimicrobials or were intermittently administered subtherapeutic levels of chlortetracycline, chlortetracycline and sulfamethazine (SMX), or virginiamycin over a 9-month feeding period *(Ref. 28)*. This study showed that strains exhibited multidrug resistance to SMX and chloramphenicol (a drug not in the antibiotic regimen) more frequently when obtained from steers fed chlortetracycline plus sulfamethazine than from cattle treated with either chlortetracycline alone or with virginiamycin. Results further suggested that the administration of chlortetracycline, even in the absence of SMX, can lead to the emergence of resistance to SMX, as well as other antibiotics, including ampicillin and chloramphenicol.

2012. Proceedings of the National Academy of Sciences. In-feed antibiotic effects on the swine intestinal microbiome. Looft et al.

This study involved pigs raised in a highly controlled environment, with one group of littermates receiving a diet containing a growth-enhancing antibiotic combination product [chlortetracycline, sulfamethazine, and penicillin (known as ASP250)] and the other receiving the same diet without the antibiotics *(Ref. 29)*. Even a low, short-term (14-day) dose of in-feed antibiotics increased the prevalence and diversity of antibiotic resistance genes, including resistance to antibiotics not administered in the study, and increased the prevalence of *E. coli*.

IV. Strategies for Controlling Antimicrobial Resistance Are Needed

As summarized above in Section III, the public health concerns associated with the use of medically important antimicrobial drugs in food-producing animals have been the subject of scientific interest for the past 40 years. FDA has considered all available information and believes that the weight of scientific evidence supports the recommendations outlined in this guidance document.

To effectively respond to the public health concerns associated with antimicrobial resistance, FDA believes it is important to broadly consider how antimicrobial drugs are being used. The scientific community generally agrees that antimicrobial drug use is a key driver for the emergence of antimicrobial-resistant bacteria. It is imperative that strategies

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for controlling antimicrobial resistance include a consideration of how antimicrobial drugs are being used and measures to address those uses that are injudicious in nature.

V. Current Regulatory Framework

FDA considers the issue of antimicrobial resistance as part of its human food safety review related to new animal drugs used in food-producing animals. FDA considers an antimicrobial new animal drug to be "safe" if the agency concludes that there is "reasonable certainty of no harm to human health" from the proposed use of the drug in food-producing animals. This standard applies to safety evaluations completed prior to new animal drug approvals, as well as to those completed for drugs after approval. If this safety standard is not met before approval, the drug cannot be approved. If safety issues arise after approval, the Federal Food, Drug, and Cosmetic Act (the Act) provides grounds for withdrawal of approval of new animal drug applications for safety reasons. For example, section 512(e)(1)(B) of the Act provides for withdrawal of new animal drug application approvals when new evidence, along with evidence contained in the application, shows that the drug is not shown to be safe under the approved conditions of use. Under this provision, if FDA initiates a withdrawal action, it must produce evidence to show that there is a reasonable basis from which serious questions may be inferred about the ultimate safety of the drug and any substance that may be formed in or on food as a result of use of such drug under approved conditions. Once the agency meets this initial burden, the burden then shifts to the sponsor to demonstrate the safety of the drug (Docket no. 00N-1571, at p. 5, Mar. 16, 2004).

In 2003, FDA implemented new policies for evaluating antimicrobial resistance associated with use of antimicrobial new animal drugs in food-producing animals through the issuance of Guidance for Industry (GFI) #152, "Evaluating the Safety of Antimicrobial New Animal Drugs with Regard to their Microbiological Effects on Bacteria of Human Health Concern" (http://www.fda.gov/downloads/AnimalVeterinary/GuidanceComplianceEnforcement/GuidanceforIndustry/UCM052519.pdf). This guidance document describes a risk-based assessment process for evaluating antimicrobial resistance associated with the use of antimicrobial new animal drugs in food-producing animals. The guidance also recommends measures for mitigating such risk.

In general, FDA's GFI #152 is premised on the concept that increasing the exposure of bacterial populations to antimicrobial drugs increases the risk of generating resistance to those antimicrobial drugs. Pursuant to this principle, the administration of medically important antimicrobial drugs to entire herds or flocks of food-producing animals (e.g., for production purposes) would represent a use that poses a qualitatively higher risk to public health than the administration of such drugs to individual animals or targeted groups of animals (e.g., to prevent, control, or treat specific diseases). In addition to factors that impact the potential extent of use of the drug, the guidance also considers such factors as the properties of the drug in question including mechanism of action and mechanism of resistance, the prevalence of zoonotic foodborne bacteria in the food-producing animal species for which the drug is intended, and the importance of the drug in question as a therapy in humans. Risk mitigating

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factors that are considered include such limitations as restricting use of the drug to use by or on the order of a veterinarian.

Although FDA developed GFI #152 primarily to assess antimicrobial resistance risks as part of the new animal drug approval process, the underlying concept described above is also applicable to safety evaluations conducted for previously-approved antimicrobial new animal drugs. Therefore, FDA considers this same concept when it conducts safety evaluations for currently approved antimicrobial drugs, including those approved for use in animal feed.

From a practical standpoint, however, some significant differences exist between applying the GFI #152 risk assessment approach to the pre-approval process and applying it to safety reviews of currently-approved products. On the pre-approval side, the GFI #152 assessment process, including the various risk mitigation measures described, is taken into consideration by drug sponsors upstream in the drug development process and, in effect, steers product development in a direction that is most consistent with the guidance. On the post-approval side, FDA may examine certain currently-approved products to determine whether such products appear consistent with GFI #152. However, initiating action to withdraw an approved new animal drug application (NADA), in whole or in part, based on the results of a post-approval safety review would require the agency to make the showing required under section 512(e)(1) of the Act.

Alternatively, concerns associated with approved NADAs can sometimes be addressed through more informal processes. For example, in certain cases FDA has worked collaboratively with the sponsor of an NADA to address concerns raised regarding their product and has initiated steps to permit the sponsor to voluntarily withdraw part or all of the NADA or to revise the product labeling to address the concern. This alternative pathway can in some cases be an effective and expedient mechanism for resolving issues associated with an NADA.

VI. Status of FDA's Current Activities

In general, the antimicrobial new animal drug applications that FDA is addressing as part of its efforts to evaluate the public health concerns associated with the use of medically important antimicrobial drugs in food-producing animals can be divided into two broad categories: 1) those NADAs submitted after the issuance of GFI #152 in 2003 and for which FDA is assessing the microbiological safety of the new animal drug on a pre-approval basis using the principles outlined in GFI #152; and 2) those NADAs approved before the final version of GFI#152 was issued in 2003. In regard to the first category, FDA believes the approach outlined in GFI #152 for evaluating microbiological safety as part of the drug approval process has been very effective. As noted above, that assessment process and the associated risk mitigation measures are usually taken into consideration by industry during the drug development process. Thus, products that ultimately move forward toward approval are those products that include use conditions that are consistent with the guidance and are intended to minimize the extent to which product use would contribute to resistance development.

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FDA believes the approach outlined in GFI #152 is scientifically sound and is protective of the public health. FDA recognizes that the list of drugs in Appendix A is not static and should be periodically reassessed and updated as necessary. Such reassessment is necessary to take into consideration such factors as the development of new antimicrobials for human therapy, the emergence of diseases in humans, or changes in prescribing practices in the United States. FDA will update Appendix A, as necessary, through a separate process that will also be subject to public comment.

The second category of products are those antimicrobial NADAs that were approved prior to the implementation of GFI #152. Some of the products in this category include products that were approved for use in food-producing animals more than 30 years ago. Of particular concern, as discussed in section IV, are those products that are approved for use in animal feed for production or growth-enhancing purposes. Although these products are FDA-approved, their approval occurred prior to implementation of current processes for assessing safety with respect to antimicrobial resistance. Furthermore, the scientific understanding regarding antimicrobial resistance has advanced significantly over this time frame and, as discussed earlier in this document, a number of scientific reports have raised public health concerns regarding the use of medically important antimicrobials in food-producing animals.

As a result, FDA is examining available information regarding medically important antimicrobial drugs currently approved for use in food-producing animals and considering potential steps for agency action.

VII. Recommended Principles Regarding Judicious Use in Animals

The continued availability of effective antimicrobial drugs is critically important for combating infectious disease in both humans and animals. This includes the continued availability of feed and water uses of such drugs for managing disease in animal agriculture. Therefore, it is in the interest of both human and animal health that we take a more proactive approach to considering how antimicrobial drugs are being used, and take steps to assure that such uses are appropriate and necessary for maintaining the health of humans and animals. Using medically important antimicrobial drugs as judiciously as possible is key to minimizing resistance development and preserving the effectiveness of these drugs as therapies for humans and animals. Although FDA applauds the efforts to date by various veterinary and animal producer organizations to institute guidelines for the judicious use of antimicrobial drugs, the agency believes additional, voluntary steps are needed.

To further address this public and animal health concern, FDA is recommending two additional principles about the appropriate or judicious use of medically important antimicrobial drugs in food-producing animals. These principles are consistent with the recommendations of a number of recent scientific panels or committees referenced earlier in this document including the 1997, 2000, and 2011 reports of the WHO, the 2003 IOM Report, and the 2005 Codex Code of Practice.

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FDA recognizes the need to collaborate with the animal health and animal producer communities on strategies for minimizing animal health impacts or industry disruption that may be associated with the implementation of changes by animal drug sponsors to voluntarily align the use conditions of affected drug products with the principles outlined below. Furthermore, FDA intends to consult with the United States Department of Agriculture (USDA) on implementation strategies, including the development of a framework for veterinary oversight and consultation requirements. FDA is committed to assuring that the public health is protected while also assuring that the health needs of animals are addressed.

Principle 1: *The use of medically important antimicrobial drugs in food-producing animals should be limited to those uses that are considered necessary for assuring animal health.*

In light of the risk that antimicrobial resistance poses to public health, FDA believes the use of medically important antimicrobial drugs in food-producing animals for production purposes (e.g., to promote growth or improve feed efficiency) represents an injudicious use of these important drugs. Production uses are not directed at any specifically identified disease, but rather are expressly indicated and used for the purpose of enhancing the production of animal-derived products. In contrast, FDA considers uses that are associated with the treatment, control, or prevention[5] of specific diseases, including administration through feed or water, to be uses that are necessary for assuring the health of food-producing animals.

Some may have concerns that the use of medically important antimicrobial drugs in food-producing animals for disease prevention purposes is not an appropriate or judicious use. However, FDA believes that some indications for prevention use are necessary and judicious as long as such use includes professional veterinary involvement. Veterinary involvement in the decision-making process associated with the use of medically important antimicrobial drugs is an important aspect of assuring appropriate use, including judicious prevention use. When determining the appropriateness of a prevention use, veterinarians consider several important factors such as determining the medical rationale for such use, and that such use is appropriately targeted at a specific etiologic agent and appropriately timed relative to the disease. For example, if a veterinarian determines, based on the client's production practices and herd health history, that cattle being transported or otherwise stressed are more likely to develop a certain bacterial infection, preventively treating these cattle with an antimicrobial approved for prevention of that bacterial infection would be considered a judicious use. Another example would be the prevention of necrotic enteritis in broiler chickens. In this case, the prevention use of an antimicrobial is important to manage this disease in certain flocks in the face of concurrent coccidiosis, a significant parasitic disease in chickens. On the other hand, FDA would not consider the administration of a drug to apparently healthy animals in the absence of any information

[5] Disease prevention involves the administration of an antimicrobial drug to animals, none of which are exhibiting clinical signs of disease, in a situation where disease is likely to occur if the drug is not administered.

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that such animals were at risk of a specific disease to be a judicious use. The decision to use a specific drug or combination drug is generally based on factors that veterinarians are uniquely qualified to consider, including the mode of antibacterial action, drug distribution in specific tissues, and the duration of effective drug levels at the site of infection.

Principle 2: *The use of medically important antimicrobial drugs in food-producing animals should be limited to those uses that include veterinary oversight or consultation.*

Most of the feed-use antimicrobial drugs are currently approved for over-the-counter use in food-producing animals for purposes that include the treatment, control, and prevention of disease as well as for production purposes (i.e., for growth promotion uses such as increased rate of weight gain). In addition to instituting voluntary measures that would limit use of medically important antimicrobial drugs in food-producing animals to uses that are considered necessary to assure the animals' health, FDA also believes it is important to phase-in the voluntary practice of including veterinary oversight or consultation in the use of these drugs. As noted above, FDA believes that this practice is an important mechanism for helping to assure appropriate use. Veterinarians can play a critical role in the diagnosis of disease and in the decision-making process related to instituting measures to treat, control, or prevent disease. FDA recognizes that the nature of veterinary involvement can vary due to numerous factors such as geographic location and animal production setting. In fact, there are limited numbers of large animal veterinarians, which can make consultation or oversight challenging in certain situations. For example, some animal disease events require immediate attention. In some cases, veterinarians may be directly diagnosing and administering therapies, while in other cases they are visiting and consulting with producers periodically to establish customized disease management protocols for that producer's herd or flock. Of key importance to FDA is the fact that, in both of these cases, the veterinarian is involved in the decision-making process regarding antimicrobial drug use. FDA recognizes that increasing veterinary involvement in the use of antimicrobial drugs has significant practical implications for animal producers, veterinary practitioners, and the veterinary profession as whole. Therefore, FDA is particularly interested in receiving comments on strategies for effectively promoting the voluntary adoption of such a change.

VIII. Conclusion

In order to minimize the development of antimicrobial resistance, FDA believes that it is important to ensure the judicious use of medically important antimicrobial drugs in animal agriculture. We recommend several steps to accomplish this including voluntary measures that would limit medically important antimicrobial drugs to uses in food-producing animals that are considered necessary for assuring animal health and that include veterinary oversight or consultation. Such limitations would reduce overall medically important antimicrobial drug use levels, thereby reducing antimicrobial resistance selection pressure, while still maintaining the availability of these drugs for appropriate use.

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End Note

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From: Jennings, Susan <Jennings.Susan@epa.gov>
To: Julius Fajardo; Patel, Jean (CDC); Schulze, Carl P - APHIS; Harbottle, Heather; Gilbert, Jeffrey M; Craig, Michael R (CDC); Hammond, Rose
Sent: 3/20/2018 2:48:24 PM
Subject: RE: Meeting?

Great, how about 9-12 (or so, maybe we can do it in 2 hours), on the 10th?

It seems that we can have at least one rep from each of the agencies.

From: Fajardo, Julius [mailto:Julius.Fajardo@ARS.USDA.GOV]
Sent: Monday, March 19, 2018 12:50 PM
To: Jennings, Susan <Jennings.Susan@epa.gov>; Patel, Jean (CDC/OID/NCEZID) <vzp4@cdc.gov>; Schulze, Carl P - APHIS <Carl.P.Schulze@aphis.usda.gov>; Harbottle, Heather (FDA/CVM) <Heather.Harbottle@fda.hhs.gov>; Gilbert, Jeffrey M (FDA/CVM) <Jeff.Gilbert@fda.hhs.gov>; Craig, Michael R. (CDC/OID/NCEZID) <bez7@cdc.gov>; Hammond, Rose <Rose.Hammond@ARS.USDA.GOV>
Subject: RE: Meeting?

Free on the 9th and the 10th (AM only). Thanks.

From: Jennings, Susan [mailto:Jennings.Susan@epa.gov]
Sent: Monday, March 19, 2018 12:16 PM
To: Patel, Jean (CDC/OID/NCEZID) <vzp4@cdc.gov>; Schulze, Carl P - APHIS <Carl.P.Schulze@aphis.usda.gov>; Fajardo, Julius <Julius.Fajardo@ARS.USDA.GOV>; Harbottle, Heather (FDA/CVM) <Heather.Harbottle@fda.hhs.gov>; Gilbert, Jeffrey M (FDA/CVM) <Jeff.Gilbert@fda.hhs.gov>; Craig, Michael R. (CDC/OID/NCEZID) <bez7@cdc.gov>; Hammond, Rose <Rose.Hammond@ARS.USDA.GOV>
Subject: RE: Meeting?

Perfect!! Glad to hear it.

Others??

From: Patel, Jean (CDC/OID/NCEZID) [mailto:vzp4@cdc.gov]
Sent: Monday, March 19, 2018 12:15 PM
To: Jennings, Susan <Jennings.Susan@epa.gov>; Carl Schultze <Carl.P.Schulze@aphis.usda.gov>; Julius Fajardo <Julius.Fajardo@ARS.USDA.GOV>; Harbottle, Heather (FDA/CVM) <Heather.Harbottle@fda.hhs.gov>; Gilbert, Jeffrey M (FDA/CVM) <Jeff.Gilbert@fda.hhs.gov>; Craig, Michael R. (CDC/OID/NCEZID) <bez7@cdc.gov>; Rose Hammond <Rose.Hammond@ARS.USDA.GOV>
Subject: RE: Meeting?

Susan – I will be in DC on the 8th and 9th for a meeting. The 10th might be best for me and I would stay an extra day.

From: Jennings, Susan [mailto:Jennings.Susan@epa.gov]
Sent: Monday, March 19, 2018 11:55 AM
To: Carl Schultze <Carl.P.Schulze@aphis.usda.gov>; Julius Fajardo <Julius.Fajardo@ARS.USDA.GOV>; Harbottle, Heather (FDA/CVM) <Heather.Harbottle@fda.hhs.gov>; Patel, Jean (CDC/OID/NCEZID) <vzp4@cdc.gov>; Gilbert, Jeffrey M (FDA/CVM) <Jeff.Gilbert@fda.hhs.gov>; Craig, Michael R. (CDC/OID /NCEZID) <bez7@cdc.gov>; Rose Hammond <Rose.Hammond@ARS.USDA.GOV>
Subject: Meeting?

Hi all,

We are about to start working on the registration review of streptomycin and oxytetracycline. As you may recall from our earlier meeting, this process is a review of existing labels and uses. Some uses that we've discussed include homeowner uses and application by air.

I will be travelling to DC the week of May 7th and was hoping that we might be able to have a face-to-face meeting on the 9th or 10th, at least for those of you who are in town? Maybe a half-day or a bit longer? We haven't met for a while and it would be a good chance to regroup and rethink our approach to these compounds, especially in light of what we have learned from the recent new uses.

Please let me know if you think you will be available.

Thanks,

Susan.

Susan Jennings
Senior Advisor for Public Health
Office of Pesticide Programs
(706) 355-8574 (office)
(703) 216-8627 (cell)

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From: Harbottle, Heather </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=55429E94C1CE44C4B031B4CFEE99A90F-HHARBOTT>
To: Jennings, Susan; Julius Fajardo; Patel, Jean (CDC); Schulze, Carl P - APHIS; Gilbert, Jeffrey M; Craig, Michael R (CDC); Hammond, Rose
Sent: 3/20/2018 2:58:43 PM
Subject: RE: Meeting?

Sure thing, just let us know where you'd like to meet. I can be there.

From: Jennings, Susan [mailto:Jennings.Susan@epa.gov]
Sent: Tuesday, March 20, 2018 10:48 AM
To: Julius Fajardo <Julius.Fajardo@ARS.USDA.GOV>; Patel, Jean (CDC) <vzp4@cdc.gov>; Schulze, Carl P - APHIS <Carl.P.Schulze@aphis.usda.gov>; Harbottle, Heather <Heather.Harbottle@fda.hhs.gov>; Gilbert, Jeffrey M <Jeff.Gilbert@fda.hhs.gov>; Craig, Michael R (CDC) <bez7@cdc.gov>; Hammond, Rose <Rose.Hammond@ARS.USDA.GOV>
Subject: RE: Meeting?

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To: Jennings, Susan <Jennings.Susan@epa.gov>; Patel, Jean (CDC/OID/NCEZID) <vzp4@cdc.gov>; Schulze, Carl P - APHIS <Carl.P.Schulze@aphis.usda.gov>; Harbottle, Heather (FDA/CVM) <Heather.Harbottle@fda.hhs.gov>; Gilbert, Jeffrey M (FDA/CVM) <Jeff.Gilbert@fda.hhs.gov>; Craig, Michael R. (CDC/OID/NCEZID) <bez7@cdc.gov>; Hammond, Rose <Rose.Hammond@ARS.USDA.GOV>
Subject: RE: Meeting?

Free on the 9th and the 10th (AM only). Thanks.

From: Jennings, Susan [mailto:Jennings.Susan@epa.gov]
Sent: Monday, March 19, 2018 12:16 PM
To: Patel, Jean (CDC/OID/NCEZID) <vzp4@cdc.gov>; Schulze, Carl P - APHIS <Carl.P.Schulze@aphis.usda.gov>; Fajardo, Julius <Julius.Fajardo@ARS.USDA.GOV>; Harbottle, Heather (FDA/CVM) <Heather.Harbottle@fda.hhs.gov>; Gilbert, Jeffrey M (FDA/CVM) <Jeff.Gilbert@fda.hhs.gov>; Craig, Michael R. (CDC/OID/NCEZID) <bez7@cdc.gov>; Hammond, Rose <Rose.Hammond@ARS.USDA.GOV>
Subject: RE: Meeting?

Perfect!! Glad to hear it.

Others??

From: Patel, Jean (CDC/OID/NCEZID) [mailto:vzp4@cdc.gov]
Sent: Monday, March 19, 2018 12:15 PM
To: Jennings, Susan <Jennings.Susan@epa.gov>; Carl Schultze <Carl.P.Schulze@aphis.usda.gov>; Julius Fajardo <Julius.Fajardo@ARS.USDA.GOV>; Harbottle, Heather (FDA/CVM) <Heather.Harbottle@fda.hhs.gov>; Gilbert, Jeffrey M (FDA/CVM) <Jeff.Gilbert@fda.hhs.gov>; Craig, Michael R. (CDC/OID/NCEZID) <bez7@cdc.gov>; Rose Hammond <Rose.Hammond@ARS.USDA.GOV>
Subject: RE: Meeting?

Susan – I will be in DC on the 8th and 9th for a meeting. The 10th might be best for me and I would stay an extra day.

From: Jennings, Susan [mailto:Jennings.Susan@epa.gov]
Sent: Monday, March 19, 2018 11:55 AM
To: Carl Schultze <Carl.P.Schulze@aphis.usda.gov>; Julius Fajardo <Julius.Fajardo@ARS.USDA.GOV>; Harbottle, Heather (FDA/CVM) <Heather.Harbottle@fda.hhs.gov>; Patel, Jean (CDC/OID/NCEZID) <vzp4@cdc.gov>; Gilbert, Jeffrey M (FDA/CVM) <Jeff.Gilbert@fda.hhs.gov>; Craig, Michael R. (CDC/OID /NCEZID) <bez7@cdc.gov>; Rose Hammond <Rose.Hammond@ARS.USDA.GOV>
Subject: Meeting?

Hi all,

We are about to start working on the registration review of streptomycin and oxytetracycline. As you may recall from our earlier meeting, this process is a review of existing labels and uses. Some uses that we've discussed include homeowner uses and application by air.

I will be travelling to DC the week of May 7th and was hoping that we might be able to have a face-to-face meeting on the 9th or 10th, at least for those of you who are in town? Maybe a half-day or a bit longer? We haven't met for a while and it would be a good chance to regroup and rethink our approach to these compounds, especially in light of what we have learned from the recent new uses.

Please let me know if you think you will be available.

Thanks,

Susan.

Susan Jennings
Senior Advisor for Public Health
Office of Pesticide Programs
(706) 355-8574 (office)
(703) 216-8627 (cell)

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From: Jennings, Susan <Jennings.Susan@epa.gov>
To: Harbottle, Heather
Sent: 4/16/2019 10:48:34 AM
Subject: RE: q about resistance

B5

B5 ?

B6

From: Harbottle, Heather <Heather.Harbottle@fda.hhs.gov>
Sent: Monday, April 15, 2019 3:41 PM
To: Jennings, Susan <Jennings.Susan@epa.gov>
Subject: RE: q about resistance

B6

B5

Let me know if any of this is not clear or if you'd like to talk more!
J H

From: Jennings, Susan <Jennings.Susan@epa.gov>
Sent: Monday, April 15, 2019 3:17 PM
To: Harbottle, Heather <Heather.Harbottle@fda.hhs.gov>
Subject: RE: q about resistance

Thanks. Here's the full proposal. B5

Looking forward to your thoughts,

Susan.

B6 ?)

From: Harbottle, Heather <Heather.Harbottle@fda.hhs.gov>
Sent: Monday, April 15, 2019 3:10 PM
To: Jennings, Susan <Jennings.Susan@epa.gov>
Subject: RE: q about resistance

Hi Susan,

B5

I'll help if I can!
J H

From: Jennings, Susan <Jennings.Susan@epa.gov>
Sent: Monday, April 15, 2019 1:06 PM
To: Harbottle, Heather <Heather.Harbottle@fda.hhs.gov>
Subject: q about resistance

Hi Heather,

B5

What do you think?

Thanks,

Susan.

Susan Jennings
Senior Advisor for Public Health
Office of Pesticide Programs
(706) 355-8574 (office)
(703) 216-8627 (cell)

From: Jennings, Susan <Jennings.Susan@epa.gov>
To: Harbottle, Heather
Sent: 4/15/2019 7:16:30 PM
Subject: RE: q about resistance
Attachments: S05-2019-0308 Borneman HLB MAC Propoposal 3_7_19_H.pdf

Thanks. B5

Looking forward to your thoughts,

Susan.

B6 ?)

From: Harbottle, Heather <Heather.Harbottle@fda.hhs.gov>
Sent: Monday, April 15, 2019 3:10 PM
To: Jennings, Susan <Jennings.Susan@epa.gov>
Subject: RE: q about resistance

Hi Susan,

B5

I'll help if I can!
J H

From: Jennings, Susan <Jennings.Susan@epa.gov>
Sent: Monday, April 15, 2019 1:06 PM
To: Harbottle, Heather <Heather.Harbottle@fda.hhs.gov>
Subject: q about resistance

Hi Heather,

B5

B5

What do you think?

Thanks,

Susan.

Susan Jennings
Senior Advisor for Public Health
Office of Pesticide Programs
(706) 355-8574 (office)
(703) 216-8627 (cell)

From: Harbottle, Heather </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=55429E94C1CE44C4B031B4CFEE99A90F-HHARBOTT>
To: Jennings, Susan
Sent: 4/17/2019 2:03:25 PM
Subject: RE: q about resistance

Hey Susan,

B5

Let me know if this is confusing, or if you'd like me to explain more!
J H

PS I really do hope CDC has B6

From: Jennings, Susan <Jennings.Susan@epa.gov>
Sent: Tuesday, April 16, 2019 6:49 AM
To: Harbottle, Heather <Heather.Harbottle@fda.hhs.gov>
Subject: RE: q about resistance

B5

B5 ?

B6

From: Harbottle, Heather <Heather.Harbottle@fda.hhs.gov>

Sent: Monday, April 15, 2019 3:41 PM
To: Jennings, Susan <Jennings.Susan@epa.gov>
Subject: RE: q about resistance

B6

B5

Let me know if any of this is not clear or if you'd like to talk more!
J H

From: Jennings, Susan <Jennings.Susan@epa.gov>
Sent: Monday, April 15, 2019 3:17 PM
To: Harbottle, Heather <Heather.Harbottle@fda.hhs.gov>
Subject: RE: q about resistance

Thanks. Here's the full proposal. B5

Looking forward to your thoughts,

Susan.

B6 ?)

From: Harbottle, Heather <Heather.Harbottle@fda.hhs.gov>
Sent: Monday, April 15, 2019 3:10 PM
To: Jennings, Susan <Jennings.Susan@epa.gov>
Subject: RE: q about resistance

Hi Susan,
That is interesting. B5

B5

B5

B5

I'll help if I can!
J H

From: Jennings, Susan <Jennings.Susan@epa.gov>
Sent: Monday, April 15, 2019 1:06 PM
To: Harbottle, Heather <Heather.Harbottle@fda.hhs.gov>
Subject: q about resistance

Hi Heather,

B5

B5

What do you think?

Thanks,

Susan.

Susan Jennings
Senior Advisor for Public Health
Office of Pesticide Programs
(706) 355-8574 (office)
(703) 216-8627 (cell)

From:	Conrath, Andrea B <Conrath.Andrea@epa.gov>
To:	Maignan, Tawanda; Kough, John; Jennings, Susan; Johnson, Marion; Chandgoyal, Tara; Rose Hammond; Gilbert, Jeffrey M; Craig, Michael R (CDC); Patel, Jean (CDC); Harbottle, Heather; Julius Fajardo; Carl Schultze
CC:	Rosenblatt, Daniel
Sent:	1/11/2017 11:57:10 PM
Subject:	RE: Resistance Monitoring Protocols from FL - Discussion
Importance:	High
Attachments:	EPA, FDA, CDC, and USDA AR discussion on FL protocols for AR monitoring.docx; Meeting Notes abc 1-11-17docx.docx

Hello all –

Thank you again for your participation in our discussion today. It was very helpful and informative!

I have attached my meeting notes of what was discussed. However, I may have missed, mis-stated, or misunderstood some of the discussion so I'd greatly appreciate you giving these a quick look and getting back to me with any additional comments or corrections.

In particular, I'd appreciate those from outside of EPA commenting on the last paragraph, on a discussion we had after the call ended about concentrations to be used for plating samples.

For your reference, I also attached the points for discussion from the meeting.

Our management is particularly interested in what transpired, so I'd appreciate your input at your earliest convenience (and more importantly, while it's still fresh in your minds!)

Thanks again, I look forward to hearing from you!

Andrea

Andrea B. Conrath
Biologist, Emergency Response Team
Registration Division ~ Office of Pesticide Programs
United States Environmental Protection Agency
Phone: 703.308.9356 Fax: 703.605.0781
conrath.andrea@epa.gov

Office & Courier:
S-7235, One Potomac Yard
2777 Crystal Drive
Arlington, VA 22202

Mailing Address:
USEPA – OPP (7505P)
1200 Pennsylvania Ave NW
Washington, DC 20004

Visit http://www.EPA.gov/pesticides/regulating/section18_training

From: Johnson, Hope <Johnson.Hope@epa.gov>
To: Jennings, Susan; Harbottle, Heather; Gilbert, Jeffrey M
CC: Giles-Parker, Cynthia; Garvie, Heather; Sow, Fatima
Sent: 2/13/2019 3:44:18 PM
Subject: RE: Streptomycin comment period for citrus

We received a high number of comments during the first comment period, including from CBD (the author of the article). We expect more to follow with this additional period.

Thanks,
Hope

Hope Johnson
Product Manager 21
Fungicide Branch
Office of Pesticide Programs
johnson.hope@epa.gov; 703-305-5410

From: Jennings, Susan
Sent: Wednesday, February 13, 2019 10:39 AM
To: Harbottle, Heather <Heather.Harbottle@fda.hhs.gov>; Gilbert, Jeffrey M <Jeff.Gilbert@fda.hhs.gov>
Cc: Giles-Parker, Cynthia <Giles-Parker.Cynthia@epa.gov>; Johnson, Hope <Johnson.Hope@epa.gov>; Garvie, Heather <Garvie.Heather@epa.gov>; Sow, Fatima <Sow.Fatima@epa.gov>
Subject: RE: Streptomycin comment period for citrus

Thanks, Heather. I haven't seen it, but maybe the others have.

From: Harbottle, Heather <Heather.Harbottle@fda.hhs.gov>
Sent: Wednesday, February 13, 2019 10:33 AM
To: Jennings, Susan <Jennings.Susan@epa.gov>; Gilbert, Jeffrey M <Jeff.Gilbert@fda.hhs.gov>
Subject: RE: Streptomycin comment period for citrus

Thanks Susan,
I was looking for the docket and came across this article. I'm sure you all have seen it. This writer did not hold back.
https://www.orlandosentinel.com/opinion/os-op-streptomycin-guest-column-20190109-story.html

Thanks,
H

From: Jennings, Susan <Jennings.Susan@epa.gov>
Sent: Wednesday, February 13, 2019 10:19 AM
To: Carl Schultze <Carl.P.Schulze@aphis.usda.gov>; Julius Fajardo <Julius.Fajardo@ARS.USDA.GOV>; Harbottle, Heather <Heather.Harbottle@fda.hhs.gov>; Patel, Jean (CDC) <vzp4@cdc.gov>; Gilbert, Jeffrey M <Jeff.Gilbert@fda.hhs.gov>; Craig, Michael R (CDC) <bez7@cdc.gov>; Rose Hammond <Rose.Hammond@ARS.USDA.GOV>; Tim Widmer <Tim.Widmer@ARS.USDA.GOV>
Subject: Streptomycin comment period for citrus

Hi All,

Because regulations.gov was down for a bit during the shutdown, we are reopening the docket for a 30-day comment period.

Hope all is well with you,

Susan.

From: Craig, Michael R. (CDC/OID/NCEZID) <bez7@cdc.gov>
To: 'Hill, Shaunta'; Patel, Jean (CDC); Harbottle, Heather; Gilbert, Jeffrey M; Wan, Ellen (CDC)
CC: 'Jennings, Susan'; 'Kough, John'; 'Chandgoyal, Tara'; 'Hicks, Karen'; 'Blackwell, Ian'
Sent: 3/15/2016 8:22:58 PM
Subject: RE: Teleconference Cancellation and EPA updates

We appreciate the update.

Thank you,
Michael

Sent with Good (www.good.com)

-----Original Message-----
From: Hill, Shaunta [Hill.Shaunta@epa.gov]
Sent: Tuesday, March 15, 2016 04:18 PM Eastern Standard Time
To: Patel, Jean (CDC/OID/NCEZID); Craig, Michael R. (CDC/OID/NCEZID); Harbottle, Heather (FDA/CVM); Gilbert, Jeffrey M (FDA/CVM); Wan, Ellen (CDC/OID/NCEZID)
Cc: Jennings, Susan; Kough, John; Chandgoyal, Tara; Hicks, Karen; Blackwell, Ian
Subject: Teleconference Cancellation and EPA updates

Good Afternoon Everyone-
First I would like to apologize for the delay in communicating details on the scheduled teleconference for tomorrow.
EPA hands have been busy working with the Section 18 – FL request, which has taken a number of turns since our initial discussion in February.
Instead of proceeding with the teleconference tomorrow, we thought we send an update email.

Status as of 3/15/16:

B5

B5

B5

Thank you for your continued assistance during this review process. We do appreciate it !

Have a great evening and I'll be in touch on the monitoring protocols soon.

Regards,
****

Shaunta Hill-Hammond, Ph. D.
Plant Pathologist
U.S. EPA: Office of Chemical Safety and Pollution Prevention
Registration Division/Fungicide Branch (PYS)
1200 Pennsylvania Avenue, NW (7505P)
Washington, DC 20460

Tel: 703.347.8961 | Fax: 703.305.6920
E-mail: hill.shaunta@epa.gov

From: Hammond, Rose <Rose.Hammond@ARS.USDA.GOV>
To: Jennings, Susan; Kough, John; Collins, Samantha; Chandgoyal, Tara; Schulze, Carl P - APHIS; Fajardo, Julius; Harbottle, Heather; Patel, Jean (CDC); Gilbert, Jeffrey M; Craig, Michael R (CDC)
CC: Giles-Parker, Cynthia; Garvie, Heather; Johnson, Hope
Sent: 7/5/2017 2:02:57 PM
Subject: RE: Trying to schedule the July interagency (time sensitive)

Dear Susan,

I am available all of those times.

Rose

Dr. Rosemarie W. Hammond, Research Plant Pathologist
USDA ARS NEA BARC Molecular Plant Pathology Laboratory
Building 004 Room 214 BARC-West
10300 Baltimore Avenue
Beltsville, MD 20705
(P) 301-504-5203 (Fax) 301-504-5449
rose.hammond@ars.usda.gov

From: Jennings, Susan [mailto:Jennings.Susan@epa.gov]
Sent: Wednesday, July 05, 2017 9:55 AM
To: Kough, John; Collins, Samantha; Chandgoyal, Tara; Schulze, Carl P - APHIS; Fajardo, Julius; Heather.Harbottle@fda.hhs.gov; Jean Patel; Jeff.Gilbert@fda.hhs.gov; Michael Craig; Hammond, Rose
Cc: Giles-Parker, Cynthia; Garvie, Heather; Johnson, Hope
Subject: Trying to schedule the July interagency (time sensitive)

Hello all,

Because of various scheduling conflicts, I am going to try again to schedule our interagency meeting to discuss the EPA assessments for streptomycin, kasugamycin, and oxytetracycline.

The only times that I could find are:

Tuesday morning, July 18 from
9 to 11
10 to 12
11 to 1

Wednesday morning, July 19, from:
9 to 11
10 to 12
11 – 1

Thursday, July 20, from 8-10.

I would really appreciate everyone's help in trying to make one of these times work for everyone.

If you each could fill respond to this email asap, I would be very appreciative.

Thanks,

Susan.

Susan Jennings
Senior Advisor for Public Health
Office of Pesticide Programs
(706) 355-8574 (office)
(703) 216-8627 (cell)

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From: Giles-Parker, Cynthia <Giles-Parker.Cynthia@epa.gov>
To: Jennings, Susan; Kough, John; Collins, Samantha; Chandgoyal, Tara; Carl Schultze; Julius Fajardo; Harbottle, Heather; Patel, Jean (CDC); Gilbert, Jeffrey M; Craig, Michael R (CDC); Rose Hammond
CC: Garvie, Heather; Johnson, Hope; Sow, Fatima
Sent: 7/5/2017 3:34:14 PM
Subject: RE: Trying to schedule the July interagency (time sensitive)

I can make myself available for the proposed dates and times. July 18th is probably the best date.

From: Jennings, Susan
Sent: Wednesday, July 05, 2017 9:55 AM
To: Kough, John <Kough.John@epa.gov>; Collins, Samantha <collins.samantha@epa.gov>; Chandgoyal, Tara <Chandgoyal.Tara@epa.gov>; Carl Schultze <Carl.P.Schulze@aphis.usda.gov>; Julius Fajardo <Julius.Fajardo@ARS.USDA.GOV>; Heather.Harbottle@fda.hhs.gov; Jean Patel <vzp4@cdc.gov>; Jeff.Gilbert@fda.hhs.gov; Michael Craig <bez7@cdc.gov>; Rose Hammond <Rose.Hammond@ARS.USDA.GOV>
Cc: Giles-Parker, Cynthia <Giles-Parker.Cynthia@epa.gov>; Garvie, Heather <Garvie.Heather@epa.gov>; Johnson, Hope <Johnson.Hope@epa.gov>
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Thanks,

Susan.

Susan Jennings
Senior Advisor for Public Health
Office of Pesticide Programs
(706) 355-8574 (office)

(703) 216-8627 (cell)

From: Harbottle, Heather </O=FDA/OU=FIRST ADMINISTRATIVE GROUP/CN=RECIPIENTS /CN=HHARBOTT>
To: Jennings, Susan; Gilbert, Jeffrey M
Sent: 7/6/2017 2:38:18 PM
Subject: RE: Trying to schedule the July interagency (time sensitive)

Hi Susan,
Sorry, I thought I had replied to this for both of us. Perhaps it never sent?

Jeff and I are both available for the times highlighted below. Sorry about that! Thanks for following up.

Best,
Heather

From: Jennings, Susan [mailto:Jennings.Susan@epa.gov]
Sent: Thursday, July 06, 2017 8:41 AM
To: Harbottle, Heather; Gilbert, Jeffrey M
Subject: FW: Trying to schedule the July interagency (time sensitive)

Heather,

Are you in this week? I need to schedule this today and I'm getting out of offices back from Jeff's email.

If I don't hear from either of you, I will just grab two times and you can pick.

Hope you enjoyed your time off.

Thanks,

Susan.

From: Jennings, Susan
Sent: Wednesday, July 05, 2017 9:55 AM
To: Kough, John <Kough.John@epa.gov>; Collins, Samantha <collins.samantha@epa.gov>; Chandgoyal, Tara <Chandgoyal.Tara@epa.gov>; Carl Schultze <Carl.P.Schulze@aphis.usda.gov>; Fajardo, Julius <Julius.Fajardo@ARS.USDA.GOV>; Heather.Harbottle@fda.hhs.gov; Jean Patel <vzp4@cdc.gov>; Jeff.Gilbert@fda.hhs.gov; Michael Craig <bez7@cdc.gov>; Rose Hammond <Rose.Hammond@ARS.USDA.GOV>
Cc: Giles-Parker, Cynthia <Giles-Parker.Cynthia@epa.gov>; Garvie, Heather <Garvie.Heather@epa.gov>; Johnson, Hope <Johnson.Hope@epa.gov>
Subject: Trying to schedule the July interagency (time sensitive)

Hello all,

Because of various scheduling conflicts, I am going to try again to schedule our interagency meeting to discuss the EPA assessments for streptomycin, kasugamycin, and oxytetracycline.

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- 9 to 11
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Thanks,

Susan.

Susan Jennings
Senior Advisor for Public Health
Office of Pesticide Programs
(706) 355-8574 (office)
(703) 216-8627 (cell)

From: Jennings, Susan <Jennings.Susan@epa.gov>
To: Carl Schultze; Julius Fajardo; Harbottle, Heather; Patel, Jean (CDC); Gilbert, Jeffrey M; Craig, Michael R (CDC); Rose Hammond; Tim Widmer; Chandgoyal, Tara; Collins, Samantha; Conde, Rosaura; Conrath, Andrea B; Cook, Colwell; Costello, Kevin; Garvie, Heather; Giles-Parker, Cynthia; Johnson, Hope; Kaul, Monisha; Koch, Erin; Kough, John; Maignan, Tawanda; Manupella, Matthew; Sow, Fatima; Zinn, Nicole
Sent: 5/9/2018 6:04:44 PM
Subject: Tomorrow's interagency meeting

Hello all,

Having received no comments on the agenda, I guess it's ok. So for tomorrow, our agenda will be:

9:00	Update from CDC, FDA and USDA
9:30	Update from the Vancouver meeting (CDC)
9:50	Registration update on Registrations (RD)
10:10	Uses for Registration Review (PRD)
10:25	AR Reports, what changes in Registration Review in ARRT assessments (John Kough)
10:50	Mitigation options for Registration Review (PRD)
11:15	Update from CDC on Azole Resistance Issue (CDC)

Here's a link on getting to PYS: https://www.epa.gov/aboutepa/visiting-epa-headquarters#tab-2 (the directions are at the bottom of the page.

When you get to the building, you will need an escort up, so please call me on my cell at 703-216-8627.

See you soon,

Susan.

Susan Jennings
Senior Advisor for Public Health
Office of Pesticide Programs
(706) 355-8574 (office)
(703) 216-8627 (cell)

OFFICE OF THE COMMISSIONER
(850) 617-7700

THE CAPITOL
400 SOUTH MONROE STREET
TALLAHASSEE, FLORIDA 32399-0800

FLORIDA DEPARTMENT OF AGRICULTURE AND CONSUMER SERVICES

COMMISSIONER ADAM H. PUTNAM

December 4, 2015

Debra Rate, Ph.D.
Acting Emergency Response Team Leader
U.S. Environmental Protection Agency
Office of Pesticide Programs (7505P)
Risk Integration, Minor Use and
Emergency Response Branch
Room S4900, One Potomac Yard
2777 Crystal Drive
Arlington, Virginia 22202

Dear Dr. Rate:

Enclosed is a FIFRA Section 18 specific exemption petition submitted on behalf of Florida Fruit and Vegetable Association (FFVA) for the use of FireWall™ 50 WP (streptomycin sulfate; EPA Reg. No. 80990-3), FireLine™ 17 WP (oxytetracycline hydrochloride; EPA Reg. No. 80990-1), and Mycoshield® (oxytetracycline calcium complex; EPA Reg. No. 55146-97) to control *Candidatus* Liberibacter asiaticus (*C*Las) bacterium in citrus.

Candidatus Liberibacter asiaticus, the bacterium causing citrus greening disease, has been documented in Florida citrus since 2005. Since its establishment, efforts to control the spread and progression of the disease have largely focused on removal of diseased trees, nutritional support, as well as rigorous efforts to control the Asian citrus psyllid, the vector for this disease. However, more recently, research efforts have shifted towards a focus on both ridding infected trees of the pathogen as well as slowing the progression of the disease through the use of antimicrobial agents.

The requested exemption stipulates that no more than 1.35 pounds streptomycin sulfate (2.07 pounds of FireWall) per acre per year and no more than 2.04 pounds oxytetracycline equivalent (potentially from FireLine and Mycoshield) per acre per year. Florida has over 388,000 acres of commercial citrus throughout the state. Additional details of the proposed use pattern are found within the narrative document of this petition.

The Department has reviewed and/or consulted with the affected agencies and determined that use of FireWall, FireLine and Mycoshield antimicrobials under the conditions of this proposed specific exemption will not pose a risk to endangered species (Department assessment to follow).

EPAREF2656-000487

Please send any correspondence on this request to: Mr. Charlie L. Clark, Environmental Administrator, Pesticide Registration Review Section, Bureau of Scientific Evaluation and Technical Assistance, Division of Agricultural Environmental Services, 3125 Conner Boulevard, Building #6, Tallahassee, Florida 32399-1650, Phone 850-617-7940, e-mail: Charlie.Clark@FreshFromFlorida.com.

Sincerely,

Adam H. Putnam
Commissioner of Agriculture

AHP/dd

Attachment

cc: Mr. Mike Joyner
Dr. Lisa Conti
Mr. Matt Joyner
Dr. Joseph Joyce
Mr. John Hoblick
Mr. Randy Dominy
Mr. Philip Beard
Dr. Fred Fishel
Mr. Daniel Botts
Mr. Michael Aerts
Dr. Michael Rogers
Dr. Harold Browning
Dr. Michelle S. Samuel-Foo
Mr. Anderson H. Rackley
Ms. Kelly Friend
Dr. Davis Daiker
Mr. Charlie Clark
Ms. Sarah Oglesby
Mr. Dale Dubberly
Mr. Neil Richmond
Ms. Jo Marie Cook
Ms. Patty Lucas
Mr. Tau Richardson
Mr. Tom Jerkins
Mr. Mark Trimmer
Mr. Bill Bewlay

EMERGENCY EXEMPTION REQUEST

(Specific Exemption)

FOR THE USE OF THE ANTIBIOTICS

FireWall™ 50WP Fungicide/Bactericide (streptomycin sulfate)

FireLine™ 17WP (oxytetracycline hydrochloride)

Mycoshield® (oxytetracycline calcium)

TO SUPPRESS

Huanglongbing (HLB) (*Candidatus* Liberibacter asiaticus)

and IMPROVE TREE HEALTH

ON

Citrus

IN FLORIDA

December 2, 2015

EPAREF2656-000490

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CONTACT PERSON(S) AND QUALIFIED EXPERTS(S) (166.20(a)(1))

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(ii) The contact people for matters relating to the technical aspects of this exemption:

For Florida, it has been agreed that questions relating to technical aspects in the field for this emergency exemption petition will work through the Florida Department of Agriculture and Consumer Services and the Emergency Response Team within EPA's OPP.

For other technical aspects related to this petition, the contact is:

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DESCRIPTION OF PESTICIDE REQUESTED (166.20(a)(2))

a. Common Chemical Names (Active Ingredients):

Streptomycin Sulfate, Oxytetracycline Hydrochloride and Oxytetracycline Calcium

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Trade Names and EPA Registration Numbers:

FireWall™ 50WP Fungicide/Bactericide
EPA Registration Number: 80990-4

FireLine™ 17WP Fungicide/Bactericide
EPA Registration Number: 80990-1

Mycoshield®
EPA Registration Number: 55146-97

Formulation:

All products are Wettable Powders

Percent Active Ingredient:

FireWall™ 50WP:	65.8% Streptomycin Sulfate (equivalent to 50% streptomycin)
FireLine™ 17WP:	18.3% Oxytetracycline Hydrochloride (equivalent to 17% oxytetracycline)
Mycoshield®:	31.5% Oxytetracycline Calcium Complex (equivalent to 17% oxytetracycline)

Manufacturers:

FireWall™ and FireLine™:	AgroSource, Inc.
Mycoshield®:	Nufarm Americas, Inc.

b. Additional labeling: see Appendix D (FireLine ™ and FireWall™) and Appendix E (Mycoshield®) for the proposed Section 18 labels.

DESCRIPTION OF PROPOSED USE (166.20(a)(3))

(i) Site to be Treated:

Rationale for Multiple Active Ingredient Products:

The Citrus Research and Development Foundation, Inc., (CRDF), a Florida based independent grower research support organization was created and funded by grower assessments to guide the search for solutions to the recently introduced disease/vector complex Huanglongbing disease/Asian citrus psyllid. This research effort has proceeded across many fronts, one of which is the discovery and development of therapeutic treatments for infected trees. This program has directly participated in the funding of

projects with registrants of agricultural antibiotics to determine the role if any these compounds may provide in addressing this industry need. These projects were initiated over the past twenty-four months and have provided indications of value in maintaining the health and productive vigor in citrus trees that are infected with the pathogen.

Initial experimentation and experience gained in commercial citrus groves with this disease/complex suggests that multiple bactericide applications will be necessary in order to improve tree health and suppress the effects of Huanglongbing (HLB) disease season-long/year-round on infected citrus trees. The information developed independently by the two registrants in cooperation with the Citrus Research and Development Foundation over the past two years indicates a measure of suppression and overall increase in tree health in HLB-infected citrus trees. Each registrant developed their research package independently of the other's involvement and the resulting data indicates the three products have efficacy when used in a season long program targeted to the flush periods in citrus. The use patterns of the oxytetracycline products, while somewhat complementary, were not based on the same treatment regimes. This petition has attempted to consolidate use patterns across those treatment regimens and develop a package that would allow the flexibility of the treatments proposed in each individual package. It is important to note that the research program to refine and finalize final use patterns are on-going and will result in label expansion actions by each registrant. It must be recognized that while all of these products have activity on other citrus plant pathogens, the reason for this petition is the need for a therapeutic treatment to prolong the life and viability of trees infected with HLB.

Additionally, the further rationale supporting the use of multiple active ingredients for this particular Section 18 request include the following:

- The *Candidatus* Liberibacter asiaticus (*C*Las) bacterium is a difficult organism to work with, starting with the fact that this organism has never been successfully cultured in the laboratory. Its potential to develop resistance to antibacterial compounds applied for its control in the field is therefore unknown.

- Since *C*Las may develop resistance if treated with just a single bactericide product, an effective resistance management strategy must be part of any antibacterial HLB management program from the start.

- The heart of any effective resistance management strategy against *C*Las will be the use of at least two bacterial control agents, each having a unique mode of action against the pathogen.

- Based on their respective and unique modes of action, streptomycin sulfate is classified as a Group 25 fungicide; oxytetracycline is classified as a Group 41 fungicide according to the Fungicide Resistance Action Committee (FRAC).

- The use of streptomycin and oxytetracycline in alternation will thus minimize any selection pressure on *C*Las for development of resistance to either streptomycin or oxytetracycline.

- Since both streptomycin and oxytetracycline are individually efficacious against *C*Las in HLB-infected citrus, attacking the situation with these multiple products in rotation constitutes an effective resistance management program for HLB management and tree health improvement, thereby ensuring the long-term efficacy of these products against the *C*Las pathogen.

- This resistance management program should also help in preventing development of resistance in non-target bacteria as well.

All citrus (statewide) is the site to be treated. The proposed crop spectrum to be treated is slightly different for the two formulations of oxytetracycline. The FireLine™ label and FireWall ™ label covers all of the Citrus Crop Group 10, whereas the Mycoshield® label is proposing use on Orange, Crop Subgroup 10-10A and Grapefruit, Crop Subgroup 10-10C. According to the latest figures available from the 2015 Citrus Reference Book (Florida Agricultural Statistics Service Citrus Summary, 2013 – 2014; February 2015), in 2014 there was a total of 515,147 acres of Florida commercial citrus acreage (452,364 acres oranges, 45,922 acres grapefruit, and 16,861 acres specialty citrus). In a subsequent report (September 17, 2015), The National Agricultural Statistics Service reported 126,613 acres of abandoned or untended citrus acreage. This acreage would be deducted from the above number resulting in potentially treated acreage of 388,534 acres. See Appendix A for Florida counties and acreages in citrus.

(ii) <u>Method of Application</u>:

Ground application only.

(iii) <u>Rates of Application (in terms of a.i. and product)</u>:

FireWall™ 50WP
0.45 pounds active ingredient (a.i.) per acre per application
0.69 pounds of formulated FireWall™ 50WP per acre per application
FireLine™ 17WP
0.27 pounds of active ingredient (a.i.) per acre per application
1.5 pounds of formulated FireLine™ 17WP per acre per application
Mycoshield®
0.255 pounds of active ingredient (a.i.) (oxytetracycline base) per acre per application
1.5 pounds of formulated Mycoshield® per acre per application

Rates of application for Mycoshield® are based on reaching a 200 ppm oxytetracycline (1.5 pounds of formulated product in 150 gallons of water)

concentration in a finished spray volume necessary to fully cover the foliage of the tree to be treated. Spray volume and use rates per acre can be scaled downward in smaller trees depending on the amounts of spray volume to provide full coverage.

Maximum Number of Applications:

FireWall™ 50WP
A maximum of 3 applications per year is proposed, totaling no more than 2.07 pounds of formulated FireWall™ 50WP per acre per year (1.35 pounds active ingredient).
Allow a minimum of 21 days between applications.

Fireline™ 17WP
A maximum of 3 applications of this formulation per year is proposed, totaling no more than 4.5 pounds of formulated FireLine™ 17WP per acre per year (0.81 pounds active ingredient).
Allow a minimum of 21 days between applications.

Mycoshield®
A maximum of 8 applications per year is proposed, totaling no more than 12 pounds of formulated Mycoshield® per acre per year (2.04 pounds oxytetracycline base). Mycoshield® would be labeled to suppress infections of HLB in foliage with applications beginning two weeks after the initiation of a new leaf flush. Closer spray intervals are conducive to better performance but limit the ability to use the product on multiple flushes. Wider spray intervals and fewer applications on a given flush may not be as effective but allows for more applications on successive flushes, especially in young small frame citrus trees.

(iv) Total Acreage (or other units) to be Treated:

During 2013-14, approximately 515,147 acres of citrus were grown in Florida. Of this acreage 388,534 acres remain under commercial management.

(v) Total Amount of Pesticide to be Used (in terms of a.i. and product):

FireWall™ 50WP
In an absolute worst-case scenario, 804,265 pounds of formulated FireWall™ 50WP Fungicide/Bactericide, or 695,448 pounds of streptomycin sulfate, would be needed. (388,534 acres X 0.69 pounds of formulated FireWall™ 50WP X 3 applications = 1,066,354 pounds FireWall™ 50WP Fungicide/Bactericide; 388,534 acres X 0.45 lbs. a.i. X 3 applications = 524,520 lbs. a.i. streptomycin sulfate).

FireLine™ 17WP
At the maximum, 1,748,403 pounds of FireLine™ 17WP or 314,712 pounds of oxytetracycline hydrochloride, would be needed. (388,534 acres X 1.5 pounds of formulated FireLine™ 17WP X 3 applications = 1,748,403 pounds FireLine™ 17WP; 388,534 acres X 0.27 pounds a.i. X 3 applications = 314,712 pounds of oxytetracycline hydrochloride).

Mycoshield®
The total amount of Mycoshield® that could be used under the specific exemption assuming all trees are treated the maximum number of recommended applications would be a total of 4,662,408 pounds of formulated Mycoshield® or 762,309 pounds of oxytetracycline calcium. (388,534 acres X 1.5 pounds of Mycoshield® X 8 applications = 4,662,408 pounds of Mycoshield®; 388,534 acres X 0.255 pounds oxytetracycline base X 8 applications = 762,309 pounds of oxytetracycline base). While the use of Mycoshield® is limited to citrus crop subgroups 10 A and 10 C, the members of crop subgroup 10B (limes and lemons) represent less than 2,000 acres of production in Florida (less than 2,550 lbs of active ingredient.

Note Oxytetracycline Formulations:

Across the two formulations of oxytetracycline, the total amount of the active ingredient oxytetracycline that would be allowed under the proposed use patterns included in this petition is equivalent to the maximum amount of active ingredient that could be applied per individual acre of treated citrus under the proposed Mycoshield® Section 18 label plus the amount adjusted for the three applications on Citrus Subgroup B, which is allowed on the proposed FireLine™ 17 Section 18 label (0.81lbs X 2,000 Acres of lemons and limes = 1,620 lbs). This is (762,309 lbs. – (2,550 lbs. (5 applications at .255 lbs.)) = 759,759 lbs. of oxytetracycline. The use across the two formulated products (on Citrus Subgoups 10 A and 10 C) would be additive over the season and capped at the maximum level of active ingredient per acre of 2.04 lbs. of oxytetracycline for Citrus Subgroups A & C and 0.81lbs. on Citrus Subgroup B. <u>We would encourage the Agency in their decision document to clearly state that the maximum amount of oxytetracycline per acre per season is capped so that if growers choose to use both products they do not exceed the maximum per acre use allowed.</u>

While the amounts of product that could be needed is projected above; it is highly probable that not all of the eligible acreage will be treated, and a portion of the treated acreage will be treated at lower use rates than the maximum rate because of smaller canopy size in the younger age classes of

trees. This will result in less material being used than the numbers projected above.

(vi) <u>Use Season (period of time for which use of chemical is requested)</u>:

Access would be needed by February 1, 2016, to coincide and overlap with the typical spring foliage flush emergence. Availability subsequent to the date of approval is requested and crucial over the ensuing 12 months, especially when considering the continued infection rates and subsequent tree losses resulting from HLB disease.

FireWall™ 50WP
FireWall™ 50WP will be applied to all varieties and cultivars included in the Citrus Crop Group 10. Make an initial application at initiation of spring flush to suppress HLB titer and disease symptoms. Make a second application mid-summer (not less than 21 days after first application). Make a third application in late summer to reduce the incidence of HLB-induced fruit drop and to further suppress HLB titer and disease symptoms (not less than 21 days after second application). Spray to near runoff. Applications of FireWall™ 50WP should be rotated with another bactericidal product having a different mode of action, to reduce risks of selecting for streptomycin-resistant organisms.

FireLine™ 17WP
FireLine™ 17WP will be applied to all varieties and cultivars included in the Citrus Crop Group 10. Make an initial application at initiation of spring flush to suppress HLB titer and disease symptoms. Make a second application mid-summer (not less than 21 days after first application). Make a third application in late summer to reduce the incidence of HLB-induced fruit drop and to further suppress HLB titer and disease symptoms (not less than 21 days after second application). Spray to near runoff.

Mycoshield®
The recommendation is to make 3 to 4 applications to growth flushes in the spring and fall. Applications to the spring flush could be initiated in February through April depending on the citrus variety and the severity of the winter. It may take until the end of May to complete the entire application program on the spring flush. Fall flushes would consist of periods of new growth initiating after September 1st.

Foliar applications of these antibiotics are not expected to cure systemic infections of HLB in the branches, trunks or roots of a diseased tree. Application flexibility is needed so growers can target periods of disease

suppression and relief of associated symptoms that best fit their overall production program.

(vii) <u>Additional Restrictions, User Precautions and Requirements, Qualifications of Applicators, etc.</u>:

All active ingredients will be applied in accordance with the proposed Section 18 label and all applicable provisions of the Section 3 registered labels. Examples of various restrictions, requirements and qualifications include but are not limited to:

FireWall™ 50WP

- A total of three (3) applications of FireWall™ 50WP may be made at no less than 21 day intervals.
- Do not apply at less than 40 days prior to harvest.
- Do not apply through irrigation systems or by aircraft.
- Do not apply more than 2.07 pounds of formulated FireWall™ 50WP (1.35 pounds active ingredient) per acre.
- Personal protective equipment for applicators and handlers includes:
  - Long sleeved shirt
  - Long pants
  - Chemical resistant gloves made of a waterproof material
  - Shoes plus socks
  - Protective eyewear
  - MSHA/NIOSH approved dust/mist respirator with any N, R, P or HE filter.
- Worker re-entry into treated areas during the restricted entry interval of 12 hours is not allowed. For early entry to treated areas that is permitted under the Worker Protection Standard and that involves contact with anything that has been treated, such as plants, soil or water, wear:
  - Coveralls over long-sleeved shirt and long pants
  - Chemical-resistant gloves made of a waterproof material
  - Shoes plus socks
  - Protective eyewear.
- Do not apply directly to water, to areas where surface water is present or to intertidal areas below the mean high water mark.
- Do not contaminate water by cleaning of equipment or disposal of equipment washwater.

- The FireWall™ 50WP label contains a CAUTION statement of hazard and this product is considered to be a "General Use" pesticide. As a non-restricted pesticide, farmers without private applicator certification,

farmers with private applicator certification, and licensed commercial applicators are allowed to apply FireWall™ 50WP.

FireLine™ 17WP

- A total of three (3) applications of FireLine™ 17WP may be made at no less than 21 day intervals.
- Do not apply at less than 40 days prior to harvest.
- Do not apply through irrigation systems or by aircraft.
- Do not apply more than 4.5 pounds of formulated FireLine™ 17WP (0.81 pounds active ingredient) per acre.
- Personal protective equipment for applicators and handlers includes:
    - Long sleeved shirt and long pants
    - Chemical resistant gloves made of a waterproof material
    - Shoes plus socks
    - Protective eyewear
    - Dust/mist filtering respirator (MSHA/NIOSH approval number prefix TC -21C) or a NIOSH approved respirator with any N , R, P or HE filter.
- Worker re-entry into treated areas during the restricted entry interval of 12 hours is not allowed. For early entry to treated areas that is permitted under the Worker Protection Standard and that involves contact with anything that has been treated, such as plants, soil or water, wear:
    - Coveralls over long-sleeved shirt and long pants
    - Chemical-resistant gloves made of a waterproof material
    - Shoes plus socks
    - Protective eyewear.
- Do not apply directly to water, to areas where surface water is present or to intertidal areas below the mean high water mark.
- Do not contaminate water by cleaning of equipment or disposal of equipment washwater.
- The FireLine™ 17WP label contains a CAUTION statement of hazard and this product is considered to be a "General Use" pesticide. As a non-restricted pesticide, farmers without private applicator certification, farmers with private applicator certification, and licensed commercial applicators are allowed to apply FireLine™ 17WP.

Mycoshield®

- A total of eight (8) applications of Mycoshield® may be made at no less than 21 day intervals.
- Do not apply at less than 21 days prior to harvest.
- Do not apply through irrigation systems or by aircraft.

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- Do not apply more than 12.0 pounds of formulated Mycoshield® (2.04 pounds oxytetracycline base) per acre.
- Personal protective equipment for applicators and handlers includes:
- Long sleeved shirt.
- Long pants.
- Chemical resistant gloves made of a waterproof material.
- Shoes plus socks.
- Protective eyewear.
- Dust/Mist filtering respirator (MSHA/NIOSH approval number prefix TC-21C) or a NIOSH approved respirator with any N, R, P or HE filter.
- Worker re-entry into treated areas during the restricted entry interval of 12 hours is not allowed. For early entry to treated areas that is permitted under the Worker Protection Standard and that involves contact with anything that has been treated, such as plants, soil or water, wear:
    - Coveralls over long-sleeved shirt and long pants
    - Chemical-resistant gloves made of a waterproof material
    - Shoes plus socks
    - Protective eyewear.
- Do not apply directly to water, to areas where surface water is present or to intertidal areas below the mean high water mark.
- Do not contaminate water by cleaning of equipment or disposal of equipment washwater.
- The Mycoshield® label contains a WARNING statement of hazard and this product is considered to be a "General Use" pesticide. As a non-restricted pesticide, farmers without private applicator certification, farmers with private applicator certification and licensed commercial applicators are allowed to apply Mycoshield®.

Other specific use directions to be followed are found on the proposed Section 18 labels and the Section 3 labels found in Appendices D and E.

ALTERNATIVE METHODS OF CONTROL (166.20(a)(4)):

(i) Detailed Explanation of Why Currently Registered Pesticides Are Not Available in Adequate Supply and/or Are Not Effective to Control the Emergency:

The Huanglongbing (HLB) disease/vector complex and its impact on the industry have been rapidly increasing since the disease was first identified in Florida in August of 2005. The fact that HLB was on the U.S. Department of Homeland Security's Select Agent List made field work next to impossible until that status was modified. As experience with the disease has progressed, it has become apparent that managing the disease at levels that

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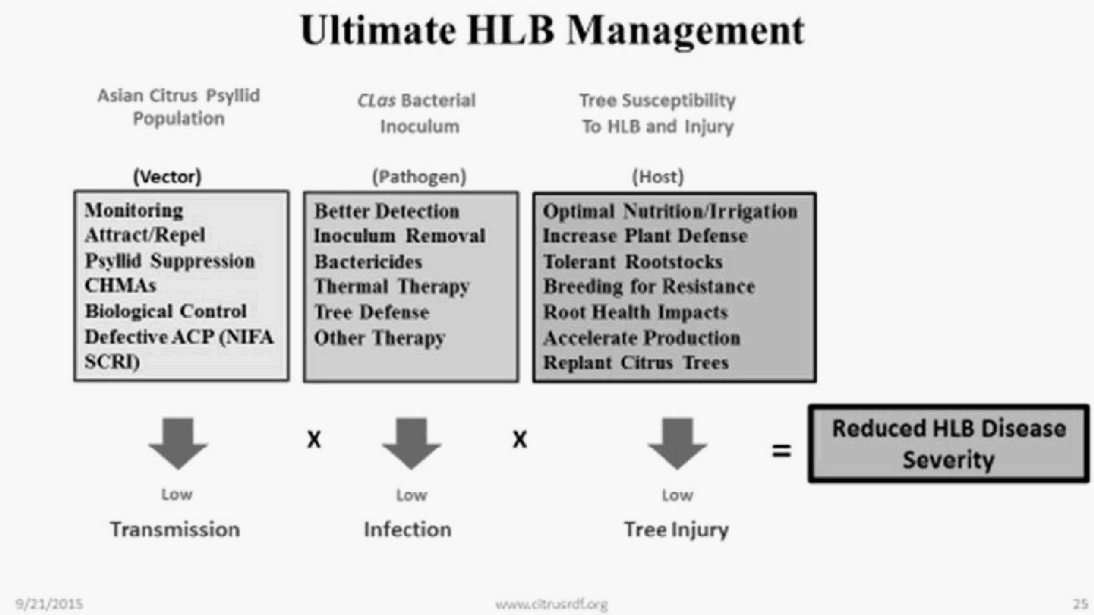
will allow continued commercial production in Florida depends on a multifaceted management strategy. This strategy includes the ability to replace non-productive trees with a realistic expectation that the newly planted replacement trees will have a reasonably productive life. Even with the complexities created by the lack of ability to culture the bacteria outside of the citrus vascular system and the digestive system of the insect, the industry has made significant strides in identifying the critical components of this management process.

From the beginning, there have been a range of approaches attempted to manage the devastation that HLB has caused to Florida citrus, and the pursuit of many parallel strategies continues. Challenges of managing HLB disease in Florida citrus are many and the application of tools that are available and emerging from research have yet to provide for a sustained leveling of disease impact or to restore tree health and productivity to trees infected with the pathogen. The graphic below highlights the breadth of effort underway in research to discover, test and deliver solutions to HLB, identifying the primary targets for intervention. Vector control, combined with therapy to reduce *C*Las titers (bacterial concentrations) in infected trees and ultimately, deployment of resistant or tolerant plant materials offers the balanced approach to disease management. Because of the absence of effective tools for bacterial therapy (the basis for this petition) and no proven plant resistance, the disease continues to impact all Florida growers and is discouraging the much-needed replanting to complement the current struggling tree inventory.



From the outset, it has been clear that vector control was tantamount to slow the spread of the disease, and many strategies were advanced to achieve this goal. Insecticidal suppression, biological control, attractants and repellants and other approaches have

been pursued, and as a result, Asian citrus psyllid (ACP) populations are well below initial levels. Similarly, as *C*Las infection spread and the numbers of infected trees grew, expansion of ACP control was necessary to protect new plants in existing groves and new plantings from becoming infected. Soil-applied neonicotinoid insecticides play a major role in protecting young trees during critical periods as they grow through the first 5 years, and these insecticides become more important as the disease reservoirs of inoculum and vector populations continue to expand. ACP suppression remains a critical component of HLB management with research and grower experience continuing to demonstrate the value of this segment of HLB management.

Florida citrus growers realized early that sustaining plant health through horticultural practices was an important response to onset and advancement of HLB disease. While trees possess considerable resilience in response to stresses, a chronically declining tree loses much of its resilience, and therefore must be managed more carefully. "Just-in-time inputs" or "spoon-feeding" trees showing advanced HLB symptoms with irrigation and fertilization can dampen limitations of compromised root systems, and cultural practices have been modified to more intensively manage tree health. In addition, plant growth regulators are being evaluated and used in an effort to assist in phloem regeneration and to limit pre-harvest fruit drop associated with HLB decline. Other cultural practices are being investigated to sustain health and productivity of infected trees and perhaps prolong productive life of these trees. Some of these same practices of intensive management are likewise being applied to newly planted trees to meet the goal of accelerating tree growth and maturity, thereby allowing for economic return to growers before HLB-induced tree decline commences. However, consistent success in this effort remains elusive.

Neither vector suppression nor cultural practices directly impact the bacterial pathogen, *C*Las, which is the target of the intervention proposed in this petition.

The goal of reducing *C*Las titer in infected trees has proven quite challenging, and relatively little progress has been made in this arena. The location of the pathogen within the plant's vascular system, difficulty of early detection of infection in citrus plants, and the inability of researchers to work with cultures of the bacteria *C*Las have limited development of *C*Las therapies to two strategies.

The first of these strategies is application of thermal therapy, where external heat is applied actively or passively to infected trees to differentially cause bacterial mortality in phloem tissues, while not harming the host plant tissues. The differential time versus temperature requirements to achieve this goal are being pursued through research and field experimentation on commercial farms.

The alternative to thermal therapy is the application of chemical therapy, wherein bactericidal chemicals are applied to trees to reduce *C*Las bacterial titer. This approach has been a priority focus for industry research efforts and extensive investment in evaluating efficacy, dose response, phytotoxicity and other parameters important to

development of a therapy tool. Chemical therapy encompasses a range of chemistries that correspond to various regulatory pathways, from conventional agricultural antibiotics to biopesticides to new active ingredients. Chemistries that fall within currently registered pesticides, 25(b) exempt list, or biopesticides offer the shorter term opportunities and these are being pursued aggressively while longer term new active ingredients are developed. Our strategy has focused most aggressively on agricultural antibiotics as these products offer an opportunity for label expansion from other U.S. crop uses as bactericides, and for which there is a broad pool of supporting data.

Processes in place to evaluate chemical therapy candidates include:

- A comprehensive laboratory bioassay system progressing from a high throughput surrogate bacterial assay to whole plant greenhouse assays;
- A range of field research spanning single plant initial trials to large scale commercial trials conducted in concert with registrants;
- Efficacy as a function of a.i., dose, timing, application method and disease intensity has been evaluated, as well as phytotoxicity, movement within the plant, and residues in plant parts.

Finally, several long-term lines of technology are being developed to identify and move the genetic components necessary to convey resistance into horticulturally important citrus cultivars. Field trials have been initiated to further investigate the potential for this to serve as a long-term means of restoring the viability of the industry. But, results are still expected to be years off.

All of this work in the state of Florida is being coordinated through the Citrus Research and Development Foundation (CRDF). This program of research to develop and deliver HLB solutions is also coordinated with existing national and international programs through USDA ARS, other research institutions, and, industry associations in Texas and California.

(ii) Alternative Control Practices:

Alternative *C*Las therapy/suppression practices are outlined above and are restricted at present to thermal therapy and chemical therapy. While there are other approaches mentioned above for vector or plant health management, none of these address reducing *C*Las titer in infected trees, and these tools are not likely to affect decline of infected trees.

Thermal therapy:

Some success has been observed with application of passive solar energy or active steam heat to young trees. These field demonstrations and trials have been evolving since the

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spring of 2014, when proof of concept was completed with solarization inside single-tree tents. Early attempts with both passive and active thermal treatment resulted in severe tree injury or actual tree death, leading to subsequent investigations to define time/temperature relationships and methods of delivery to achieve the differential thermal effects on bacteria while preventing tree injury. At present, all systems operating in the field to advance this approach are designed to treat individual trees up to a maximum height of about 3 meters. Results appear most predictable when trees are in early stage in infection and disease onset. While delivery systems and time/temperature characteristics are being resolved, predictability of response and expected duration of effects are in early stages of evaluation. Practical limitations of the number of trees that can be treated with thermal therapy and the expected outcomes in balancing bacterial titer reduction with increasing injury to leaves, limbs and fruit on treated trees are being evaluated in small-scale field trials in Florida. Research and commercialization funding is encouraging innovation to solve issues of practical application of this *C*Las suppression strategy, but progress is slow at present. It is anticipated that this approach will emerge on a commercial scale as a tool for managing early infection that will perhaps be limited to young (small) trees.

Chemical Therapy of *C*Las:

Chemical therapy of *C*Las is under intensive investigation in Florida citrus, with relatively few candidate materials advanced to commercial use or demonstrated effectiveness. The only antibiotics available for use in the agricultural sector include streptomycin, oxytetracycline and kasugamycin. Among the groups of chemistries under consideration, the bactericides labelled for use in other crops are the front-runners in terms of available data and performance testing in Florida citrus. These are the subjects for this Emergency Exemption petition.

Alternatives available for field use against *C*Las are few. *C*Las bioassay and field trials are being conducted on the biopesticides that are labelled for pest or disease control in citrus to determine how effective these materials might be under current field use patterns. Field research is ongoing, but results that could indicate a clear effect are not yet available. Optimism around these products exists but none of these materials are currently considered as demonstrable *C*Las therapy.

Other alternative chemistries that are being evaluated in Florida citrus for HLB suppression or tree health management include products based on plant essential oils. Some of these oils appear on the EPA 25(b) exempt list. Several products containing plant essential oils are available in Florida [e.g., Thymeguard (AgroResearch), and Ecotrol Plus (Keyplex®)]. These products are being field evaluated by growers to determine their impact on HLB through foliar application.

Field trials are underway to quantify the impact of these potential tools, but it is too early to have meaningful results. Similarly, field evaluations by Florida growers in conventional and organic citrus blocks have failed to demonstrate a measurable effect of these plant

essential oils. While these tools may complement the bactericides being considered in this petition, there is limited evidence for their effectiveness in reversing HLB.

EFFECTIVENESS OF USE PROPOSED UNDER SECTION 18 (166.20(a)(5)) (166.20(a)(5))

FireWall™ 50WP and FireLine™ 17WP

To assess the potential management of HLB disease, foliar applications of two bactericides, streptomycin sulfate and oxytetracycline hydrochloride were applied to commercially-grown grapefruit and oranges at 17 Florida field test locations in 2014 (year 1) and 2015 (year 2). Trials were located in the Indian River, the Central Ridge and the Peace River regions of Florida's citrus industry. Prior to treatment applications, all trees at each location were confirmed to test "positive" for HLB, based on PCR (polymerase chain reaction) analysis. Treatment effects for streptomycin and oxytetracycline applications were determined by quarterly DNA titer assays of the bacterium *Candidatus* Liberibacter asiaticus present in leaf samples collected from each treatment plot. In addition, multiple assessments of tree health were made, including improvement in tree canopy density (e.g. health), increased tree height and reductions in leaf drop, fruit drop, visual HLB symptoms, branch dieback and increases in fruit load in treated versus untreated trees. Foliar applications with streptomycin or oxytetracycline to grapefruit and orange trees in year-1 resulted in a statistically significant reduction ($p < 0.05$) in *C*Las titer, and this remained evident 4 to 5 months after the last application of streptomycin or oxytetracycline. In addition, significant improvements ($p < 0.05$) in leaf drop, fruit drop, visual HLB symptoms, and visual tree health, were noted in treated year-1 trees. Significant treatment effects ($p < 0.05$) were also recorded for these same parameters plus tree height in year-2. Results from these trials showed that foliar applications of streptomycin and oxytetracycline bactericides to commercially grown citrus significantly reduces titer for *C*Las in HLB-infected trees, and results in significant improvements to overall tree health. These field evaluations serve to illustrate that the reduction in *C*Las titer from the PCR results has correlation to healthier citrus trees in a production grove environment.

Mycoshield®

Mycoshield® oxytetracycline calcium complex was first registered in 1979 for control of fire blight (*Erwinia amylovora*) of pear and bacterial spot (*Xanthomonas arboricola* pv. *pruni*) of peach. Apple (fire blight) and nectarine (bacterial spot) were added to the label in later years. Oxytetracycline hydrochloride was first approved for agricultural use in 2004. EPA has determined that oxytetracycline calcium complex and oxytetracycline hydrochloride rapidly convert to oxytetracycline when added to water and "both OTC calcium complex and OTC-HCL will be mainly introduced into the environment as OTC." Thus, it was determined that environmental fate data for OTC calcium complex and OTC-

HCL are interchangeable. Disease control with the two forms is expected to be equivalent because the spray deposits would be oxytetracycline.

Oxytetracycline is produced naturally by *Streptomyces rimosus*. Commercial production of Mycoshield® is achieved by fermentation of the natural organism. This is followed by an extraction and concentration process to obtain a manufacturing concentrate that is used to make the final end product. OTC is a reversible bacteriostat that inhibits protein synthesis at the ribosome. Susceptible bacteria may resume development if the exposure period is inadequate for action by a secondary mortality factor such as senescence, attempted cell division, environmental stress or a host plant response.

Potted seedlings of various citrus cultivars were sprayed to run off with daily foliar applications of oxytetracycline at 100 ppm in a 1975 report (A. L. Martinez, 1975). A majority of the plants demonstrated partial recovery with obvious improvements in color and shoot production. However, none of the plants were completely cured. Injections of tetracycline to Sakkan orange and Fuju mandarin at 500 to 1000 ppm were effective at reducing disease symptoms and preserving higher yields in a 1991 article (K. Chung and W. Zhisheng, 1991). The trees were not cured and growth of the disease was evident one year later. Injection of tetracycline resulted in phytotoxic effects such as rotten tissue around the injection points and leaf drop. Oxytetracycline was not considered to be of value in the early stages of the Florida epidemic because of the inability to cure infected trees.

The following characteristics are required for bactericides to make definitive claims for direct suppressive activity on HLB and have practical utility for use in the field:

1. **Proven activity on *Liberibacter spp.* in culture**. It must inhibit *Candidatus* Liberbacter crescens, the closest cultured relative of *Candidatus* Liberibacter asiaticus, at low concentrations. Oxytetracycline strongly inhibits *Candidatus* Liberbacter crescens culture growth by more than 90 percent at a concentration of 0.54 µM, a level suitable for field use. Thus, it is believed that oxytetracycline can inhibit *Candidatus* Liberbacter asiaticus.

2. **Phloem mobility**. The chemical structure of oxytetracycline suggests that it can penetrate the phloem where the causal agent, *Candidatus* Liberibacter asiaticus, resides in the tree.

3. **Excellent crop safety**. Mycoshield® applied twice weekly to citrus at 1000 ppm for 12 weeks (24 total applications) did not cause noticeable injury in a 2013 field trial by the University of Florida's Dr. Eric Triplett (personal communication).

Zebra chip disease is caused by *Candidatus* Liberibacter solanacearum, a very close relative of *Candidatus* Liberbacter asiaticus. As in HLB disease, the *Liberibacter* pathogen resides in the phloem after having been vectored by a phloem-feeding insect (potato psyllid). Testing bactericides against zebra chip disease on tomato or potato generates

results much faster than can be obtained on citrus. Symptoms on tomato appear in 10 days but can take many months on citrus. Disease suppression through the use of an effective bactericide can be observed in less than three weeks in tomato but can take many months on citrus.

Zebra chip is not endemic to Florida, but laboratory and field research can be conducted in south Texas where the disease and potato psyllid are widely established. Dr. Erik Mirkov (Texas A&M AgriLife Research) has shown in laboratory studies that oxytetracycline effectively manages the symptoms of Zebra chip disease on tomato and dramatically reduces the number of bacteria residing in the plant (data in preparation for publication). Dr. Manuel Campos (Texas A&M AgriLife Research) conducted a field trial on potato in 2015. Five weekly applications of Mycoshield® at 200 ppm resulted in 13 percent infected tubers as compared to 90 percent in the untreated. This study demonstrated that oxytetracycline can reduce disease caused by a phloem-limited pathogen very closely related to *Candidatus* Liberbacter asiaticus.

Nufarm conducted experimental field trials in 2014 and 2015 (Better Crops, LLC, 2014 / 2015) evaluating the suppressive activity of Mycoshield® foliar sprays against HLB in Florida groves with HLB symptoms. This was a commercial grapefruit grove with 7 – 10 year old trees.

In 2014, the treatment list was based on anecdotal information suggesting that a combination of a bactericide with a strong penetrant (Pentra-Bark®) plus fertilizers would provide the best results. Unfortunately, the treatments with Pentra-Bark®/fertilizer combinations (with or without a bactericide) resulted in phytotoxic effects in the form of severe leaf and fruit drop. Although 2014 growth information was confounded by the crop injury, qPCR data demonstrated that oxytetracycline foliar applications suppressed the incidence of HLB infection in new growth. Samples of mature foliage collected prior to the initiation of the program revealed an infection incidence of 75 – 100 percent throughout the study area. Samples of mature foliage collected after the treatment program (4 applications at 3 week intervals) had the same incidence of infection.

However, samples of new foliage that was flushing during the treatment period showed that all Mycoshield® foliar treatments (treatments 6 – 12) only had an infection incidence of 25 – 50 percent. The untreated, fertilizer + Pentra-Bark® alone, Agri-Mycin® 17 streptomycin (with and without Pentra-Bark®) and Mycoshield® trunk spray had an infection incidence of 50 – 75 percent.

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Table 1: Mycoshield® HLB Foliar Suppression - Grapefruit - St. Lucie W 2014 Percent of Plots Positive for HLB / Old vs. New Foliage

Treatment	% Old Infect 7-27	% Old Infect 10-29	% New Infect 10-29
Untreated	75	75	75
Fertilizer (F) + Pentra-Bark® (P)	75	75	50
Agri-Mycin® Low Vol (AL)	100	100	50
AL + P	100	100	75
Mycoshield® + P Trunk	75	75	50
Mycoshield® Low Vol (ML)	100	100	25
ML + P	75	75	50
Mycoshield® High Vol (MH) + P	75	75	25
ML + F + P	100	100	25
MH + F + P	100	100	25
MH + RTREX Plus	100	100	25
MH + KeyPlex® 1400 DP	100	100	25

Antibiotic Foliar and Trunk Applications: 7-27, 8-15, 9-12, 10-11
Fertilizer Foliar Application: 7-27, 9-12
Fertilizer: 1 gal chelated iron + 5 lb. zinc sulfate + 5 lb. manganese sulfate / A
Agri-Mycin® 17 and Mycoshield® Low Vol: 1.5 lb. product in 100 GPA
Mycoshield® High Vol: 1.5 lb. product in 150 GPA
Mycoshield® Trunk: 1.5 lb. in 12.5 GPA @ approximately 8 oz./tree
Pentra-Bark®: Applied at 0.5% v/v foliar; 2.5% v/v trunk
Infection Incidence: % of plots testing positive for HLB based on PCR of old or young foliage

Table 2: Mycoshield® HLB Foliar Suppression - Grapefruit - St. Lucie W 2014 Percent of Tree Canopy a Contiguous Leaf Wall

Treatment	% leaf Wall Area 3-31-2015
Untreated	49 b
Fertilizer (F) + Pentra-Bark® (P)	48 b
Agri-Mycin® Low Vol (AL)	53 ab
AL + P	67 a
Mycoshield® + P Trunk	59 ab
Mycoshield® Low Vol (ML)	69 a
ML + P	67 a
Mycoshield® High Vol (MH) + P	71 a
ML + F + P	63 ab
MH + F + P	64 ab
MH + RTREX Plus	58 ab
MH + KeyPlex® 1400 DP	58 ab

Percent Leaf Wall: Visual assessment of canopy fullness averaged for 4 angles of perspective on each tree.

The 2014 study area recovered from the phytotoxicity and increased spring growth of the new canopy in 2015 was evident in all oxytetracycline foliar treatments relative to the untreated (9 – 22% denser canopy than the untreated). Several of the treatments were significantly superior to the untreated (5% probability level).

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Table 3: Mycoshield® HLB Foliar Suppression /Grapefruit - St. Lucie W 2015

Treatment	Vigor Rating 7-21-2015
Untreated	5.2 c
Mycoshield® + Pentra-Bark® Trunk	5.5 bc
Phostrol® 4.5pt/100 gal	5.5 bc
Mycoshield® LV	5.6 bc
Mycoshield® HV	6.8 abc
Mycoshield® + Phostrol® LV	6.3 abc
Mycoshield® + Tactic® 0.125% LV	6.7 abc
Mycoshield® + Tactic® 0.125% HV	6.2 abc
Mycoshield® + Tactic® 0.125% LV 4 appl*	6.8 abc
Mycoshield® + Dyne-Amic® 0.25% LV	5.7 bc
Mycoshield® + Dyne-Amic® 0.25% HV	6.2 abc
Mycoshield® + LI 700 0.25% LV	7.1 ab
Mycoshield® + LI 700 0.25% LV	7.7 a

Three applications to spring 2015 flush @ 2 week intervals
* A 4th application made 6 days after the 3rd
Mycoshield® Low Vol: 1.0 lb. product in 100 GPA
Phostrol® Low Vol: 4.5 pints in 100 GPA
Mycoshield® High Vol: 1.5 lb. product in 150 GPA
Mycoshield® Trunk: 1.5 lb. in 12.5 GPA @ approximately 8 ounces per tree
Pentra-Bark®: Applied at 0.5% v/v foliar; 2.5% v/v trunk
Tree Vigor Rating: 0 = dead; 10 = completely healthy growth

The 2015 grapefruit study was established on different trees. Application timing focused on periods of new growth flush in the spring, summer and fall. Periods of new growth are the optimal times for infection by *C*Las and it was expected that phloem penetration of oxytetracycline would occur at a greater concentration in newer foliage.
Many of the treatments involved the identification of additives that would improve performance without causing crop injury and the comparison of two spray volumes (100 and 150 gal/acre). Most treatments involved three applications at two week intervals initiated at a flush of new growth. Approximately six weeks after flush initiation, the foliage hardens, becomes less attractive to psyllid feeding and is less amenable to the penetration of oxytetracycline. One tank mix treatment of Mycoshield® + Tactic included a fourth spray applied six days after the third application. A trunk spray of Mycoshield® + Pentra-Bark® was added as a comparison with the foliar sprays which were applied to the point of runoff. Mid-season tree vigor ratings (0 – 10 scale) showed that all oxytetracycline foliar treatments were numerically higher than the untreated, trunk spray and Phostrol® alone. The mixture of Mycoshield® + LI 700 at 100 and 150 gal/acre was significantly superior to the untreated (5% probability level). Oxytetracycline degrades quicker at a neutral pH than under acidic conditions. LI 700 is an acidifying penetrating surfactant which may be stabilizing the applied residues and extending the period for leaf absorption.

Leaves were collected from selected treatments in the 2015 grapefruit trial and forwarded to Dr. Xiaoan Sun (Florida Department of Agriculture and Consumer Services,

Division of Plant Industry) for residue analysis. Dr. Sun uses a method that has a lower limit of quantification (1 ppm). Values lower than this may represent false detects. The analysis proved that oxytetracycline penetrated the foliage and was still detectable in the single treatment that was collected four days after application. As predicted the residues were higher in young leaves than old leaves. However, oxytetracycline was not found at the limit of quantification in leaves at 10 days after application. The grapefruit leaf residue analysis supports that the application needs to be less than 10 days to prevent HLB bacteria from recovering and resuming growth.

Table 4: Mycoshield® - Grapefruit Leaf Residues 2015

Treatment	Additive	# Appl	Last Appl	Sampled	Foliage Residues (ppm)	
					Mature	New
Untreated	none	0	NA	22 May	ND – all Reps	ND, 0.5
Mycoshield® Foliar 1.0 lb./100 GPA	none	3	12 May	22 May	ND – all Reps	ND, 0.5
Mycoshield® Foliar 1.5 lb./100 GPA	none	3	12 May	22 May	ND – all Reps	ND, 0.7
Phostrol® Foliar 4.5 pt./100 GPA	none	3	12 May	22 May	ND – all Reps	ND – all Reps
Mycoshield® + Phostrol® /100 GPA	none	3	12 May	22 May	ND – all Reps	ND – all Reps
Mycoshield® Foliar 1.0 lb./100 GPA	Tactic	3	12 May	22 May	ND – all Reps	ND – all Reps
Mycoshield® Foliar 1.0 lb./100 GPA	Tactic	4	18 May	22 May	1.4 ,0.9, 0.6, 0.8	2.9, 0.8, 1.6, 0.8
Mycoshield® Foliar 1.0 lb./100 GPA	LI 700	3	12 May	22 May	ND – all Reps	ND – all Reps
Mycoshield® Foliar 1.0 lb./100 GPA	Dyne-Amic®	3	12 May	22 May	ND – all Reps	ND – all Reps

Comparison of oxytetracycline residues in mature and new flush foliage collected from the same trees.
Residues determined by *Bacillus subtilis* bioassay.
Leaf samples collected by John Curtis, Better Crops, LLC.
Leaf analysis conducted by Dr. Xiaoan Sun, FDACS, Div. of Plant Industry.

Table 5: Mycoshield® - Orange Leaf Residues 2015

Treatment	Additive	# Appl	Last Appl	Sampled	Foliage Residues (ppm)	
					Mature	New
Untreated	none	0	NA	19 Aug	ND	ND
Untreated	none	0	NA	22 Aug	ND	ND
Mycoshield® Foliar 1.5 lb./150 GPA	none	1	18 Aug	19 Aug	3.2	7.3
Mycoshield® Foliar 1.5 lb./150 GPA	none	1	18 Aug	22Aug	ND	ND

Comparison of oxytetracycline residues in mature and new flush foliage collected from the same trees.
Residues determined by *Bacillus subtilis* bioassay.
Leaf samples collected by Henry Younce, KAC Agricultural Research, Inc.
Leaf analysis conducted by Dr. Xiaoan Sun, Florida Department of Agriculture and Consumer Services, Div. of Plant Industry

Similar results were obtained from a residue analysis of treated orange (Hamlin) foliage from another location. One day after application, the oxytetracycline residue concentration in new flush foliage was 7.3 ppm, which exceeded the concentration in mature leaves by more than 2X. At the orange site, residues were not detected in foliage at four days after application

Based on this information then, the following use instructions are proposed for the specific exemption:

- A use concentration of 200 ppm that provides disease suppression in field trials and is consistent with the current maximum use concentration on the Mycoshield® label.

- Full coverage foliar application to the point of run-off. Oxytetracycline residues are rapidly degraded and inactivated in the soil. High volume applications that result in the run-off of excess material would be of no performance value.

- Testing the crop safety of tank mixtures to avoid potential phytotoxicity issues.

- Targeting applications to periods of new leaf flushes. This is supported by disease suppression results, leaf residue analysis and the infection properties of HLB.

- Apply at 21 day intervals. Although there were distinct benefits with 2- and 3-week intervals in 2014 and 2015 field trials, there was room for improvement. As a bacteriostat, the activity of oxytetracycline is improved by extended intervals of exposure. Residues were not detected in foliage at 10 days after application in the grapefruit trial and at four days after application in the orange trial. Applications at 3 – 7 day can be made for labeled use for control of fire blight on apples and pears.

- Use in combination with an Asian citrus psyllid management programs recommended by local experts. Imperfect vector control and suppression of HLB would be complementary strategies.

- Studies (Xia, 2012) have shown that high summer temperatures reduce the HLB levels in infected trees and in the psyllid. Thus, this emergency exemption request recommends targeting spring and fall flushes with oxytetracycline applications when the greatest benefit is expected. The exception would be a grower that intends to use oxytetracycline in combination with vector control to delay the infection of newly planted trees. In this situation, all flushes would need to be targeted with both technologies. Additional research is needed to investigate the use of oxytetracycline in a preventative program and large treatment areas are needed to optimize the activity of the vector control component. The expanded treatment acreage allowed under this emergency exemption request will enable the investigation of large area HLB prevention programs.

DISCUSSION OF RESIDUES IN FOOD (166.20(a)(6)) (166.20(a)(6))

FireWall™ 50WP and FireLine™ 17WP

AgroSource, Inc. and the IR-4 Project have performed Magnitude of Residue studies for streptomycin sulfate and oxytetracycline in/on citrus commodities. Field residue studies have been conducted and this information has been submitted to the Agency or is being

submitted to the Agency. Dietary and drinking water exposure and risk assessment with the current crop uses plus citrus have been performed using DEEM-FCID version 4.02 and citrus residue data from recent citrus field studies treated with three foliar applications at the proposed Section 18 label rates of both streptomycin and oxytetracycline each application. Based on available information, a temporary streptomycin tolerance of 0.5 ppm and a temporary oxytetracycline tolerance of 0.1 ppm on citrus are proposed.

For the streptomycin dried pulp fraction, the proposed tolerance will be 3.5 ppm and for the oil and juice fractions the proposed tolerance is 0.005 ppm (50% of the LOQ).

For oxytetracycline, no residues (LOQ=0.01 ppm) were found in whole fruit, orange peel, juice or dried pulp in crop residue trials. Residues of oxytetracycline in orange oil ranged from ND (<0.002 ppm) to <LOQ (0.01 ppm). Therefore, the NAFTA MRL of 0.01 ppm on the citrus fruit group 10-10 is proposed as the tolerance.

The summary of the residue data and the corresponding risk assessments to support the use of FireWall ™ and FireLine ™ for on citrus is included in the Appendix D – 3 and D – 4)

Mycoshield®

A GLP residue study on citrus fruit sponsored by Nufarm Americas Inc. was initiated in March 2015 to support a tolerance petition and registration application for the use of Mycoshield® on the Citrus Fruit Crop Group 10-10 commodities. The study is expected to be completed by the end of June 2016. Residue data are currently available for several of the field trials and include data for raw agricultural commodities and processed fractions. Based on available data, Nufarm is proposing the establishment of time-limited tolerances for residues of oxytetracycline in or on orange, Crop Subgroup 10-10A, at 0.4 ppm and grapefruit, Crop Subgroup 10-10C, at 0.4 ppm. A summary of analytical results is provided in the Appendix E - 3.

The proposed time-limited tolerances for orange and grapefruit commodities are consistent with the tolerances of 0.35 ppm already established for apples, pears and peaches. The processing study was conducted at the exaggerated rate of 5 times the proposed application rate of 1.5 pounds Mycoshield®/acre (7.5 lb. Mycoshield®/acre). No detectable residues were found in orange juice. Residues in whole oranges and grapefruit were approximately 0.2 and 0.02 ppm, respectively.

To mitigate the small dietary risk posed by the specific exemption use on Florida orange and grapefruit crop subgroups 10-10A and 10-10C, a maximum of 8 applications per year and a maximum annual rate of 12 pounds of Mycoshield® per acre are proposed (compared to the 12 applications and the total rate of 21 pounds of Mycoshield® per acre used for the conduct of the residue study on citrus). In addition, a retreatment interval of 21 days is proposed instead of the 2-day retreatment interval used in the residue

trials. With these risk mitigation measures in place, it is very unlikely that any residues detected in treated citrus commodities will exceed the proposed time-limited tolerances for oxytetracycline in/on orange and grapefruit crop subgroups 10-10A and 10-10C. The incremental risk associated with the Section 18 use is therefore expected to be below the Agency's level of concern.

The summary of the residue data and the corresponding risk assessments to support the use of Mycoshield on citrus subgroup 10(A) and 10(C) is included in the Appendix E – 3 and E – 4)

Proposed Time Limited Tolerance

It is anticipated that a single time limited tolerance would be set for the use of Oxytetracycline under the Section 18. As a result of the status of the supporting data across both registrants we would propose the following:

- Fruit, citrus, subgroup 10-10A at 0.4 ppm (the highest of the tolerance level needed for both FireLine 17WP and Mycoshield)
- Fruit, citrus, subgroup 10-10B at 0.1 ppm (needed to cover anticipated residues resulting from the use of FireLine 17WP only)
- Fruit, citrus, subgroup 10-10C at 0.4 ppm (the highest of the tolerance level needed for both FireLine 17WP and Mycoshield)

DISCUSSION OF RISK INFORMATION (166.20(a)(7))

Description of application sites, including proximity to residential areas, aquatic systems, endangered or threatened species habitats, soil types, etc.:

FireWall™ 50WP and FireLine™ 17WP

FireWall™ 50WP and FireLine™ 17WP will only be applied to commercial citrus groves. These groves are typical of those found in Florida. Commercial groves are intensive and no unreasonable risks to human health, endangered or threatened species, beneficial organisms, or the environment are expected from the proposed use of this product.

Also included in the Appendix is an executive summary of work done in association with FDA requirements #152, Resistance Risk Assessment for Foliar Applications of FireWall™ and FireLine™ to citrus crops. With integration of the effective resistance management options, this situation does not significantly change the existing Qualitative Risk Assessment for the emergence of streptomycin or oxytetracycline resistance among clinical pathogenic bacteria. Since this proposed new use of streptomycin and oxytetracycline on citrus crops to improve tree health

and manage HLB is unlikely to represent a source for potential emergence of streptomycin or oxytetracycline resistance among clinical pathogens, approval of the proposed new use of streptomycin and oxytetracycline on citrus crops is believed to be in the public interest.

Mycoshield®

Mycoshield® will be applied to commercial orange and grapefruit plantings, including all citrus fruit belonging to the citrus crop subgroups 10-10A and 10-10C (Calamondin; citron; citrus hybrids; grapefruit; Japanese summer grapefruit; Mediterranean mandarin; orange (sour); orange (sweet); pummelo; satsuma mandarin; tachibana orange; tangelo; tangerine (mandarin); tangor; trifoliate orange; uniq fruit; cultivars, varieties, and/or hybrids of these). Use under the Section 18 will occur in all areas of the state with commercial citrus groves.

Possible risks posed by use:

FireWall™ 50WP and FireLine™ 17WP

FireWall™ 50WP Fungicide/Bactericide and FireLine™ 17WP Fungicide/Bactericide are approved products registered by the U.S. Environmental Protection Agency that have been used in the field for more than 40 years. Possible risks were evaluated during Section 3 registration and reregistration processes for both compounds. FireWall™ is currently registered for use on crops such as beans, celery, peppers, potatoes, tomatoes, apples and pears, and FireLine™ is currently registered for use on crops such as apples, pears, peaches and nectarines. No unreasonable adverse effects to man or the environment are anticipated with this proposed use of three applications of streptomycin and three applications of oxytetracycline to Florida citrus. Additional information for FireWall™ and FireLine™ on these subjects can be obtained from Taw Richardson with AgroSource. His phone number is (908) 215-3500.

Facts associated with the potential for increasing the risk of human resistance to streptomycin and oxytetracycline have also been addressed in the TRED for oxytetracycline and the R.E.D. Facts publications for streptomycin, streptomycin sulfate and oxytetracycline. The streptomycin R.E.D. EPA report says that "regarding the problem of drug resistance, EPA has no data indicating that streptomycin residues remaining in the food supply have a significant or even a measurable potential for increasing human resistance to that drug." The Regulatory Conclusion of that same publication says that "all currently registered pesticide products containing streptomycin or streptomycin sulfate as the active ingredient are not likely to cause unreasonable adverse effects in people or the environment." The TRED for streptomycin says that "antibiotic resistance from pesticidal use of streptomycin is unlikely to result directly from dietary residues of streptomycin because dietary residues are very low. The drug dose is 3,000 times greater than the estimated pesticidal dietary exposure. The small dose from

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(streptomycin) pesticidal exposure would not be expected to select for resistant bacteria because very few bacteria would be killed by this small dose."

The streptomycin FDA #152 study summary paper notes that "streptomycin has been safely and effectively used in plant agriculture since 1955, yet a direct connection to the emergence of streptomycin resistance among clinical pathogens as a consequence of this use pattern remains undocumented. EPA has previously determined that the dietary exposure to streptomycin is below its level of concern. The use of streptomycin to manage HLB in commercially grown citrus crops does not increase the chronic aggregate exposure to a level of concern, since the combined aggregate residential and chronic dietary exposure to all agricultural applications of streptomycin, including the proposed us of streptomycin on citrus crops is 2,491 times less than the No Observed Adverse Effects Level (NOAEL) for the total U.S. population and 719 times less than the NOAEL for the most affected population subgroup, non-nursing infants. Dietary intake of streptomycin does not constitute a source of selection pressure for streptomycin resistance among enteric gut flora, since the dietary exposure from streptomycin applications to plant agriculture is so low and oral absorption for streptomycin is extremely low (<1%). Recent studies have revealed streptomycin-resistant isolates of many plant pathogenic bacteria exist as stable populations in the environment, even where streptomycin has never been applied, giving indication that factors other than streptomycin applications in the field influence the emergence of streptomycin resistance among plant pathogenic bacteria."

Similarly, the R.E.D. publication for oxytetracycline says that the "use of the active ingredients hydroxytetracycline monohydrochloride and oxytetracycline calcium in accordance with approved labeling will not result in unreasonable adverse effects to human health or the environment." Facts pertaining to risks have also been addressed in association with the potential for increasing the risk of human resistance to oxytetracycline in EPA's TRED for oxytetracycline, as well as the FDA #152 assessment. The EPA oxytetracycline TRED concluded that "because anticipated dietary residues are extremely low, it is unlikely that antibiotic resistance from pesticidal use of oxytetracycline would result from food exposure," and "the drug dose is 50,000 times greater than the estimated pesticidal dietary exposure (25 mg/kg/day dose divided by maximum aggregate dietary exposure of 0.000473 mg/kg/day). The small dose from pesticidal exposure would not be expected to select for resistant bacteria because very few bacteria would be killed by this small dose." In the latest oxytetracycline dietary risk assessment, the drug dose is nearly 82,000 times greater than the estimated pesticidal dietary exposure [25 mg/kg/day dose divided by maximum aggregate dietary exposure of 0.000305 mg/kg/day for non-nursing infants (the highest population sub-group)]. Therefore, anticipated dietary residues of oxytetracycline are extremely low, and it is also unlikely that antibiotic resistance from the pesticidal use of oxytetracycline would result from food exposure.

The AgroSource oxytetracycline FDA #152 study summary paper notes that "oxytetracycline has been safely and effectively used in plant agriculture for more than 40 years yet a connection to the emergence of oxytetracycline resistance among clinical pathogens remains undocumented. EPA has previously determined that dietary exposure to oxytetracycline is below its level of concern. The use of oxytetracycline to combat HLB in citrus crops does not significantly increase the chronic aggregate exposure to oxytetracycline. Dietary intake of oxytetracycline is not expected to constitute a source of selection pressure for oxytetracycline resistance among enteric gut flora since the combined aggregate residential and chronic dietary exposure to all agricultural applications of oxytetracycline, including the proposed us of oxytetracycline on citrus crops, by non-nursing infants is 164 times less than the NOAEL, and approximately 82,000 times less than the commonly prescribed therapeutic dose for this most affected population subgroup."

As a condition of the approval of a Section 18 exemption for the use of FireWall™ 50WP for the management of citrus canker (*Xanthomonas citri* pv. *citri*) on commercially-grown grapefruit in Florida, field studies were conducted during the 2014 season designed to detect potential development of streptomycin resistance in the culturable microbial communities from both phyllosphere and rhizosphere zones of FireWall™ 50WP treated (tested) and untreated (control) trees. Two commercial grapefruit grower cooperators provided a total of five unique test sites, all located within the Indian River Citrus growing region of southeastern Florida. No test site had previously received any treatments with streptomycin or streptomycin-based products. FireWall™ 50WP was applied to the test sites following the Section 18 label directions. Samples for culturable bacteria (as found in soils from beneath each tree and leaves taken from each tree) were collected at four dates beginning in August 2014 (T0) and ending in December 2014 (T3). Samples from all FireWall™ 50WP treated and corresponding untreated plots were analyzed for evidence of streptomycin-resistant bacteria. When the data were analyzed across all five test sites, results indicated no consistent and significant change ($p=0.05$) in phyllosphere or rhizosphere microbial populations. More importantly, results revealed no evidence for development of streptomycin resistance among bacterial populations resident in FireWall™ 50WP treated grapefruit trees or soils in response to the use of FireWall™ 50WP on Florida grapefruit for management of citrus canker.

Mycoshield®

Mycoshield® is currently registered for use on apples, pears, peaches and nectarines. Occupational exposure and risk are not expected to exceed the Agency's level of concern since airblast application at the same maximum rate of 1.5 pounds of formulated product per acre per application is already registered for peaches, nectarines and apples. EPA stated in the 2008 Health Effects Division (HED) Scoping Document for Registration Review of oxytetracycline that an

occupational assessment was not needed because of the low level of exposure anticipated from application of oxytetracycline products and the personal protective equipment required by the Section 3 label that includes protective clothing, chemical-resistant gloves, protective eyewear and a respirator. The occupational exposure and risk associated with the proposed Section 18 use on Florida citrus is therefore expected to be well below the Agency's level of concern.

The proposed time-limited tolerances of 0.4 ppm for residues of oxytetracycline in or on orange, Crop Subgroup 10-10A, and grapefruit, Crop Subgroup 10-10C, are based on data available to date from the ongoing magnitude of residue study (included in the Appendix E). Twelve foliar airblast applications of Mycoshield® were made at the maximum use rate of 1.5 pounds of formulated product per acre per application with a 2-day retreatment interval plus two trunk applications of Mycoshield® at 1.5 pounds of formulated product per acre per application. This resulted in a total application rate of 21 pounds of formulated product/acre (3.57 lb. oxytetracycline/acre) whereas the proposed Section 18 label limits application to 12 pounds of formulated product/acre (2.04 lb. oxytetracycline/acre) total per year.

In the 2008 EPA Health Effects Division's Scoping Document for Registration Review of oxytetracycline, EPA concluded that expected dietary (food and water) risk for the U.S. population and all subpopulations was conservative and below the level of concern. Acute dietary exposure was not estimated because no acute toxicity was identified in any of the relevant studies in the oxytetracycline database. As a result, EPA determined that acute dietary risks are not of concern.

In order to investigate potential exposure and risk associated with the proposed Section 18 use on Florida citrus, Nufarm sponsored a chronic aggregate dietary assessment for currently registered uses of oxytetracycline and the proposed use on citrus in Florida. The available data from Nufarm's residue study on citrus were used to assess dietary exposure. The resulting chronic risk estimates are not of concern for any population assessed. Based on this assessment, there are no dietary exposure issues that would preclude the specific exemption use on citrus trees in Florida. Since there is no residential use of oxytetracycline, an assessment that aggregates more than food plus water is not needed.

A drinking water exposure assessment was also conducted for currently registered uses of Mycoshield® and the proposed Section 18 use on Florida citrus trees. The resulting drinking water concentrations were used in the dietary risk assessment. Concentrations were calculated to be very low or practically non-existent (report included in the aggregate dietary risk assessment). The impact of the Section 18 use on the ecological risk is not expected to exceed the Agency's level of concern. Oxytetracycline residues degrade rapidly in citrus foliage. As discussed in the section "Effectiveness of Proposed Use under Section 18", leaf residue analysis has shown that oxytetracycline residues were no longer detectable in foliage 10 days

after application to a grapefruit location and 4 days after application to an orange site.

Nufarm has responded to Data Call-In notices issued for the TRED and Registration Review of Oxytetracycline. Several studies including environmental fate and ecotoxicology studies were conducted to support the continued registration of Mycoshield®. Most of these studies have already been submitted to the EPA or will be submitted in the near future.

Regarding the potential for resistance development, it is unlikely that antibiotic resistance from pesticidal use of oxytetracycline would result from food exposure. Anticipated dietary residues for existing agricultural uses of oxytetracycline and the proposed Section 18 for Florida citrus are extremely low (conservatively estimated at 0.000076 mg/kg/day for the general U.S. population). The maximum aggregate dietary exposure calculated is very small when compared to pharmaceutical or veterinary doses. The small dose from pesticidal exposure would not be expected to select for resistant bacteria because very few bacteria would be killed by this small dose. An assessment of the potential for antibiotic resistance to develop as a result of the use of Mycoshield® on citrus was conducted following FDA Guidance #152 and is included in Appendix E-4. Additional information for Mycoshield® on these subjects can be obtained from Bill Bewlay with Nufarm.

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Proposals to mitigate risks:

Existing use restrictions already listed on both the streptomycin and oxytetracycline labels will further reduce risk. These label restrictions include: do not apply directly to water, or to areas where surface water is present, or to intertidal areas below the mean high watermark; do not contaminate water when disposing of equipment wash water; do not apply by aircraft; do not apply these products through any type of irrigation system; and, only three applications of streptomycin and three applications of oxytetracycline are allowed per season. Current labeling directives are sufficient to mitigate any potential risks. Full reports of tests and investigations made with respect to the safety of streptomycin and oxytetracycline, including all information pertaining to the methods and controls used in conducting these tests and investigations have been submitted and reviewed by the Agency.

The enforcement analytical methods for both products are available to monitor residues of streptomycin and oxytetracycline in citrus.

FQPA INFORMATION (OCTOBER 24, 1996 EPA LETTER)

EPA requested that additional information be submitted with Emergency Exemption requests to address new risk considerations associated with requirements of the Food Quality Protection Act. This information has been provided to the Agency. Since these products are approved for other Section 3 registrations an initial FQPA review has already occurred.

COORDINATION WITH OTHER AFFECTED FEDERAL, STATE, AND LOCAL AGENCIES (166.20(a)(8))

As EPA's state lead agency, the Florida Department of Agriculture and Consumer Services should provide this information.

NOTIFICATION OF REGISTRANT (166.20(a)(9))

AgroSource, Inc. and Nufarm Americas Inc. have been notified of this request. The companies are supportive of this emergency exemption petition (see the Appendix for registrant support letters).

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DESCRIPTION OF ENFORCEMENT PROGRAM (166.20(a)(10))

As EPA's state lead agency, the Florida Department of Agriculture and Consumer Services should provide this information.

REPEAT USES (166.20(a)(11))

This is the first request for the use of each of the requested products, streptomycin and oxytetracycline on citrus by Florida for management of HLB and improvement of overall citrus tree health. The use of antibiotics under this Emergency Exemption Request will suppress HLB in new growth but will not cure the infection in the branches, trunk and roots. The reservoir of bacteria in the lower portions of the tree is a source for constant reinfection. Even new plantings are subjected to continuous pressure from 'hot' psyllids. A Section 18 Emergency Use Exemption would be needed until the Section 3 registrations are obtained.

PROGRESS TOWARD REGISTRATION (166.25(b)(2)(ii))

FireWall™ 50WP and FireLine™ 17WP

AgroSource, in conjunction with the IR-4 Project, continues to make progress toward new registrations for the use of streptomycin and oxytetracycline on the citrus crop group and a variety of other crops. The company is preparing or has prepared and submitted the necessary documentation for a Section 3 registration for citrus. The application to amend the Section 3 label for streptomycin has been submitted to EPA (Decision Number: 486863) and a Pesticide Registration Improvement Extension Act (PRIA) due date of 05/04/2015 had been assigned. EPA subsequently decided to require that this request go through a "public participation process". As part of preparation for this process, EPA issued a deficiency letter to AgroSource (to provide more benefits information) and both parties "mutually agreed" on a new PRIA date of June 2016. Subsequently, the new submission goal for oxytetracycline on citrus is now October 1st, 2015 and for streptomycin the new citrus submission goal is November 1st, 2015.

Mycoshield®

A GLP residue study on citrus fruit sponsored by Nufarm Americas Inc. was initiated in March 2015 to support the registration of Mycoshield® on the Citrus Fruit Crop Group 10-10. The study is expected to be completed by the end of June 2016. It will then be submitted to the EPA in support of a tolerance petition and Section 3 registration application. Nufarm anticipates submitting the application by August 1st, 2016. Assuming a timeline of 15 months for the EPA review, the registration could possibly be granted by the end of November 2017.

Nufarm is the basic registrant for Oxytetracycline Calcium and is responding to Data Call-In notices issued for the TRED and the Registration Review of Oxytetracycline. Several studies were required including environmental fate and ecotoxicology studies that also support the Registration Review of Oxytetracycline Hydrochloride (Appendix E-5).

NAME OF PEST (166.20(b)(1))

Scientific Name:

Candidatus Liberibacter asiaticus (*C*Las)

Common Name:

Disease:
Huanglongbing (HLB) or Citrus Greening or Yellow Dragon Disease

Vector:
Asian Citrus Psyllid (ACP) (*Diaphorina citri* Kuwayama)

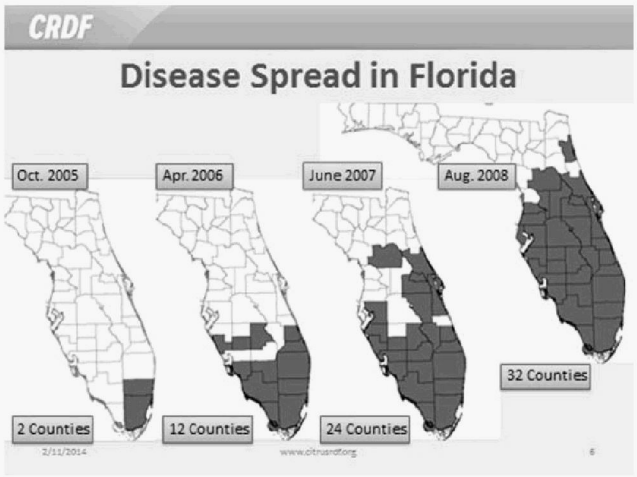
DISCUSSION OF THE EMERGENCY CONDITION (166.20(b)(2))

Citrus huanglongbing has been known in China for more than 100 years. In 1929, a disease with similar symptoms appeared in South Africa and was named 'yellow branch' in Western Transvaal and 'greening' in Eastern Transvaal. The agent associated with the disease was transmitted by graft-inoculation from citrus to citrus for the first time by Lin in China in 1956. This work remained unknown outside China; McLean and Oberholzer demonstrated independently that South African greening was graft-transmissible. Because 'huanglongbing' was the name used in the paper describing graft-transmission of the agent for the first time, it has priority over other names and has been unanimously adopted as the official name of the disease by the International Organization of Citrus Virologists (IOCV) at the 12th Congress of IOCV, Fuzhou, China, 1995.

In the 1960s, the agent was shown to be transmitted by two insects: the African citrus psyllid *Trioza erytreae* in Africa and the Asian citrus psyllid *Diaphorina citri* in Asia.

Symptoms of HLB were reported in Sao Paulo state in Brazil in 2004. Then, in 2005, HLB, was found to be present in Florida. This disease is caused by the pathogen *Candidatus* Liberibacter asiaticus and is spread by the Asian citrus psyllid (*Diaphorina citri* Kuwayama), which is an invasive pest to Florida, first discovered in 1998. HLB is considered to be the most serious disease of citrus worldwide and has greatly limited commercial production of citrus in countries where it is present. Since its discovery in Florida, this disease has rapidly spread throughout citrus production area to all

commercial production areas in the state. The graphic below illustrates the rapidity with which HLB invaded Florida commercial citrus counties:



(Source: CRDF Presentation to EPA, February 5, 2014)

HLB is a prime example of how an unintentional, but illegal, plant introduction into a country can cause multi-billion dollar crop losses, unemployment and industry-wide financial strain. The HLB bacterium lives in the vascular system component (phloem) that conducts synthesized food materials from the tree to the roots. Like the human blood vessels, a blockage of these vascular system conducting tissues by any foreign substance produces deleterious effect. The presence of *C*Las in the phloem prevents the tree from effectively transporting water, nutrients and minerals between the leaves, fruit and the roots in the ground, thereby driving the tree into decline. Since this disease's appearance, citrus production has been compromised with the loss of millions of trees, and HLB has subsequently been detected in every county with commercial citrus and in residential dooryard citrus as well. Trees infected with HLB will continuously decline and eventually die, even when incorporating all management options available to the industry at this time. The HLB-causing bacterium found in Florida is the Asian species that occurs in warm low altitude areas. HLB survives and multiplies within the psyllid vector throughout the psyllid's lifetime. The psyllid was first found in Florida in June 1998.

The severity of HLB and declining tree health far exceeds that of any previously known citrus disease, and all citrus species and their hybrids are confirmed to be affected by HLB. Infected trees first produce leaf symptoms; typically leaf yellowing on one or more branches, then leaves develop a blotchy (irregular spotted) appearance with grades of color. Infected trees typically also show symptoms that resemble micronutrient deficiency, especially, zinc and manganese. Fruit set becomes thin, fruit appear lopsided, the lopsided fruit may contain aborted seeds, and juice quality is unacceptable.

Impacts from HLB are numerous. On infected trees fruit are few in number, small, lopsided with a curved central core, and they fail to color properly, remaining green at the stylar end (hence the name "greening"). Excessive fruit drop occurs prematurely on

afflicted trees, and this has been reported in the past three harvest seasons in Florida to exceed 10 percent per season across all varieties. Even if fruit remain on the tree until harvest, the fruit are undersized and contain bitter juice, rendering it of reduced economic value. From a fruit size standpoint, HLB-infected trees have a significantly greater portion of fruit in smaller size categories compared to healthy trees (more than 95% of symptomatic fruit are less than 2.25 inches in diameter). Total juice volume produced is less from HLB-positive trees because of the smaller fruit size as well. Extensive research has been done to characterize the off-flavors associated with HLB-infected trees, highlighting both the general brix/acid ratio impacts as well as the components that contribute to flavor. This work is presented in detail by Baldwin, et al. 2010, Ikpechukwu et. al, 2011, Plotto et. al., 2013 and Massenti et. al. 2015.

HLB disease and the lack of any tree health improvement antibiotic has already pushed untold numbers of farmers out of the industry. Between 2004 and 2014, the amount of Florida land planted with citrus shrunk by nearly one-third, from 748,555 acres down to 515,147 acres (USDA, FASS). During that same timeframe, overall citrus production in the state dropped from 292 million boxes of fruit down to 124 million boxes (a 58% reduction). Average orange yields sunk from 428 boxes per acre in 2004 down to 250 boxes an acre in 2014 (a 42% reduction), despite the higher-density new plantings of orange trees, almost solely resulting from HLB infection.

Also contributing to the situation (and the continued higher grove maintenance costs) are Asian citrus psyllid management requirements. Since the psyllid's discovery, annual production costs have more than doubled. The majority of these increased costs are derived from psyllid management requirements and the necessary modified cultural practices. Psyllid management is an absolute necessity with respect to controlling HLB spread; the threshold for psyllid treatment has become "less than zero" in the industry. A high proportion of psyllids are now infected with the bacteria and capable of transmitting the disease. Florida citrus growers are currently spending more than $240 million a year on insecticides directed solely to manage psyllids, which is about 30 percent more than they were spending in 2004, even though they're farming about 30 percent less land and yielding half as much fruit.

Citrus production and research experts believe that looking forward, the pursuit of interventions to reduce Asian citrus psyllid populations, reducing HLB bacterial populations within infected trees, and promotion of optimal tree health in the presence of HLB are the keys to the citrus industry's sustainability. The industry to this point has pursued a three-pronged approach to combating HLB, focusing on interventions on the three components of the disease pathosystem. The first component involves managing the psyllid. The second is understanding the bacterium itself, with the goal of hopefully neutralizing impact on psyllids or trees. Access to antibiotic materials such as streptomycin and oxytetracycline is vital to induce the improvement of tree health and subsequently keep trees viable until these other HLB management approaches can be developed. The third component is to breed new citrus trees that will hopefully tolerate or resist infection.

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HLB is truly a limiting factor for citrus production. In the attempt to improve tree health to the degree possible, cultural practices such as foliar micronutrient sprays are employed once HLB infects a tree, but these effects are short-lived and certainly will not sustain the industry. HLB is already directly responsible for the loss of thousands of acres of Florida citrus trees. An emergency exemption involving multiple antibacterial strategies that enables improved fruit production must be gained in order to counter the impact of this bacterium/vector complex that is threatening the short- and long-term viability of the state's $7 billion citrus industry. Without such antibiotic access and without anything else changing, within five to eight years of becoming infected, diseased trees will no longer be economically productive.

Limitations on replanting to replace declining tree inventories have made it critical to extend the productive life of the more than sixty million mature citrus trees in commercial groves. Continued production from this inventory of mature (infected) trees while new trees come on line is the process by which the Florida citrus industry can avoid failure and loss of critical nursery, production, harvesting, processing, packing and marketing infrastructure.

HLB infection rates in new plantings

Groves ~2 years of age (2014)

Psyllid pressure	HLB infection range	Average infection rate	# of groves
1 - low	0 – 4.05%	1.02%	20
2 – medium	1.73 – 65.6%	17.7%	20
3 - high	0 – 36.9%	20.96%	21

The graphic above emphasizes the point that despite ACP management programs, new plantings are still becoming infected and these would be primary targets for bactericide treatment.

Biology of *C*Las and Disease Onset/Progression

The complicated biology of HLB and the interactions between vector, pathogen and host citrus plant make development of solutions challenging. Following inoculation of *C*Las into uninfected citrus trees, a period of latency follows during which time there is no

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evidence of infection. Early symptom development is manifested through mottled foliage, followed progressively by smaller and narrower leaves, reduced mature fruit size and thinning of canopies. Chronic symptoms include limb dieback, fruit yield and quality reduction, and pre-harvest shedding of mature fruit. The time period of this disease progression varies with tree age and inoculum pressure, but generally in mature trees chronic decline appears within three to four years of initial infection.

New information on Root Impacts

Research reported over the past three years (Graham et. al., 2012, Johnson et. al., 2014, and Graham and Morgan 2015) has revealed that *C*Las infection of citrus involves early movement of bacteria to root systems, where direct impacts on root health result. Root systems of infected trees have relatively fewer feeder root densities, diminishing water and nutrient uptake efficiencies and exposing diseased trees to additional stress. Further evidence from field research has demonstrated that HLB-infected trees are susceptible to lower populations of Phytophthora propagules than healthy trees, indicating that HLB infection allows soil diseases to overcome or break rootstock tolerance.

Significant economic loss has been experienced through lower fruit quality and smaller fruit size as described below, and proposed bacterial therapies have the potential to improve this aspect of the disease as root systems are restored. Strategies that address reduction in *C*Las titers in infected plants are few, but focus on reduction of bacterial levels early in disease development.

While research continues to further elucidate the impacts of early migration of *C*Las into root systems, it has become necessary for growers to apply additional treatments for Phytophthora, root weevils and other soil stressors. It is expected that this root health compromise will also impact the ability of citrus trees to respond to weather disruptions like freeze events or sustained heavy rainfall.

<u>Non-Routine Emergency Situation:</u>

The rapid decline of HLB-infected mature citrus trees as evidenced by reduction in fruit size and quality and with the dramatic increase of fruit drop as fruit reaches harvest maturity.

Dr. Ariel Singerman of the University of Florida, IFAS, Citrus Research and Education Center has updated grower estimates of the spread of HLB in Florida and its impacts on production. This study is included in the Appendix and is posted at http://www.crec.ifas.ufl.edu/extension/economics/. Here are highlights regarding HLB incidence in Florida:

- 57 percent of growers surveyed report that 100 percent of their groves were infected, while 24 percent and 13 percent reported 80-99 percent and 60-80 percent infection, respectively.

- On a tree-by-tree basis, 15 percent reported 100 percent of their trees were infected, while 49 percent and 21 percent reported 80-99 percent and 60-80 percent tree infection rates, respectively.

- 80 percent of respondents reports yield losses in the range of 20-60 percent, with 13 percent of respondents reporting more than 60 percent yield loss.

These estimates reinforce official crop production figures from USDA/FASS reported elsewhere in this petition and highlight the level of impact on individual growers as the disease decline continues.

DISCUSSION OF ECONOMIC LOSS (166.20(b)(4))

The damage resulting from HLB infection is considerable. Diseased trees decline, yields are reduced, and fruit quality is affected. As the disease severity increases, yield is reduced through a combination of smaller crop set, preharvest fruit drop from affected branches and smaller fruit size. The yield reduction can reach 30 to 100 percent, depending on proportion of affected canopy. This level of disease progression makes the grove economically nonviable 7 to 10 years after planting. As disease severity increases, the percentage of affected fruit increases, reaching more than 40 percent. The affected fruit are smaller, lighter, very acidic, with reduced Brix, ratio, percentage of juice and soluble solids per box, and juice quality is negatively impacted. Millions of citrus trees in Florida have been affected by HLB and subsequently destroyed. The last projected value that has been established as a direct cost of HLB to Florida's citrus industry is around $300 million annually.

The loss of production is felt by more people than just the famers that grow citrus. As production declines, packing houses do not run, box makers do not sell their products, shipping companies do not operate, etc.

Dr. Ariel Singerman, Assistant Professor of Agricultural Economics at the University of Florida, IFAS, Citrus Research and Education Center, has recently evaluated the impact of HLB on citrus production costs across the three general production regions of the state. His work is posted on http://www.crec.ifas.ufl.edu/extension/economics/.
Below is a summary of Dr. Singerman' s findings from citrus production operations in the three regions:

Central Florida (Ridge) Cost of Production for Processed Oranges:

The Table below shows total costs growers incurred for 2014-15, which includes cultural costs, tree replacement plus other costs such as management, regulatory and opportunity costs. The total cost of production for processed oranges for 2014-15 is reported to be $2,282.19 per acre. Contributions to cultural operations include foliar

sprays at $705.30 per acre; Citrus Health Management Area (CHMA) sprays $56.65 per acre; fertilizer expense at $469.80, and weed control at $246.31. With thinner tree canopies and open spots where HLB has caused tree death, even weed management costs have escalated. This can be compared to production costs averaging $700-800 per acre prior to HLB.

Table 6: Total Costs of Production per Acre for Processed Oranges in Central Florida (Ridge), 2014/15.

Total Cultural Costs with Tree Replacement		1819.74
Other Costs	Interest on Operating (Cultural) Costs	90.99
	Management Cost	81.75
	Property Tax/Water Management Assessment	35.37
	Interest on Average Capital Investment	254.34
Total Other Costs		462.45
Total Costs		**2282.19**

Southwest Florida Cost of Production for Processed Oranges:

Similarly, costs for production of oranges in southwest Florida continue to climb, in the Table below excerpted from this section of the Singerman report. In this case, foliar sprays average $666 per acre plus $20.55 for CHMA sprays. Fertilizer costs were $486.90 per acre, and weed control averaged $248.19. The total cultural operations costs of $1,998.10 per acre are more than double those experienced prior to HLB impact.

Table 7: Total Costs of Production per Acre for Processed Oranges in Southwest Florida, 2014/15

Total Cultural Costs		1998.10
Other Costs	Interest on Operating (Cultural) Costs	99.91
	Management Cost	63.34
	Property Tax/Water Management Assessment	28.73
	Interest on Average Capital Investment	254.34
Total Other Costs		446.31
Total Costs		**2444.41**

Indian River Cost of Production for Fresh Grapefruit:

In the case of the Florida's premier production area for fresh grapefruit, the Indian River, the production costs mirror the increases observed in the other regions for processed

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oranges, but are magnified due to the need for fresh fruit quality and its impacts on production costs. The Table below from the Indian River portion of the report indicates a total of $2,478.61 cultural costs for 2014-15 and an overall per acre average production cost of $3,073.38 per acre. Relevant operational costs are $1,300.40 per acre for foliar sprays and $14.75 for coordinated sprays (CHMA); fertilizer costs average $452.55 per acre and weed control averaged $190.60 per acre. This compares to fresh fruit production costs prior to HLB that averaged $1,000-1,200 per acre per year.

Table 8: Total Costs of Production per Acre for Fresh Market Grapefruit Grown in Indian River, 2014/15.

Total Cultural Costs with Tree Replacement		2478.61
Other Costs	Interest on Operating (Cultural) Costs	123.93
	Management Cost	75.00
	Property Tax/Water Management Tax	18.50
	Fly protocol	16.00
	Water Drainage District Assessment	107.00
	Interest on Average Capital Investment	254.34
Total Other Costs		594.77
Total Grower Costs		**3073.38**

Integrating the increased production costs for Florida citrus with statewide declines in per-acre yields illustrates the emergency status and the business failure that is being witnessed in Florida. Small- and medium-sized operations are economically abandoning blocks of citrus which have fallen below break-even levels for several consecutive years, reducing any further losses associated with continued investment in the face of continuing decline in production. An option considered by some is reduction in inputs to offset smaller crop size and quality. Experience over recent years indicates that this pull-back in intensity of management of tree health accelerates the disease decline and only hastens economic abandonment. At the same time, these unmanaged groves become a source for inoculum for the pathogen and reservoir for the vector ACP.

Large citrus operations in Florida are facing similar decisions on the declining return or loss due to HLB, and are risk assessing individual blocks each year to determine where investments are warranted. They, too, are removing groves that have fallen below economic return thresholds from active management.

This scenario also is not favorably affecting growers' interest in replanting, as the uncertainties of being able to sustain production on new trees is influenced heavily by their experience with standing groves. Data on declines in nursery tree production in the past year attests to this uncertainty, despite availability of industry and other incentive programs to replant. The health of Florida's citrus industry is usually mirrored in nursery production. As industry production falls or fruit prices weaken, citrus nursery tree orders suffer. A total of 54 citrus nurseries propagated 4,438,128 trees in 2014-15, which is a decrease (5.8%) from last year. Nursery activity was strong for several new nurseries

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that began producing trees this year; 6 new nurseries accounted for over 5 percent of the total nursery propagations. Existing nurseries mostly saw a decline in budding and tree orders. A total of 33 nurseries had reduced production from the previous year and only 15 saw an increase. Overall, tree production based on reports decreased by 274,311 trees. Taking into account that six new nurseries contributed to the production figures, it signified a downward trend for most nurseries. (FDACS Budwood Certification Program, Annual Report 2014-15).

The Economic Impact of HLB on the Florida Citrus Industry:

As described in a recent publication, this disease and the resulting loss of production cost the industry over $7 billion in lost revenue by 2012 (Hodges A.W., Spreen T. H., 2012). This loss of production translates to more than 8,000 lost jobs over the same five-year period. As trees succumb to the effects of the disease, the industry is faced with the challenge of replanting groves to replace the lost production. Although these figures have not been formally updated, the losses have risen considerably since this analysis was published.

Economic Effects of HLB in Florida:

Florida's iconic citrus industry is an essential part of the economy of Florida, especially in the 28 central and southern counties of Florida where citrus is grown and processed. The most recent study before HLB became endemic put the overall economic impact at $8.91 billion and provision of 75,827 jobs.

However, in 2012 economists calculated that over $4.5 billion in economic impact had been lost because of the effects of HLB on the Florida orange juice industry for the period 2006 to 2010. The report details the category of losses, i.e., direct economic impacts, indirect economic impacts and induced impacts. On average, Florida's economy suffered with the loss of $908.2 million dollars each year, and 8,257 permanent jobs.

These losses are mainly because of the reduced production of Florida oranges versus a scenario without the effects of HLB in the citrus growing environment. Losing orange production is exacerbated by further losses of the value-added segment of the industry, that is fruit processing, juice manufacturing, and juice packaging and distribution. Since most of the orange juice sold in the United States is produced solely in Florida, this becomes a loss of economic benefits for Florida residents.

As the disease progresses, more losses are expected each year. An estimate of the most current losses are explained by looking at Florida citrus production statistics over the period prior to first detection of HLB in Florida (1996-1997 through 2005-2006) and the decline in production experienced in the recent three years as a result of both accumulation of disease across the state as well as the cumulative decline due to multi-year chronic HLB infection (Table 9).

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Table 9: Florida Citrus Production Statistics during the Period 1996-1997 through 2013-2014.

Crop Production by Fruit Type 1996-1997 through 2014-2015				
Crop Year	**Oranges**	**Grapefruit**	**Other Citrus**	**Total**
	(1,000 Boxes)			
1996-1997	226,200	55,800	13,315	295,315
1997-1998	244,000	49,550	10,900	304,450
1998-1999	186,000	47,050	10,115	243,165
1999-2000	233,000	53,400	12,030	298,430
2000-2001	223,300	46,000	9,505	278,805
2001-2002	230,000	46,700	10,565	287,265
2002-2003	203,000	38,700	9,305	251,005
2003-2004	242,000	40,900	8,900	291,800
2004-2005	149,800	12,800	6,650	169,250
2005-2006	147,700	19,300	7,600	174,600
2006-2007	129,000	27,200	5,850	162,050
2007-2008	170,200	26,600	7,000	203,800
2008-2009	162,500	21,700	5,000	189,200
2009-2010	133,700	20,300	5,350	159,350
2010-2011	140,500	19,750	5,800	166,050
2011-2012	146,600	18,850	5,440	170,890
2012-2013	133,600	18,350	4,280	156,230
2013-2014	115,000	16,500	4,400	135,900
2014-2015	96,700	12,950	2,980	112,630

Source: USDA, National Agricultural Statistics Service, FASS, Florida Citrus Statistics. 2011-2012, published February 12, 2013. Data for crop years 2012-2013 and estimates for 2013-2014 provided by USDA, NASS, FASS, Citrus Forecast, January 10, 2014. 2014-15 July 10, 201 Final Forecast for Season.

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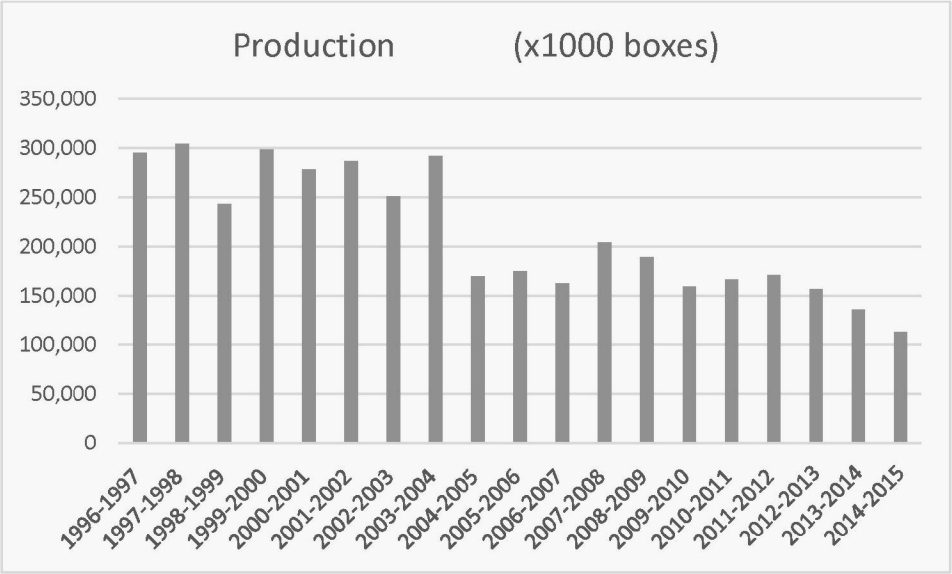

Note: The above graph depicts the data in the table for total production, all varieties, and is included as an alternative data presentation, or to be used elsewhere in the petition.

Losses have now reached levels that annual citrus production is less than half of what it was as recently as 2003-2004. The decrease in fruit in successive harvests over the past three seasons is shown here:

2010-2011 to 2011-2012		**9%**
2012-2013 to 2013-2014		**11%**
2013-2014 to 2014-2015		**17%**
Net loss (3 years)	**=**	**34%**

With the rapid spread of HLB disease, and the increasing infection rates within standing groves, the situation that we are experiencing now in Florida is a combination of:

- Widespread infection of citrus trees throughout the growing region of Florida.
- Heavy inoculum in infected trees available for acquisition by the vector, ACP. Recent samples indicate up to 100 percent of field-collected ACP are positive for *C*Las, the pathogen.
- Limited removal of infected trees means that local spread can be rapid if psyllids are not managed effectively. With high rates of infection within a block, tree removal is not practical.

- The accumulation of years of progressive infection by *C*Las means that a higher percentage of trees are beginning to show chronic infection, including more widespread symptoms within trees, thinner canopies and impaired root systems.

- These factors all contribute to the reduced fruit production (yield), even though the official acreage of citrus plantings has not declined significantly in the last few years. And,

- Fruit quality is declining, in size, flavor and maturity.

Thus, the productive population of mature trees is declining in health and productivity, and will likely continue to do so without effective therapeutics, which currently are not available. In addition, new citrus trees that are either inter-planted in existing groves of mature trees or planted solid in new blocks are at high risk to infection via the ACP vector bringing inoculum from *C*Las reservoirs. It is these new trees that will provide the ability for economic production of citrus to continue, and the confidence to replant is, at present, limited by early and fatal infection of young trees by *C*Las through psyllid transmission. Trees in the first 4-5 years of growth are particularly vulnerable since they grow new flush off-cycle when other trees are not producing new leaves. This makes them more attractive to ACP colonization and vulnerable to disease transmission.

The importance of management of HLB in Florida citrus is reduced to two major considerations. The first is to delay further health decline in existing mature trees that will further erode production. Second, and more vital, is the ability to manage ACP populations in young plants, thereby providing confidence to growers to replant. Both of these considerations could be positively impacted by availability of effective bactericides.

Consideration of Expected Economic Benefits of Improved HLB Management, Particularly Through Availability of Bactericides

This overview adds insights by attempting to quantify potential economic benefits to Florida if research efforts change the trajectory of any one of several factors that affect the economic impact of citrus production (specifically oranges) in the state. The initial overview focuses on the various aspects of production, such as acreage, yields, fruit loss to drop and quality reduction and other measures of decline due to HLB that would be expected to show improvement with implementation of an effective bactericidal program, as well as the trends in replanting, which likewise would be expected to improve as bactericidal therapy is made available.

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To understand the economics of expected response to exposure of HLB-infected trees to a time course of one or more bactericidal treatments, it is important to outline the disease progression associated with this disease and to determine which aspects of the disease impact would be improved through treatment. As stated earlier in this petition, infection of citrus by *C*Las is initially invisible, followed in a multi-year time course by a series of symptoms and injury which begin as foliar mottling and chlorosis and progressing to reduction in canopy density, and leaf size, and overall appearance of decline in one or more branches of the infected tree. General decline reflects root injury and limited movement of plant products through the impaired vascular system. With time, the appearance of small fruit, further thinning of canopies, and leaf and premature fruit drop signal more advanced imbalance in the tree. Leaf symptoms also include general chlorosis (yellowing) and their noticeable appearance as thinned canopies, with bare patches within the canopy of chronically infected trees. These advanced symptoms, and the continued decline to death of chronically infected trees, may not appear for several years following infection, or even following first visual symptoms. The general decline is symptomatic of the breakdown of several plant systems, including roots (lower feeder root density), reduced vascular movement (phloem plugging) of nutrients from sources to areas of need (leaves to roots, roots to developing fruit, etc.), and impaired photosynthesis due to canopy loss.

Thus, in evaluating the expected response to treatment of *C*Las in infected trees, the forgoing description also defines the measures necessary to determine stabilization or recovery from disease symptoms. Expected changes in the following parameters can be predicted from previous research on epidemiology of HLB in citrus and are the metrics associated with field evaluation of therapies as pursued by the registrants of the candidate bactericides.

- Reduction in *C*Las titer in infected trees following bactericidal regimen: The first measurable impact of bactericidal treatment would be expected to be reduction in bacterial titer in infected tissues. This is best measured at present using qPCR, and the numerical scale changes in samples over time reflect increase or decrease in bacteria in tissues sampled. Following a time-course of bactericidal treatments, it would be expected to see a gradual increase in PCR CT values, indicating a decline in titer in infected plant parts sampled. This may occur as step-wise reduction following individual applications, as evidenced in the data summaries provided. This in itself is not a metric of improved plant health or economic benefit, but portends resumption of growth and response as bacterial levels decline.

- Improved tree growth response: Biological response to the lessening of pathogen pressure in infected trees is manifest in a series of indicators that trees are returning to more normal growth and development. As in the description of the onset of disease symptoms above, the progressive lessening of disease injury would be expected to show itself through leaf, branch, root and fruit symptoms. This has been observed in field experiments where therapies (both chemical and thermal) have been applied, and specific field results are presented in this petition for the products being field tested.

- Foliage response: Larger, greener, more robust flush appear in flushing periods following treatment, and the degree to which flushing phenology and the strength of new foliage resume a "normal pattern" is indicative of reduced disease.

- Canopy density improvement: Increased photosynthetic capacity is a by-product of new, healthy flush and drives plant health. Tree growth, including laying down of new phloem also can follow.

- Root health improvement: Photosynthate movement and lessening of root decline due directly to *C*Las follows resumption of tree flushing, and it is yet unclear to what extent this will occur following a treatment regime of bactericides.

- Increased capacity to utilize irrigation and nutritional applications, including improved foliar uptake. Restoration of root health has immediate impacts on the tree's ability to utilize nutrients and healthy roots buffer periods of dry and wet weather.

- Ability to combat other stresses (root disease, cold, drought). Resumption of balanced flush with restored roots has the added advantage of providing the defense against other stresses that exist in groves. Overcoming these stresses also contributes to resumption of tree health and productivity.

- Fruit set and productivity: Since successful fruiting is dependent on support from the canopy, the above improvements in tree health can be expected to contribute to improved fruiting, and in conjunction with lower *C*Las titer, less size and fruit quality issues. Metrics associated with fruit yield, size and quality thus are direct indicators of effect of treatment success.

It should be clear that expected response in diseased citrus trees from application of a regimen of bactericidal applications will first be improvement in bacterial titers, followed by reduced visual symptoms, then impacts on the production and quality of fruit. While

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this is likely to occur across a full production season, it is also likely that accrued benefit of the suppression of *C*Las in infected plants will occur over multiple seasons.

While none of the above discussion pinpoints economic benefit of grower use of the proposed bactericides in this petition, it provides the context for that economic assessment. Based on the preceding discussion, improvement in tree health should lead to following economic drivers:

Fruit yield and quality improvement –
- Larger fruit set and retention through the production season;
- Increased capacity to hold fruit on the tree season-long; less pre-harvest fruit drop;
- Improved fruit size;
- Improved internal fruit quality;

Normal growth progression for young trees (up to 5 years old) to full productivity (multi-year impact); and,

Increases in new plantings with availability of tools to deter disease progression.

Impacts at the Processing Facility:

The economic loss resulting from HLB-induced reduction of quality can be measured by downgrading, which initially can be done while fruit are still on the tree. Quality standards are established for juice fruit and fresh fruit harvest per fruit variety, and delays in maturity, caused by HLB infection, postpone harvest, and allow an extended period for pre-harvest fruit drop to occur. Increasingly, harvesting of fruit, even for processing, is not "clean-picked", where the entire crop is removed at once, then graded and routed to fresh and processing streams. In the presence of HLB, fewer groves are harvested in this manner, and the fruit left behind due to irregular shape, small size, and other quality parameters is lost production.

Fresh-fruit harvest has traditionally used "spot-picking" to begin the season, where fruit of the desired size and maturity are harvested, allowing remaining, smaller fruit to "size up" and mature for later harvest. Under HLB conditions, some groves from which fresh fruit are harvested are spot-picked 3 times, dramatically increasing harvest and handling costs. In the past two seasons, fruit left after initial spot picking did not continue to size, another result of HLB disease. Ultimately, the remaining fruit on these trees are clean-picked for routing to processing plants.

The second stage for quality downgrading comes at fruit load receipt at either packing houses (fresh) or processing plants (juice). Typically, fresh packing operations sort, grade and pack cartons of fruit to specifications. The percent of fruit arriving at the packinghouse that ends up in cartons is referred to as pack-out. Even with spot-picking to select higher quality fruit, pack-out percentages have dropped 20 to 40% in the past 3

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years. The fruit not packed into cartons is redirected to processing streams, resulting in lower returns. For the 2014 fruit season, oranges averaged $16.31/box when utilized for fresh and $12.09/box average for processing (USDA, NASS Florida Agriculture Quick Statistics). The differential is even greater for grapefruit, where 2014 fresh grapefruit were valued at an average of $14.44 per box for fresh and $6.38 per box for processing utilization.

Fruit arriving at processing plants is sampled by load and the quality is assessed. The FDACS State Test House measures percent brix (sugar), percent acid and the ratio of brix/acid. This ratio is the initial basis for juice quality, and provides the quality data for payment to the grower. Additional data recovered from the load sampling includes pounds solids per weight of fruit, percent juice and overall weight of the load. The formula for payment is quality based and calculated for the pounds solids delivered from the entire load.

HLB-affected loads of fruit net a lower brix and lower ratio, and due to smaller size, have less percent juice, yielding less juice from processing. Based on the State Test House results, fruit loads are assigned a grade, and lower grades are discounted. In the case of shared pool processing situations, the grade determines your "pool share" at season's end, and this can be as much as 15-20 % discount for grade B compared to grade A fruit loads. The more serious impact is when lower grade loads of fruit are routed for juice concentrate production rather than inclusion in the not-from-concentrate juice processing stream. A significant differential occurs between these two forms of orange juice utilization, and this varies by processor and by season.

All of these parameters have declined progressively over the past 3 years, and are expected to continue in chronically infected trees. Treatment to suppress HLB in these infected trees would be expected to reverse this process and restore value for each of these variables.

Impacts at the Fresh Fruit Packing House:

In addition to the impact on the processing industry, the fresh fruit industry has paralleled the losses due to HLB.

The loss in fresh utilization is due to:

- Tree loss
- Increased fruit drop
- Lower pack outs, due to smaller size and quality issues associated with HLB.

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Table 10: Reduction in shipments of Fresh Fruit Varieties in Florida as a result of the impact of HLB

Change 2014-2015 from 2007-2008		
Variety	**Fresh Boxes (In 000)**	**% Reductions**
Oranges	(476)	-10.8%
Grapefruit	(4,645)	-46.8%
Tangelos	(74)	-46.1%
Early Tangerines	(730)	-63.3%
Honey Tangerines	(909)	-63.3%
All Fresh	(6,834)	-38.6%

Data sourced from: Duke Chadwell, Citrus Administrative Committee

For one Florida shipper, the 3-year average pack out (fresh utilization) for the 2005, 2006, and 2007 seasons was 70.4%. The average pack out for the 2013, 2014, and 2015 seasons was 53.7%. This 16.7% pack out reduction is due to HLB impacts on the size and quality of fresh fruit produced from our groves.

Improving pack outs to pre-HLB levels would increase our company's fresh output by 126,487 boxes, or 33.0%, without considering any potential yield increases.

Industry Wide Impacts:

The following is a summary of previously published and presented material supplemented with data from the 2012-13 fruit season. This report was prepared by Bob Norberg, Economist, Florida Citrus Mutual, Economic and Market Research Associates, January 2014. It summarizes several previously published reports regarding the economics of the Florida Citrus Industry and the impacts of HLB on Florida Citrus economics. Data from the most recent seasons is used to generate supplemental impacts based on the logic from the previous reports.

The three factors examined in this economic evaluation were: tree mortality rates, re-planting rates, and fruit yields. Reducing the mortality, and/or increasing the replanting rate, and/or improving fruit yields all have positive economic impacts. The following chart shows the combined effects on crop size with gradual improvements to these factors over the next 10 years. Reducing the mortality rate from 4 to 3 percent in 10 years, increasing the planting rate from 2 percent to 3 percent over 10 years, and raising yields 1 percent per year would generate a total of 140 million additional boxes of fruit over the forecast horizon. Those additional boxes generate direct, indirect and induced economic impacts that would not be generated without them.

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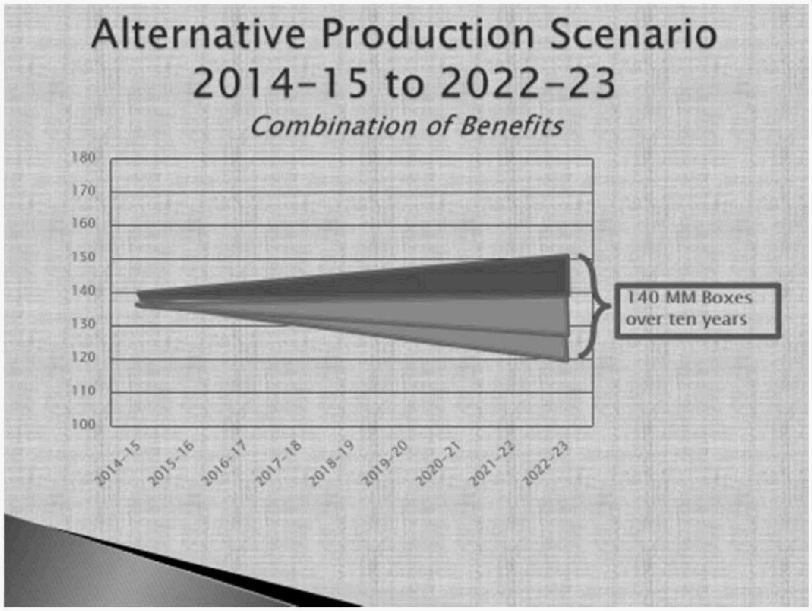
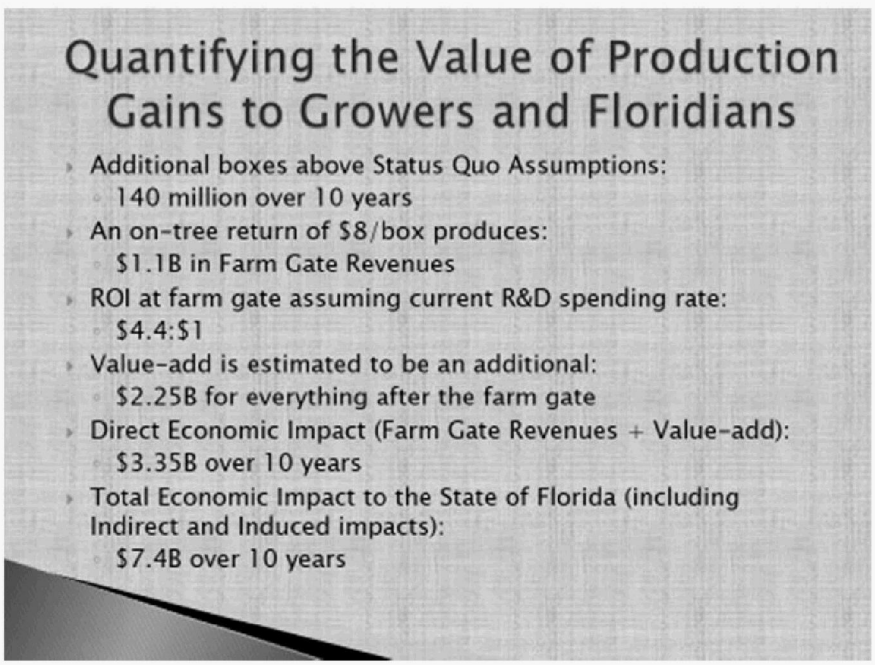


The following chart from the presentation concludes that those boxes are worth $7.4 billion dollars during those ten years. Farm gate revenues would be enhanced by $1.1 billion dollars.



Further increases in pre-season fruit drop and reductions in fruit size were forecasted in the January 2014 estimate highlighted in the table above and are expected to continue that trend in future production estimates. The reduced yields have contributed to the smallest orange crop since the freeze impacted crop of 1989/90. It is uncertain, but

likely, that these yield effects will be seen in future seasons without dramatic advances in production management practices, disease mitigation strategies, and solutions from the comprehensive research efforts.

Update on Economic Impacts, January, 2014:

Using the methodology previously established by Hodges and Spreen in their 2012 analysis, an updated estimate of the annual economic impacts of HLB (and other calamities) can be calculated. Although unit FOB values have risen recently, these increases do not compensate for the loss of volumes since the value-added portion of total economic output is a significant factor and is directly correlated to volumes of orange juice case goods produced and distributed.

The following table shows the losses to be $3.3 billion over the period from 2011/12 to 2013/14 (January forecast) and 10,089 annual jobs. Combined with the losses estimated previously, losses to date from the 2006/07 season are $7.8 billion.

The annual rate of losses in both economic output and jobs is accelerating from the previous estimate. The average annual loss was $908.2 million per year between 2006/07 and 2010/11, while the annual loss rate for the period 2011/12 to 2013/14 is $1.1 billion. Currently total economic losses versus a non-HLB forecast is estimated to be $1.8 billion for the 2013/14 season based on the January crop forecast.

Table 11: Impact of HLB to the Florida Citrus Industry the three Previous Seasons

CROP SEASONS 2011/12 – 2013/14	Non-HLB	HLB	Difference
FOB REVENUES (MM)	$7,356	$6,103	($1,253)
DIRECT ECONOMIC OUTPUT (MM)	$7,088	$5873	($855)
TOTAL ECONOMIC OUTPUT	$19,245	$16,096	($3,329)
ANNUAL EMPLOYMENT	58,865	48,776	(10,089)

This information has not been updated to include the 17 percent production loss experienced during the 2014-15 citrus season.

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ESTIMATED REVENUES FOR THE SITES TO BE TREATED (166.20(b)(4)(ii) & (iii)) (166.20(b)(4)(ii) & (iii))

Florida accounts for:
66 percent of the total U.S. value for oranges;
65 percent of the total U.S. value for grapefruit.

Florida currently ranks 1st in the U.S. in the value of both the production of oranges and grapefruit.

Table 12: Florida Production Information, Oranges

Florida Orange Production Information*					
Season	Total Bearing Acres	Total Production (1000 boxes**)	Yield per Acre (total boxes)	Price per Box	Total On-Tree Value (Millions)
2013-14	418,700	104,600	250	$7.58	$ 792.7
2012-13	429,200	133,600	311	$7.43	$ 992.5
2011-12	433,400	146,700	338	$9.92	$1,455.7
2010-11	440,000	140,500	319	$8.41	$1,181.9
2009-10	451,000	133,700	296	$6.96	$ 929.9
5-Year Average	434,460	131,820	303	$8.06	$1,070.5

* Source: Latest Available Florida Agricultural Statistics Service Citrus Summary, February 2015.
** Box = 90 pounds

Table 13: Florida Production Information, Grapefruit

Florida Grapefruit Production Information*					
Season	Total Bearing Acres	Total Production (X 1000 boxes)	Yield per Acre (total boxes)	Price per Box	Total On-Tree Value (Millions)
2013-14	43,100	15,650	363	$6.44	$100.8
2012-13	44,900	18,350	409	$6.47	$118.7
2011-12	45,500	18,850	414	$7.17	$135.3
2010-11	46,500	19,750	425	$6.72	$132.7
2009-10	48,100	20,300	422	$7.50	$152.2
5-Year Average	45,620	18,580	407	$6.86	$127.9

* Source: Latest Available Florida Agricultural Statistics Service Citrus Summary, February 2015.
** Box =85 pounds

Economics associated with HLB and potential impacts of Section 18 bactericidal treatments:

Processed Oranges Metrics (>90% of Florida citrus Crop)

Table 14: Emergency Loss When compared to Baseline Florida Orange Production Prior to HLB.

Factor	Baseline (pre-HLB) 2005-06	2014-15 Harvest Season	Change (%)
Bearing Orange Acreage	529,241 acres	441,628 acres	-16.6
Annual Production (million boxes)	147,700,000	96,800,000	-34.5
Yields per acre (90 lb. box)	301 boxes/acre	250 boxes/acre	-17
Fruit Size (average number/box)	221 (2007-08)	244	10.4
Pre-harvest fruit drop (Valencia)	15 % (2007-08)	25%	10

Source: USDA, Florida Agricultural Statistics Service

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Expected Benefit Due to Bactericide Treatments:

Expected impacts are calculated based on historic statistics and expected impacts of the proposed treatment on citrus productivity and fruit quality. The factors that are most likely to show improvement following season-long treatments as described in the petition are improvement in fruit size, retention of more fruit on tree, and return crop production increases.

Reduction in Fruit Drop: One of the most devastating impacts of HLB is loss of yield through fruit drop just prior to harvest. The impacts of 20 percent and 50 percent reduction in fruit drop are calculated here.

A 20 percent reduction in the current 25 percent fruit drop rate would restore five percent to harvested yield for the same crop load. This five percent retention adds 12.5 boxes per acre and at $12.09, on-tree value of $151.13 per acre. **That translates into 5,520,350 boxes of fruit saved from falling to the ground with a 25 percent reduction in the amount of fruit drop, and this is valued at $66,743,240 for orange acreage per year.**

Using the same calculations for fifty percent reduction in fruit drop would restore 12.5 percent to yield. This translates into 31.25 boxes per acre additional impact on yield and, at $12.09, is valued at $378 per acre per season. **Calculated benefit across all orange acreage provides addition of 13,800,875 boxes of fruit, or an economic benefit of $166,935,384 to Florida orange growers per season.**

Similar calculations can also be made for other citrus varieties and for the added value of fresh market, especially for grapefruit.

Improvement in Fruit Size: HLB has reduced fruit size, and tree health recovery is expected to improve fruit size. The impact is calculated for 20 percent reduction and 50 percent reduction in fruit size.

Comparison of fruit size shows 23 additional fruit were needed to fill a 90 pound box because of HLB in 2014-15.

A 20 percent treatment improvement in fruit size would lead to 4.6 fewer fruit per box (239.4 fruit/box), across 250 boxes per acre, for a total of 1,150 pieces, and at 239.4 fruit/box, this would add 4.8 boxes per acre. **The per-acre economic benefit of a 20 percent change in fruit size reduction would lead to 4.8 boxes x $12.09 (on-tree price, 2014-15) or $58.03 per acre. Across all orange acreage (441,628 acres), this benefit would be 2,119,814 additional boxes of oranges, and $25,628,556 per season for just this minor improvement to fruit size.**

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A 50 percent treatment improvement in fruit size reduction would similarly lead to 11.5 fewer fruit needed to fill a 90 pound box (232.5 fruit), across 250 boxes per acre, for a total of 2,875 pieces, and at 232.5 fruit/box, that improves yield by 12.4 boxes per acre. **The per-acre economic benefit of a 50 percent change in fruit size reduction would therefore lead to 12.4 additional boxes x $12.09, or $149.50 per acre. Across all orange acreage, this would add 5,343,699 boxes of yield worth $64,605,321 per season at 2014-15 prices.**

Similar calculations could be developed for non-orange varieties, and additional value could be calculated for considering fresh fruit value-added for the portion of the crop that is marketed fresh.

Both of the above improvements to orange yields are possible within the existing crop load of fruit, and reflect within season improvements that could occur with effective bactericidal treatment. Additional value could be obtained with expected improvements in fruit quality (brix/acid ration, pounds solids and flavor-impacting components. These benefits are not included in the size and fruit drop considerations above.

Improved annual production (successive years): In crop years following application of the emergency treatments, it is expected that restored tree health would lead to higher fruit set and increased yields above and beyond the benefits discussed above.

Calculations of the value of this for varying rates of improved yield are:

> Five percent yield response would increment yield of 250 boxes to 262.5 per acre, or an increase of $151.13 per acre. **The all-orange impact would be 5,520,350 boxes and $66,736.800 per season, the same benefit (additive) to the reduction in fruit drop.**
>
> 10 percent yield response would increment yield of 250 boxes by 25 boxes per acre, or $302.25. **Across all orange acres, this 10% improvement in current tree productivity would add 11,040,700 boxes of fruit and an economic benefit of $133,482,063 per season.**
>
> 25 percent yield response nets 62.5 boxes per acre additional fruit, or $755.63 per acre benefit. Across all orange acreage, this estimated benefit is 27,601,750 boxes, or when added to 2014-15 season yields, 124,401,750 boxes per season. **The estimated economic value of the additional production improvement of 25 percent is $333,705,158 per season.**
>
> The actual benefit can be approximated by adding the improvement in fruit drop reduction, increased fruit size, and finally the gain in production that treatment to reduce *C*Las titer in infected trees might bring. Again, these calculations represent oranges and the acreage currently dedicated to this major element of the industry. Similar composite benefits could be calculated.

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Using the minimal improvements calculated above (20% reduction in fruit drop, 20% improvement in fruit size reduction and 5% production increase in new crop) the economic benefit calculated for the orange acreage in Florida is $66,743,240 + $25,628,556 + $66,736,800 or $159,108,596 per season.

Finally, the treatment benefits would encourage new plantings, and the new benefit would then by be multiplied as new plantings come into production.

From:	Hill, Shaunta <Hill.Shaunta@epa.gov>
To:	Patel, Jean (CDC); Craig, Michael R (CDC); Harbottle, Heather; Gilbert, Jeffrey M; Wan, Ellen (CDC)
CC:	Jennings, Susan; Kough, John; Chandgoyal, Tara; Hicks, Karen; Blackwell, Ian
Sent:	4/19/2016 6:12:47 PM
Subject:	Final meeting minutes 2-10-16 CDC-EPA-FDA teleconference
Attachments:	Meeting minutes_02102016_EPA-CDC-FDA_Final_031616.pdf; Sec 3 grpfrt_tomato strep 152.pdf; Section 18 citrus 152 review_final.pdf

Hello everyone,
I just realized that I neglected to send the final meeting minutes to everyone concerning our Feb 2016 teleconference. Please see the final version which is attached. I am also including the final 152 reviews for the citrus section 18 (FL) and grapefruit/tomato section 3.

Thank you all for your inputs.

Regards,
****

Shaunta Hill-Hammond, Ph. D.
Acting Ombudsman
Antimicrobials Division, 7510P
Office of Pesticide Programs
U.S. Environmental Protection Agency
Washington, DC 20460
Tel: 703.347.8961

From:	Jennings, Susan <Jennings.Susan@epa.gov>
To:	Carl Schultze; Julius Fajardo; Harbottle, Heather; Patel, Jean (CDC); Gilbert, Jeffrey M; Craig, Michael R (CDC); Rose Hammond
CC:	Conrath, Andrea B; Maignan, Tawanda; Johnson, Marion
Sent:	12/19/2016 3:39:39 PM
Subject:	FW: Antibiotic - Sec18 Protocols for Resistance Testing; also use and efficacy information
Importance:	High
Attachments:	_AgroSource 2017 THS18_Resistance Monitoring Protocol (v 2) (2).pdf; 12-5-16 recd from FDACS THS18 Monitoring Protocol -- for review.docx; NuFarm Antibiotic Resistance Monitoring Protocol - Oxytetracycline in Citrus Sec18.pdf

Hi All,

Attached are the protocols that we discussed last week. I apologize for not sending these out sooner. Tawanda or Andrea, cc:'d above, will contact you shortly about getting your feedback

Attachments are: (Andrea, if you want them to see any other materials, please forward. No one in the workgroup is cleared for CBI)

1. AgroSource protocol
2. Nufarm protocol
3. A draft rec'd from FDACS on 12-5-16 of an overall "generic" protocol they have developed for resistance monitoring.

Any questions or comments, please Respond All.

Thanks,

Susan.

From: Jennings, Susan <Jennings.Susan@epa.gov>
To: Harbottle, Heather; Gilbert, Jeffrey M; Julius Fajardo; Rose Hammond
CC: Johnson, Hope; Garvie, Heather; Patel, Jean (CDC); Craig, Michael R (CDC)
Sent: 8/1/2017 12:54:28 PM
Subject: FW: comments from CDC

Hello all,

Thanks for your comments. Below is what we've received from CDC.

Thanks to all,

Susan.

From: Patel, Jean (CDC/OID/NCEZID) [mailto:vzp4@cdc.gov]
Sent: Friday, July 28, 2017 11:35 AM
To: Johnson, Hope <Johnson.Hope@epa.gov>
Cc: Jennings, Susan <Jennings.Susan@epa.gov>; Craig, Michael R. (CDC/OID/NCEZID) <bez7@cdc.gov>
Subject: comments from CDC

Sorry for being a bit late.

Streptomycin & Tetracycline

B5

From: Johnson, Hope [mailto:Johnson.Hope@epa.gov]
Sent: Thursday, July 20, 2017 10:54 AM
To: Sow, Fatima <Sow.Fatima@epa.gov>; Jennings, Susan <Jennings.Susan@epa.gov>; Kough, John <Kough.John@epa.gov>; Collins, Samantha <collins.samantha@epa.gov>; Chandgoyal, Tara <Chandgoyal.Tara@epa.gov>; Garvie, Heather <Garvie.Heather@epa.gov>; Giles-Parker, Cynthia <Giles-

Parker.Cynthia@epa.gov>; Carl Schultze <Carl.P.Schulze@aphis.usda.gov>; Julius Fajardo <Julius.Fajardo@ARS.USDA.GOV>; Harbottle, Heather (FDA/CVM) <Heather.Harbottle@fda.hhs.gov>; Patel, Jean (CDC/OID/NCEZID) <vzp4@cdc.gov>; Gilbert, Jeffrey M (FDA/CVM) <Jeff.Gilbert@fda.hhs.gov>; Craig, Michael R. (CDC/OID/NCEZID) <bez7@cdc.gov>; Rose Hammond <Rose.Hammond@ARS.USDA.GOV>
Cc: Cook, Colwell <cook.colwell@epa.gov>; Britton, Cathryn <Britton.Cathryn@epa.gov>; Kaul, Monisha <Kaul.Monisha@epa.gov>
Subject: RE: Federal interagency Antibiotic Resistance Call

Thank you all again for your participation today on the call. Attached are all the Resistance Review documents for your review in one place. Our BEAD division is determining whether or not we can provide the draft Benefits documents as an FYI. The Benefits documents include discussion on efficacy and alternatives. We will forward those documents to you if we can as soon as possible.

We would appreciate any comments you have- please send as soon as possible and hopefully no later than COB Wednesday 7/26/2017.
Please send any comments to Susan Jennings and cc: myself (Hope Johnson) and Fatima Sow.

Again, please note that we are in the Risk Management stage of the review. In the coming few weeks, we will begin briefings for our Management along with drafting the Proposed Decision documents for each AI (active ingredient) in preparation for the Public Process. We hope to begin the Public Process by the beginning of October of this year. It will include a 30 day comment period and allows the public to look at all supporting documents associated with the Proposed Decision (Health Effects Division risk assessment, Environmental Fate and Effects Division risk assessment, Biological and Economic Analysis Division Benefits assessment, Resistance Review (former 152), proposed labels). The Proposed Decision will discuss any mitigation we are proposing for that specific AI's new use.

After the comment period has closed, the Agency responds to comments received and incorporates these responses along with any revisions to the Proposed Decision into a Final Decision document. This is then uploaded to the docket, the Registrations are signed, and the Final Rule is published establishing tolerances. We are striving to meet a January 2018 timeframe for the Final Decisions.

Please feel free to contact me if you have questions on the process.

Thank you,

Hope A. Johnson
Product Manager 21
U.S. Environmental Protection Agency
Office of Pesticide Programs
Registration Division
Fungicide Branch
Phone: 703-305-5410
Mail Code 7505P

From: Johnson, Hope
Sent: Thursday, July 20, 2017 8:18 AM
To: Sow, Fatima <Sow.Fatima@epa.gov>; Jennings, Susan <Jennings.Susan@epa.gov>; Kough, John <Kough.John@epa.gov>; Collins, Samantha <collins.samantha@epa.gov>; Chandgoyal, Tara <Chandgoyal.Tara@epa.gov>; Garvie, Heather <Garvie.Heather@epa.gov>; Giles-Parker, Cynthia <Giles-

Parker.Cynthia@epa.gov>; Carl Schultze <Carl.P.Schulze@aphis.usda.gov>; Julius Fajardo <Julius.Fajardo@ARS.USDA.GOV>;Heather.Harbottle@fda.hhs.gov; Jean Patel <vzp4@cdc.gov>;Jeff.Gilbert@fda.hhs.gov; Michael Craig <bez7@cdc.gov>; Rose Hammond <Rose.Hammond@ARS.USDA.GOV>
Cc: Cook, Colwell <cook.colwell@epa.gov>; Britton, Cathryn <Britton.Cathryn@epa.gov>
Subject: RE: Federal interagency Antibiotic Resistance Call

The original streptomycin grapefruit/tomato 152 review is attached here. Previously only the addendum was attached. This is the complete document .

Hope A. Johnson
Product Manager 21
U.S. Environmental Protection Agency
Office of Pesticide Programs
Registration Division
Fungicide Branch
Phone: 703-305-5410
Mail Code 7505P

From: Sow, Fatima
Sent: Wednesday, July 19, 2017 4:49 PM
To: Jennings, Susan <Jennings.Susan@epa.gov>; Kough, John <Kough.John@epa.gov>; Collins, Samantha <collins.samantha@epa.gov>; Chandgoyal, Tara <Chandgoyal.Tara@epa.gov>; Garvie, Heather <Garvie.Heather@epa.gov>; Johnson, Hope <Johnson.Hope@epa.gov>; Giles-Parker, Cynthia <Giles-Parker.Cynthia@epa.gov>; Carl Schultze <Carl.P.Schulze@aphis.usda.gov>; Julius Fajardo <Julius.Fajardo@ARS.USDA.GOV>;Heather.Harbottle@fda.hhs.gov; Jean Patel <vzp4@cdc.gov>;Jeff.Gilbert@fda.hhs.gov; Michael Craig <bez7@cdc.gov>; Rose Hammond <Rose.Hammond@ARS.USDA.GOV>
Subject: RE: Federal interagency Antibiotic Resistance Call

Documents to be discussed are attached.

-----Original Appointment-----
From: Jennings, Susan
Sent: Monday, June 19, 2017 10:19 AM
To: Jennings, Susan; Kough, John; Collins, Samantha; Chandgoyal, Tara; Garvie, Heather; Johnson, Hope; Giles-Parker, Cynthia; Carl Schultze; Julius Fajardo;Heather.Harbottle@fda.hhs.gov; Jean Patel;Jeff.Gilbert@fda.hhs.gov; Michael Craig; Rose Hammond
Cc: Sow, Fatima
Subject: Federal interagency Antibiotic Resistance Call
When: Thursday, July 20, 2017 8:00 AM-10:00 AM (UTC-05:00) Eastern Time (US & Canada).
Where: Conference call # 866-299-3188, code 7063558524

Documents to be discussed are attached to this invitation.

This is just a hold until we find a time that works for Federal Partners. Final meeting will be scheduled for 2 hours (but may be shorter).

From: Jennings, Susan <Jennings.Susan@epa.gov>
To: Gilbert, Jeffrey M; Harbottle, Heather
CC: Manupella, Matthew
Sent: 11/16/2016 7:42:16 PM
Subject: Link for FDA Doc on anti-microbial resistance

Jeff and Heather,

We cannot recall exactly which FDA document that you were referring to for a statement on antimicrobial resistance.

Could you please point us in the right direction?

Thanks,

Susan.

Susan Jennings
Senior Advisor for Public Health
Office of Pesticide Programs
(706) 355-8574 (office)
(703) 216-8627 (cell)

From: Jennings, Susan <Jennings.Susan@epa.gov>
To: Patel, Jean (CDC); Carl Schultze; Fajardo, Julius; Harbottle, Heather; Gilbert, Jeffrey M; Craig, Michael R (CDC); Rose Hammond
Sent: 10/24/2016 2:58:28 PM
Subject: RE: Action Items from AR Interagency Meeting

Great, thanks for the feedback. Looks like EPA can also participate in the statement.

Just leaves USDA and FDA?

From: Patel, Jean (CDC/OID/NCEZID) [mailto:vzp4@cdc.gov]
Sent: Thursday, October 20, 2016 4:52 PM
To: Jennings, Susan <Jennings.Susan@epa.gov>; Carl Schultze <Carl.P.Schulze@aphis.usda.gov>; Fajardo, Julius <Julius.Fajardo@ARS.USDA.GOV>; Harbottle, Heather (FDA/CVM) <Heather.Harbottle@fda.hhs.gov>; Gilbert, Jeffrey M (FDA/CVM) <Jeff.Gilbert@fda.hhs.gov>; Craig, Michael R. (CDC/OID/NCEZID) <bez7@cdc.gov>; Rose Hammond <Rose.Hammond@ARS.USDA.GOV>
Cc: Johnson, Marion <Johnson.Marion@epa.gov>; Maignan, Tawanda <Maignan.Tawanda@epa.gov>; Giles-Parker, Cynthia <Giles-Parker.Cynthia@epa.gov>; Johnson, Marion <Johnson.Marion@epa.gov>; Garvie, Heather <Garvie.Heather@epa.gov>; Jones, Arnet <Jones.Arnet@epa.gov>; Chandgoyal, Tara <Chandgoyal.Tara@epa.gov>; Yourman, Leonard <Yourman.Leonard@epa.gov>; Britton, Cathryn <Britton.Cathryn@epa.gov>; Manupella, Matthew <Manupella.Matthew@epa.gov>; Leshin, Jonathan <Leshin.Jonathan@epa.gov>; Collins, Samantha <collins.samantha@epa.gov>; Conrath, Andrea B <Conrath.Andrea@epa.gov>; Kaul, Monisha <Kaul.Monisha@epa.gov>; Herndon, George <Herndon.George@epa.gov>; Kough, John <Kough.John@epa.gov>
Subject: RE: Action Items from AR Interagency Meeting

Susan – A brief update from the CDC:

1. **B5** I hope to have more information soon
2. CDC can participate in a joint statement

All the best,

Jean

From: Jennings, Susan [mailto:Jennings.Susan@epa.gov]
Sent: Friday, September 30, 2016 11:08 AM
To: Carl Schultze <Carl.P.Schulze@aphis.usda.gov>; Fajardo, Julius <Julius.Fajardo@ARS.USDA.GOV>; Harbottle, Heather (FDA/CVM) <Heather.Harbottle@fda.hhs.gov>; Patel, Jean (CDC/OID/NCEZID) <vzp4@cdc.gov>; Gilbert, Jeffrey M (FDA/CVM) <Jeff.Gilbert@fda.hhs.gov>; Craig, Michael R. (CDC/OID /NCEZID) <bez7@cdc.gov>; Rose Hammond <Rose.Hammond@ARS.USDA.GOV>
Cc: Johnson, Marion <Johnson.Marion@epa.gov>; Maignan, Tawanda <Maignan.Tawanda@epa.gov>; Giles-Parker, Cynthia <Giles-Parker.Cynthia@epa.gov>; Johnson, Marion <Johnson.Marion@epa.gov>; Garvie, Heather <Garvie.Heather@epa.gov>; Jones, Arnet <Jones.Arnet@epa.gov>; Chandgoyal, Tara <Chandgoyal.Tara@epa.gov>; Yourman, Leonard <Yourman.Leonard@epa.gov>; Britton, Cathryn <Britton.Cathryn@epa.gov>; Manupella, Matthew <Manupella.Matthew@epa.gov>; Leshin, Jonathan <Leshin.Jonathan@epa.gov>; Collins, Samantha <collins.samantha@epa.gov>; Conrath, Andrea B <Conrath.Andrea@epa.gov>; Kaul, Monisha <Kaul.Monisha@epa.gov>; Herndon, George <Herndon.George@epa.gov>; Kough, John <Kough.John@epa.gov>
Subject: Action Items from AR Interagency Meeting

Hi,

Thanks to all for helping to make Wednesday's meeting so productive. I have attached a copy of the meeting

minutes. If everyone could please review and make sure that I have not overlooked, misinterpreted, or erred on anything I would truly appreciate it.

The minutes detail the action items (highlighted with ***), but for clarity I am also going to include them here (again, please let me know if this list can be improved):

B5

I'm looking forward to working with all of you on this.

Thanks,

Susan.

Susan Jennings
Senior Advisor for Public Health
Office of Pesticide Programs
(706) 355-8574 (office)
(703) 216-8627 (cell)

From: Jennings, Susan <Jennings.Susan@epa.gov>
To: Harbottle, Heather; Gilbert, Jeffrey M
Sent: 1/17/2017 1:25:14 PM
Subject: RE: data from drug arm??

Let's go with all human pathogens. We have workers to consider too.

Thanks,

Susan.

From: Harbottle, Heather [mailto:Heather.Harbottle@fda.hhs.gov]
Sent: Friday, January 13, 2017 3:12 PM
To: Jennings, Susan <Jennings.Susan@epa.gov>; Gilbert, Jeffrey M <Jeff.Gilbert@fda.hhs.gov>
Subject: RE: data from drug arm??

Hi Susan,
Ok, so this is what NARMS offers: https://www.cdc.gov/narms/reports/

E. coli, Salmonella enterica serotypes, and Campylobacter, and Shigella data isolated from humans in all 50 states. They are tested against tetracycline and streptomycin (not oxy tet). The most recent report was published for 2014 isolates. There's also data on Vibrios, but only for tet, not strep or oxytet.

We can reach out asap to the FDA drug arm; however, these are old drugs and likely any data they had on resistance is over 30 years old from the original approval package. We can of course ask if any newer data has been submitted in more recent packages (if any have been submitted for new drug indications) but I'm thinking that is unlikely. When we do ask, are you looking for any resistance data for any human pathogen that might have been submitted, or those which may be more likely to be in the environment (commensals like E. coli)?

I'll send an email out that way asap when I hear back from you. J

Thanks,
H

From: Jennings, Susan [mailto:Jennings.Susan@epa.gov]
Sent: Friday, January 13, 2017 2:55 PM
To: Harbottle, Heather; Gilbert, Jeffrey M
Subject: RE: data from drug arm??

Yes. Human isolates. The third is oxytetracycline.

Thanks,

Susan.

From: Harbottle, Heather [mailto:Heather.Harbottle@fda.hhs.gov]
Sent: Friday, January 13, 2017 2:53 PM
To: Jennings, Susan <Jennings.Susan@epa.gov>; Gilbert, Jeffrey M <Jeff.Gilbert@fda.hhs.gov>
Subject: RE: data from drug arm??

Hi Susan,

B5

B5 Are we looking for something different?

Thanks!
Heather

From: Jennings, Susan [mailto:Jennings.Susan@epa.gov]
Sent: Friday, January 13, 2017 2:50 PM
To: Gilbert, Jeffrey M; Harbottle, Heather
Subject: data from drug arm??

Hi Jeff and Heather,

According to my notes you were going to check with FDA's drug arm to determine whether there was any data in-house for the three compounds? We're particularly interested in any data that could address the resistance issue.

Thanks,

Susan.

From:	Patel, Jean (CDC/OID/NCEZID) <vzp4@cdc.gov>
To:	Jennings, Susan; Carl Schultze; Julius Fajardo; Harbottle, Heather; Gilbert, Jeffrey M; Craig, Michael R (CDC); Rose Hammond; Avery, Lacey (CDC*)
Sent:	12/30/2016 2:20:47 PM
Subject:	RE: detailed outline attached for joint statement
Attachments:	detailed outline 12 14 16CDCedits.docx

Susan

Attached is a version with some suggestions from CDC. The revisions address comments I have included in the document. In addition, the revisions are meant to make the document evergreen (i.e., will not be outdated as science progresses).

Thanks for considering these suggestions.

Jean

From: Jennings, Susan [mailto:Jennings.Susan@epa.gov]
Sent: Friday, December 16, 2016 9:14 AM
To: Carl Schultze <Carl.P.Schulze@aphis.usda.gov>; Julius Fajardo <Julius.Fajardo@ARS.USDA.GOV>; Harbottle, Heather (FDA/CVM) <Heather.Harbottle@fda.hhs.gov>; Patel, Jean (CDC/OID/NCEZID) <vzp4@cdc.gov>; Gilbert, Jeffrey M (FDA/CVM) <Jeff.Gilbert@fda.hhs.gov>; Craig, Michael R. (CDC/OID /NCEZID) <bez7@cdc.gov>; Rose Hammond <Rose.Hammond@ARS.USDA.GOV>
Subject: detailed outline attached for joint statement

Hi all,

Attached is the detailed outline that we discussed on Wednesday. If you could all read through it and send comments back, using REPLY ALL, that would be great.

Our goal was to have this finalized by early next week.

Thanks,

Susan.

From: Jennings, Susan <Jennings.Susan@epa.gov>
To: Harbottle, Heather; Gilbert, Jeffrey M
Sent: 10/11/2017 12:09:49 PM
Subject: RE: Draft Decision Document Interagency discussion

A response to a petition for approval/registration of new uses of oxytetracycline. We'll be issuing it shortly.

I'm really just looking to make sure that your web language is still current (I quoted from the web to make sure we don't need concurrence).

Please let me know if you have any more questions.

Thanks,

Susan.

From: Harbottle, Heather [mailto:Heather.Harbottle@fda.hhs.gov]
Sent: Tuesday, October 10, 2017 6:15 PM
To: Jennings, Susan <Jennings.Susan@epa.gov>; Gilbert, Jeffrey M <Jeff.Gilbert@fda.hhs.gov>
Subject: RE: Draft Decision Document Interagency discussion

Hi Susan,
We'll get back to you asap. When is your deadline? Also what is the draft risk management decision? Do you mean a response to a petition for approval/registration or a more general agency document?
Thanks!
Heather

From: Jennings, Susan [mailto:Jennings.Susan@epa.gov]
Sent: Tuesday, October 10, 2017 9:49 AM
To: Patel, Jean (CDC) <vzp4@cdc.gov>; Harbottle, Heather <Heather.Harbottle@fda.hhs.gov>; Gilbert, Jeffrey M <Jeff.Gilbert@fda.hhs.gov>; Rose Hammond <Rose.Hammond@ARS.USDA.GOV>; Julius Fajardo <Julius.Fajardo@ARS.USDA.GOV>
Cc: Garvie, Heather <Garvie.Heather@epa.gov>; Johnson, Hope <Johnson.Hope@epa.gov>
Subject: Draft Decision Document Interagency discussion

Hi all,

Below is some language that we would like to include in the draft risk management decision. I pulled the language for each of your agencies from the web, link is provided at the end of each paragraph.

Could each of you please read through this and let me know if there are any issues? I want to stick as closely to web language as possible since we don't have time for interagency concurrence.

Thanks,

Susan.

==========
Other agencies in the federal government (CDC, FDA, USDA) are aware of the potential for resistance to develop from the use of antibiotics in agriculture and have been working within their areas of expertise to address the problem. CDC cites "Improving Antibiotic Prescribing/Stewardship" as one of

its Four Core Actions to Fight Resistance. CDC believes antibiotic stewardship is the "commitment to always use antibiotics appropriately and safely -- only when they are needed to treat disease, and to choose the right antibiotics and to administer them in the right way in every case." For more on CDC's views, see https://www.cdc.gov/drugresistance/about.html/.

FDA is committed to further advancing antimicrobial stewardship by focusing on the following key initiatives: (1) aligning antimicrobial drug products with the principles of antimicrobial stewardship in veterinary settings; (2) supporting efforts to foster stewardship of antimicrobials in veterinary settings; and (3) assessing the impact of strategies intended to curb the emergence of antimicrobial resistance associated with the use of antimicrobial drugs in veterinary settings. For more on FDA's views, see https://www.fda.gov/AnimalVeterinary/SafetyHealth/AntimicrobialResistance/JudiciousUseofAntimicrobials/ucm535158.htm]

USDA is funding research where the focus addresses studying the role of agriculture in antimicrobial resistance, reducing potential negative impacts from the use of antibiotics, and identifying alternative strategies for mitigating AMR in the food chain. The goal is to reduce or negate any potential negatively adverse impact of antimicrobials used in agriculture that may have potentially adverse effects on the treatment of human diseases. For more on USDA's views, see https://nifa.usda.gov/antimicrobial-resistance]

EPA believes that the management of pesticide resistance development is an important part of sustainable pest management and, in conjunction with alternative pest management strategies and IPM programs, can make significant contributions to reducing risks to humans and the environment. In support of these goals, EPA is assessing the potential development of antibiotic resistance as an adverse effect under FIFRA.

==========

From:	Hill, Shaunta <Hill.Shaunta@epa.gov>
To:	Harbottle, Heather; Jennings, Susan
CC:	Gilbert, Jeffrey M
Sent:	2/10/2016 3:02:11 PM
Subject:	RE: EPA - Pending antibiotic request for Streptomycin, request for a teleconference
Attachments:	6. FL Citrus Greening Section 18 Antimicrobial Request petition and lett....pdf; 7. FDA 152 FireWall Resistance Risk Assessment HLB and Canker 10-19-15.pdf; 8. FDA 152, FireLine Resistance Risk Assessment, 10-2-15.pdf

From: Hill, Shaunta
Sent: Wednesday, February 10, 2016 6:32 AM
To: 'Harbottle, Heather' <Heather.Harbottle@fda.hhs.gov>; Jennings, Susan <Jennings.Susan@epa.gov>
Cc: Gilbert, Jeffrey M <Jeff.Gilbert@fda.hhs.gov>
Subject: EPA - Pending antibiotic request for Streptomycin, request for a teleconference

This is the second email for Wednesday's teleconference.
If you have any questions / trouble with the files, please let me know.
Thank you

Regards,
****

Shaunta Hill-Hammond, Ph. D.
Plant Pathologist
U.S. EPA: Office of Chemical Safety and Pollution Prevention
Registration Division/Fungicide Branch (PYS)
1200 Pennsylvania Avenue, NW (7505P)
Washington, DC 20460

Tel: 703.347.8961 I Fax: 703.305.6920
E-mail: hill.shaunta@epa.gov
URL Address: www.epa.gov/pesticides

From: Harbottle, Heather [mailto:Heather.Harbottle@fda.hhs.gov]
Sent: Tuesday, February 09, 2016 4:58 PM
To: Hill, Shaunta <Hill.Shaunta@epa.gov>; Jennings, Susan <Jennings.Susan@epa.gov>
Cc: Gilbert, Jeffrey M <Jeff.Gilbert@fda.hhs.gov>
Subject: RE: EPA - Pending antibiotic request for Streptomycin, request for a teleconference

Hi Shaunta,
We'll be happy to call in. Is there a call in number and agenda yet for the teleconference tomorrow at 11am?
Thanks!
Heather

From: Hill, Shaunta [mailto:Hill.Shaunta@epa.gov]
Sent: Monday, February 08, 2016 12:16 PM
To: Harbottle, Heather; Jennings, Susan
Cc: Gilbert, Jeffrey M
Subject: RE: EPA - Pending antibiotic request for Streptomycin, request for a teleconference

Hello Heather,
We did meet during the IR-4 meeting. Happy to hear that you and Jeff will be joining our discussion.
The meeting agenda will be finalized shortly and I will forward it along with several reference documents for our discussion.
In the meantime, I wanted to provide some background information on pesticide registrations.

The type of registrations permitted under FIFRA (i.e. Section 3 and Section 18) can be found here: http://www.epa.gov/pesticide-registration/types-registrations-under-fifra

Information on the general registration process can be found here: http://www.epa.gov/pesticide-registration/pesticide-registration-manual-chapter-1-overview-requirements-pesticide

I hope you find this initial information helpful.
If you have any questions, please let me know.

Regards,
****
Shaunta Hill-Hammond, Ph. D.
Plant Pathologist
U.S. EPA: Office of Chemical Safety and Pollution Prevention
Registration Division/Fungicide Branch (PYS)
1200 Pennsylvania Avenue, NW (7505P)
Washington, DC 20460

Tel: 703.347.8961 | Fax: 703.305.6920
E-mail: hill.shaunta@epa.gov
URL Address: www.epa.gov/pesticides

From: Harbottle, Heather [mailto:Heather.Harbottle@fda.hhs.gov]
Sent: Friday, February 05, 2016 8:35 AM
To: Hill, Shaunta <Hill.Shaunta@epa.gov>; Jennings, Susan <Jennings.Susan@epa.gov>
Cc: Gilbert, Jeffrey M <Jeff.Gilbert@fda.hhs.gov>
Subject: FW: EPA - Pending antibiotic request for Streptomycin, request for a teleconference
Importance: High

Good morning Ms. Hill and Ms. Jennings,

My name is Heather Harbottle and I believe we met during the IR-4 Bacterial Challenges Mini-Summit meeting "Understanding the ABCs (Awareness of Bacterial Challenges) with Antibiotics In Crops" in September of 2014. As you may remember, I delivered a presentation regarding FDA's use of GFI #152 due to our extensive use of this guidance assessing risk for the use of antimicrobials in food producing animals. I've been asked by Bill Flynn and my team leader, Dr. Jeff Gilbert, to get in touch with you regarding your email below. Dr. Gilbert and I would be happy to attend the teleconference on Wednesday, and provide any assistance with GFI #152 as it pertains to your application for streptomycin or any other antimicrobial.

Please let us know how we can be of help.

Best,
Heather Harbottle

From: Hill, Shaunta [mailto:Hill.Shaunta@epa.gov]
Sent: Thursday, February 04, 2016 9:59 AM
To: Flynn, William T
Cc: Jennings, Susan
Subject: EPA - Pending antibiotic request for Streptomycin, request for a teleconference

Hello Dr. William;

My name is Shaunta Hill and I am a Risk Assessor/Plant Pathologist with EPA's Office of Pesticide Programs – Registration Division.
I received your name from Dr. Jean Patel at CDC as a potential contact.

As EPA manages antibiotics for pesticidal use, we are interested in accessing the resistance risk potential along with human and environmental risks. We have previously worked with CDC and FDA (via David White) utilizing the FDA Guidance for Industry #152 for this purpose.

We have a number of applications currently pending and have scheduled a teleconference for **Wednesday Feb 10 at 11 am** to begin discussions.
I am hopefully that you are available to participate in this discussion as FDA input is valued.
The primary application for consideration next week is Streptomycin sulfate use on grapefruit and tomatoes via FIFRA Section 3 Registration.

If you are available, I can provide additional background information in addition to our meeting agenda.
Should you have any questions, please let us know. I have cc'ed on this communication Susan Jennings, who serves as our Public Health Coordinator and is available to address questions on this meeting request as well.

Thank you for your time and I look forward to hearing from you.

Regards,
****
Shaunta Hill-Hammond, Ph. D.

Plant Pathologist
U.S. EPA: Office of Chemical Safety and Pollution Prevention
Registration Division/Fungicide Branch (PYS)
1200 Pennsylvania Avenue, NW (7505P)
Washington, DC 20460

Tel: 703.347.8961 | Fax: 703.305.6920
E-mail: hill.shaunta@epa.gov
URL Address: www.epa.gov/pesticides

From: Hill, Shaunta <Hill.Shaunta@epa.gov>
To: Harbottle, Heather
CC: Gilbert, Jeffrey M
Sent: 2/10/2016 4:09:19 PM
Subject: RE: EPA - Pending antibiotic request for Streptomycin, request for a teleconference

Wonderful !

From: Harbottle, Heather [mailto:Heather.Harbottle@fda.hhs.gov]
Sent: Wednesday, February 10, 2016 10:40 AM
To: Hill, Shaunta <Hill.Shaunta@epa.gov>
Cc: Gilbert, Jeffrey M <Jeff.Gilbert@fda.hhs.gov>
Subject: RE: EPA - Pending antibiotic request for Streptomycin, request for a teleconference

Got it!

From: Hill, Shaunta [mailto:Hill.Shaunta@epa.gov]
Sent: Wednesday, February 10, 2016 10:18 AM
To: Harbottle, Heather
Cc: Gilbert, Jeffrey M
Subject: FW: EPA - Pending antibiotic request for Streptomycin, request for a teleconference

Hello Heather,
Hopefully it works this time…

Please see the following files which are attached.
-4. EPA review memo (image2016-02-01)
- 5. Proposed label (080990-00003.20151123. revised Master Label)
- Meeting Agenda

From: Hill, Shaunta
Sent: Wednesday, February 10, 2016 10:04 AM
To: 'Gilbert, Jeffrey M' <Jeff.Gilbert@fda.hhs.gov>; 'Harbottle, Heather' <Heather.Harbottle@fda.hhs.gov>
Subject: FW: EPA - Pending antibiotic request for Streptomycin, request for a teleconference

Heather –
There are 6 files attached to this message (including the agenda).

From: Hill, Shaunta
Sent: Wednesday, February 10, 2016 6:31 AM
To: Jennings, Susan <Jennings.Susan@epa.gov>
Cc:
Subject: EPA - Pending antibiotic request for Streptomycin, request for a teleconference

Good Morning Heather and Jeff,
Please see the attached agenda and support files for our teleconference Wednesday – Feb 10, 2016 at 11 am.
The conference line information is noted on the agenda.

**Due to the file sizes, two emails will be sent.*

If you would not mind, could you please provide contact information and title for both you and Jeff.
Thank you

From: Harbottle, Heather [mailto:Heather.Harbottle@fda.hhs.gov]
Sent: Tuesday, February 09, 2016 4:58 PM
To: Hill, Shaunta <Hill.Shaunta@epa.gov>; Jennings, Susan <Jennings.Susan@epa.gov>
Cc: Gilbert, Jeffrey M <Jeff.Gilbert@fda.hhs.gov>
Subject: RE: EPA - Pending antibiotic request for Streptomycin, request for a teleconference

Hi Shaunta,
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Cc: Gilbert, Jeffrey M
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I hope you find this initial information helpful.
If you have any questions, please let me know.

Regards,

****

Shaunta Hill-Hammond, Ph. D.
Plant Pathologist
U.S. EPA: Office of Chemical Safety and Pollution Prevention
Registration Division/Fungicide Branch (PYS)
1200 Pennsylvania Avenue, NW (7505P)
Washington, DC 20460

Tel: 703.347.8961 | Fax: 703.305.6920
E-mail: hill.shaunta@epa.gov
URL Address: www.epa.gov/pesticides

From: Harbottle, Heather [mailto:Heather.Harbottle@fda.hhs.gov]
Sent: Friday, February 05, 2016 8:35 AM
To: Hill, Shaunta <Hill.Shaunta@epa.gov>; Jennings, Susan <Jennings.Susan@epa.gov>
Cc: Gilbert, Jeffrey M <Jeff.Gilbert@fda.hhs.gov>
Subject: FW: EPA - Pending antibiotic request for Streptomycin, request for a teleconference
Importance: High

Good morning Ms. Hill and Ms. Jennings,

My name is Heather Harbottle and I believe we met during the IR-4 Bacterial Challenges Mini-Summit meeting "Understanding the ABCs (Awareness of Bacterial Challenges) with Antibiotics In Crops" in September of 2014. As you may remember, I delivered a presentation regarding FDA's use of GFI #152 due to our extensive use of this guidance assessing risk for the use of antimicrobials in food producing animals. I've been asked by Bill Flynn and my team leader, Dr. Jeff Gilbert, to get in touch with you regarding your email below. Dr. Gilbert and I would be happy to attend the teleconference on Wednesday, and provide any assistance with GFI #152 as it pertains to your application for streptomycin or any other antimicrobial.

Please let us know how we can be of help.

Best,
Heather Harbottle

From: Hill, Shaunta [mailto:Hill.Shaunta@epa.gov]
Sent: Thursday, February 04, 2016 9:59 AM
To: Flynn, William T
Cc: Jennings, Susan
Subject: EPA - Pending antibiotic request for Streptomycin, request for a teleconference

Hello Dr. William;

My name is Shaunta Hill and I am a Risk Assessor/Plant Pathologist with EPA's Office of Pesticide Programs – Registration Division.

I received your name from Dr. Jean Patel at CDC as a potential contact.

As EPA manages antibiotics for pesticidal use, we are interested in accessing the resistance risk potential along with human and environmental risks. We have previously worked with CDC and FDA (via David White) utilizing the FDA Guidance for Industry #152 for this purpose.

We have a number of applications currently pending and have scheduled a teleconference for **Wednesday Feb 10 at 11 am** to begin discussions.
I am hopefully that you are available to participate in this discussion as FDA input is valued.
The primary application for consideration next week is Streptomycin sulfate use on grapefruit and tomatoes via FIFRA Section 3 Registration.

If you are available, I can provide additional background information in addition to our meeting agenda.
Should you have any questions, please let us know. I have cc'ed on this communication Susan Jennings, who serves as our Public Health Coordinator and is available to address questions on this meeting request as well.

Thank you for your time and I look forward to hearing from you.

Regards,
****

Shaunta Hill-Hammond, Ph. D.
Plant Pathologist
U.S. EPA: Office of Chemical Safety and Pollution Prevention
Registration Division/Fungicide Branch (PYS)
1200 Pennsylvania Avenue, NW (7505P)
Washington, DC 20460

Tel: 703.347.8961 I Fax: 703.305.6920
E-mail: hill.shaunta@epa.gov
URL Address: www.epa.gov/pesticides

From: Jennings, Susan <Jennings.Susan@epa.gov>
To: Harbottle, Heather; Cox, Edward M
CC: Friedlander, Lynn G; Gilbert, Jeffrey M
Sent: 2/2/2018 2:25:23 PM
Subject: RE: EPA request re: antimicrobials in humans

Thanks, you too.

From: Harbottle, Heather [mailto:Heather.Harbottle@fda.hhs.gov]
Sent: Friday, February 02, 2018 9:13 AM
To: Jennings, Susan <Jennings.Susan@epa.gov>; Cox, Edward M <Edward.Cox@fda.hhs.gov>
Cc: Friedlander, Lynn G <Lynn.Friedlander@fda.hhs.gov>; Gilbert, Jeffrey M <Jeff.Gilbert@fda.hhs.gov>
Subject: RE: EPA request re: antimicrobials in humans

Hi Susan,
Lynn Friedlander works in CVM, in my division. We estimate the acceptable daily intake for antimicrobial residues in animal tissues, and Lynn's group sets tolerances in that context. We only deal with edible animal tissues, so I'm not sure that Lynn is the person you may need. I've copied her on this email as well as Jeff.

If you are looking for residue exposure in the agricultural crops listed in the registrations, I'm not sure who in our Center for Food Safety and Applied Nutrition may work on that.

Have a good weekend,
Heather

From: Jennings, Susan [mailto:Jennings.Susan@epa.gov]
Sent: Friday, February 02, 2018 8:58 AM
To: Cox, Edward M <Edward.Cox@fda.hhs.gov>; Harbottle, Heather <Heather.Harbottle@fda.hhs.gov>
Subject: RE: EPA request re: antimicrobials in humans

Thanks.

We're looking to discuss the exposure from all sources: pesticide and from the therapeutic use combined. And you are correct, we are still working out what we would like for this round of discussions.

Two other people provided Lynn Friedlander as a name to contact. Once we've ironed out exactly what we're looking for (likely early next week) I'll contact both of you and we can work from there.

Thanks in advance for your help on this issue,

Susan.

Susan Jennings
Senior Advisor for Public Health
Office of Pesticide Programs
(706) 355-8574 (office)
(703) 216-8627 (cell)

From: Cox, Edward M [mailto:Edward.Cox@fda.hhs.gov]
Sent: Thursday, February 01, 2018 4:36 PM
To: Jennings, Susan <Jennings.Susan@epa.gov>; Harbottle, Heather <Heather.Harbottle@fda.hhs.gov>

Subject: RE: EPA request re: antimicrobials in humans

Hi Susan and Heather,

Thanks for your e-mails. I read through and took a quick look at the letter. I couldn't tell exactly what's needed here and it sounds like maybe you are still working to figure that out. We may be able to contribute depending on the assessment needed.

B5

If you need us, just let me know.

Thanks.
-Ed

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To: Harbottle, Heather <Heather.Harbottle@fda.hhs.gov>; Cox, Edward M <Edward.Cox@fda.hhs.gov>
Subject: RE: EPA request re: antimicrobials in humans

Thanks, Heather.

B5

Because of the tight timeframes, I am hoping to identify the right contact now so that we can move more quickly when needed.

Thank you for your help,

Susan.

Susan Jennings
Senior Advisor for Public Health
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(703) 216-8627 (cell)

From: Harbottle, Heather [mailto:Heather.Harbottle@fda.hhs.gov]
Sent: Thursday, February 01, 2018 2:14 PM
To: Cox, Edward M <Edward.Cox@fda.hhs.gov>; Jennings, Susan <Jennings.Susan@epa.gov>
Subject: EPA request re: antimicrobials in humans

Good afternoon Dr. Cox,
Susan Jennings from EPA has been leading a working group with regard to the registration of antimicrobials in agricultural crops (CVM has been consulting) and is looking for a contact at FDA who works with antimicrobial approvals for humans. She's tasked with setting a tolerance and has some questions about human therapeutic use of antimicrobials. I fear that if I try to explain further, I may not be correct in my explanation. I suggested she contact your group in hopes that someone there is the correct person and if not, you may know who would be the best person for her to contact.

Thanks for your help.

Best,

Heather Harbottle, Ph.D.
Microbiologist
Microbial Food Safety Team
Division of Human Food Safety
Office of New Animal Drug Evaluation
Center for Veterinary Medicine, FDA
240-402-0791

From: Jennings, Susan <Jennings.Susan@epa.gov>
To: Gilbert, Jeffrey M; Harbottle, Heather
Sent: 2/2/2018 2:24:53 PM
Subject: RE: EPA request re: antimicrobials in humans

OK. Thank you both for your help.

From: Gilbert, Jeffrey M [mailto:Jeff.Gilbert@fda.hhs.gov]
Sent: Friday, February 02, 2018 9:16 AM
To: Harbottle, Heather <Heather.Harbottle@fda.hhs.gov>; Jennings, Susan <Jennings.Susan@epa.gov>
Subject: RE: EPA request re: antimicrobials in humans

I discussed with Lynn – she may give you a call, Susan. We may need to involve the Toxicology Team, as they may have been the genesis of that letter. Stay tuned……

From: Harbottle, Heather
Sent: Friday, February 02, 2018 9:13 AM
To: Jennings, Susan <Jennings.Susan@epa.gov>; Cox, Edward M <Edward.Cox@fda.hhs.gov>
Cc: Friedlander, Lynn G <Lynn.Friedlander@fda.hhs.gov>; Gilbert, Jeffrey M <Jeff.Gilbert@fda.hhs.gov>
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Susan Jennings
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Office of Pesticide Programs
(706) 355-8574 (office)

(703) 216-8627 (cell)

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-Ed

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Thank you for your help,

Susan.

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Thanks for your help.

Best,

Heather Harbottle, Ph.D.
Microbiologist
Microbial Food Safety Team
Division of Human Food Safety
Office of New Animal Drug Evaluation
Center for Veterinary Medicine, FDA
240-402-0791

From: Patel, Jean (CDC/OID/NCEZID) <vzp4@cdc.gov>
To: Jennings, Susan; Gilbert, Jeffrey M
Sent: 8/29/2016 2:37:51 PM
Subject: RE: EPA's Interagency AR Meeting

I may be able to meet on Sept 28th. Would that day work? If yes, I will check to see if I can adjust my travel arrangements.

From: Jennings, Susan [mailto:Jennings.Susan@epa.gov]
Sent: Monday, August 29, 2016 10:31 AM
To: Gilbert, Jeffrey M (FDA/CVM) <Jeff.Gilbert@fda.hhs.gov>; Patel, Jean (CDC/OID/NCEZID) <vzp4@cdc.gov>
Subject: RE: EPA's Interagency AR Meeting

Since Jean and I are both going to be in DC that week, it seems like a great opportunity to piggy back on this meeting as well.

I've written back to Jean and hopefully we'll find a day that works.

Thanks,

Susan.

From: Gilbert, Jeffrey M [mailto:Jeff.Gilbert@fda.hhs.gov]
Sent: Sunday, August 28, 2016 10:23 AM
To: Jennings, Susan <Jennings.Susan@epa.gov>; Patel, Jean (CDC) <vzp4@cdc.gov>
Subject: RE: EPA's Interagency AR Meeting

29th best, either OK – but looks like Jean is busy – options?

From: Jennings, Susan [mailto:Jennings.Susan@epa.gov]
Sent: Thursday, August 25, 2016 3:08 PM
To: Gilbert, Jeffrey M; Patel, Jean (CDC)
Subject: EPA's Interagency AR Meeting

Hi,

I would like to hold the meeting sometime during the week of 9/26, preferably Wed or Th, the 28th or 29th?

Will either of these days work for you both?

Thanks,

Susan.

Susan Jennings
Senior Advisor for Public Health
Office of Pesticide Programs
(706) 355-8574 (office)
(703) 216-8627 (cell)

From: Jennings, Susan <Jennings.Susan@epa.gov>
To: Harbottle, Heather
CC: Gilbert, Jeffrey M
Sent: 3/16/2018 3:24:33 PM
Subject: RE: FDA Input on Tolerance Decisions for Oxytetracycline and Streptomycin - Revised FDA response

That's ok. Thanks for trying. Ed responded and I'll be getting back to him shortly.

From: Harbottle, Heather [mailto:Heather.Harbottle@fda.hhs.gov]
Sent: Friday, March 16, 2018 11:08 AM
To: Jennings, Susan <Jennings.Susan@epa.gov>
Cc: Gilbert, Jeffrey M <Jeff.Gilbert@fda.hhs.gov>
Subject: RE: FDA Input on Tolerance Decisions for Oxytetracycline and Streptomycin - Revised FDA response

Oh no! B5

B5

Has anyone responded from Ed's group?

Sorry Susan, B5

Best,
Heather

From: Jennings, Susan [mailto:Jennings.Susan@epa.gov]
Sent: Friday, March 16, 2018 11:02 AM
To: Harbottle, Heather <Heather.Harbottle@fda.hhs.gov>
Subject: RE: FDA Input on Tolerance Decisions for Oxytetracycline and Streptomycin - Revised FDA response

Yes, but the times are changing and it won't work.

Thanks for trying.

From: Harbottle, Heather [mailto:Heather.Harbottle@fda.hhs.gov]
Sent: Friday, March 16, 2018 11:00 AM
To: Jennings, Susan <Jennings.Susan@epa.gov>
Subject: FW: FDA Input on Tolerance Decisions for Oxytetracycline and Streptomycin - Revised FDA response

Hi Susan,
Did you see the attached edited letter that does not reference CDER at all? We are hoping that this will work for you now. B5

Thanks,
Heather

From: Harbottle, Heather
Sent: Thursday, March 15, 2018 3:19 PM

To: 'Jennings, Susan' <Jennings.Susan@epa.gov>; Long, Charli <Charli.Long-Medrano@fda.hhs.gov>
Cc: Goodis, Michael <Goodis.Michael@epa.gov>; Gilbert, Jeffrey M <Jeff.Gilbert@fda.hhs.gov>; Giles-Parker, Cynthia <Giles-Parker.Cynthia@epa.gov>; Johnson, Hope <Johnson.Hope@epa.gov>
Subject: RE: FDA Input on Tolerance Decisions for Oxytetracycline and Streptomycin - Revised FDA response

Dear Dr. Jennings,
Per your February 27, 2018 request, we have attached an edited response to your request letter. We hope this letter satisfies your request, as it is modeled after our previous response to your request in 2006. Please feel free to contact us with any further questions.

B5

https://www.fda.gov/downloads/AnimalVeterinary/GuidanceComplianceEnforcement/GuidanceforIndustry/UCM124674.pdf

We look forward to collaborating with you in the future in this respect and regarding the risk for the development of antimicrobial resistance.

Best regards,
Heather Harbottle

Heather Harbottle, Ph.D.
Microbiologist
Microbial Food Safety Team
Division of Human Food Safety
Office of New Animal Drug Evaluation
Center for Veterinary Medicine, FDA
240-402-0791

From: Jennings, Susan [mailto:Jennings.Susan@epa.gov]
Sent: Tuesday, February 27, 2018 3:42 PM
To: Long, Charli <Charli.Long-Medrano@fda.hhs.gov>
Cc: Goodis, Michael <Goodis.Michael@epa.gov>; Gilbert, Jeffrey M <Jeff.Gilbert@fda.hhs.gov>; Harbottle, Heather <Heather.Harbottle@fda.hhs.gov>; Giles-Parker, Cynthia <Giles-Parker.Cynthia@epa.gov>; Johnson, Hope <Johnson.Hope@epa.gov>
Subject: FDA Input on Tolerance Decisions for Oxytetracycline and Streptomycin

Dr. Long:

Thank you for allowing Drs. Jeffrey Gilbert and Heather Harbottle to collaborate with us on our registrations for new uses for antibiotic pesticides. They have provided valuable input into our draft decisions and analyses and, along with our colleagues at CDC and USDA, helped EPA's decision be more robust and balanced.

While working on these decisions, **B5**
B5
B5 EPA is required by the Federal Food, Drug and Cosmetic Act to consider this information when establishing tolerances on agricultural

commodities. The attached letter, signed by Michael Goodis (Director, Registration Division) provides more information and serves as the official request. If it all possible, we would appreciate receiving a response to this letter by March 7, 2018. If this is not possible, please let us know so that we can readjust our schedules accordingly.

Again, thank you for your time and consideration, as well as your division's continued collaboration on antibiotic pesticide activities.

Susan Jennings
Senior Advisor for Public Health
Office of Pesticide Programs
(706) 355-8574 (office)
(703) 216-8627 (cell)

From: Hill, Shaunta <Hill.Shaunta@epa.gov>
To: Patel, Jean (CDC); Harbottle, Heather; Craig, Michael R (CDC); Gilbert, Jeffrey M
Sent: 3/2/2016 5:14:23 PM
Subject: RE: Follow-up: Streptomycin and Oxytetracycline pesticide requests pending with EPA

Hello Jean,
Your comments by Monday morning will be fine.
Thank you
-Shaunta

From: Patel, Jean (CDC/OID/NCEZID) [mailto:vzp4@cdc.gov]
Sent: Wednesday, March 02, 2016 12:11 PM
To: Hill, Shaunta <Hill.Shaunta@epa.gov>; Harbottle, Heather (FDA/CVM) <Heather.Harbottle@fda.hhs.gov>; Craig, Michael R. (CDC/OID/NCEZID) <bez7@cdc.gov>; Gilbert, Jeffrey M (FDA/CVM) <Jeff.Gilbert@fda.hhs.gov>
Subject: RE: Follow-up: Streptomycin and Oxytetracycline pesticide requests pending with EPA

Shaunta

Could I please send comments/edits on the notes by Monday, March 6th. I will send in the am.

Also, March 16th works best for me. I think for Michael as well, but will let him respond if not.

Thanks,

Jean

From: Hill, Shaunta [mailto:Hill.Shaunta@epa.gov]
Sent: Tuesday, March 01, 2016 4:22 PM
To: Harbottle, Heather (FDA/CVM) <Heather.Harbottle@fda.hhs.gov>; Patel, Jean (CDC/OID/NCEZID) <vzp4@cdc.gov>; Craig, Michael R. (CDC/OID/NCEZID) <bez7@cdc.gov>; Gilbert, Jeffrey M (FDA/CVM) <Jeff.Gilbert@fda.hhs.gov>
Subject: RE: Follow-up: Streptomycin and Oxytetracycline pesticide requests pending with EPA

Hello everyone,

That comment is relative to EPA's request for a written position from CDC and FDA that we could share with management.

I believe B5

B5

As time would be needed to provide such a memo, we would appreciate concurrence on the meeting minutes. (Assuming we have captured the thoughts/concerns correctly).

B5

B5

Please let me know if you have additional questions.

Regards,
****

Shaunta Hill-Hammond, Ph. D.
Plant Pathologist
U.S. EPA: Office of Chemical Safety and Pollution Prevention
Registration Division/Fungicide Branch (PYS)
1200 Pennsylvania Avenue, NW (7505P)
Washington, DC 20460

Tel: 703.347.8961 I Fax: 703.305.6920
E-mail: hill.shaunta@epa.gov

From: Harbottle, Heather [mailto:Heather.Harbottle@fda.hhs.gov]
Sent: Tuesday, March 01, 2016 10:40 AM
To: Hill, Shaunta <Hill.Shaunta@epa.gov>; Patel, Jean (CDC) <vzp4@cdc.gov>; Craig, Michael R (CDC) <bez7@cdc.gov>; Gilbert, Jeffrey M <Jeff.Gilbert@fda.hhs.gov>
Subject: RE: Follow-up: Streptomycin and Oxytetracycline pesticide requests pending with EPA

Good Morning Shaunta, Jean, and Michael,

I've been reading over the minutes that Shaunta sent out and making comments to send back for inclusion. I noticed that there's a line item for FDA and CDC and wondered if I could get some clarification.

"CDC and FDA jointly will provide:
1. Position statement on the use of streptomycin as a pesticide"

Could you please clarify what you'd like us to send? Jean, Michael, have you yet addressed this?

Thanks,
Heather

From: Hill, Shaunta [mailto:Hill.Shaunta@epa.gov]
Sent: Thursday, February 25, 2016 1:38 PM
To: Patel, Jean (CDC); Craig, Michael R (CDC); Harbottle, Heather; Gilbert, Jeffrey M
Cc: Jennings, Susan; Kough, John; Chandgoyal, Tara; Hicks, Karen
Subject: Follow-up: Streptomycin and Oxytetracycline pesticide requests pending with EPA

Good Afternoon Everyone,
Thank you for participating in the teleconference on Feb 10, 2016. As promised, I am

following-up with the group to share the draft meeting minutes. I would greatly appreciate your review of the minutes and any comments/corrections you find by 3/3/16.

B5

The proposed meeting times are:

- Tuesday – March 8, 9 am
- Thursday - March 10, 1 pm
- Wednesday – March 16, 1 pm

Thank you and enjoy the rest of your day.

Regards,
****

Shaunta Hill-Hammond, Ph. D.
Plant Pathologist
U.S. EPA: Office of Chemical Safety and Pollution Prevention
Registration Division/Fungicide Branch (PYS)
1200 Pennsylvania Avenue, NW (7505P)
Washington, DC 20460

Tel: 703.347.8961 I Fax: 703.305.6920
E-mail: hill.shaunta@epa.gov

Jean – could you please forward the materials to Ellen.

From: Hill, Shaunta <Hill.Shaunta@epa.gov>
To: Craig, Michael R (CDC); Patel, Jean (CDC); Wan, Ellen (CDC); Harbottle, Heather; Gilbert, Jeffrey M
CC: Jennings, Susan
Sent: 3/2/2016 5:32:50 PM
Subject: RE: Follow-up: Streptomycin and Oxytetracycline pesticide requests pending with EPA

Thank you Michael.
It seems that we have a consensus for **March 16, 2016 at 1 pm.**
We should have the agenda/teleconference information available next week.

In meantime – if there are any questions, comments on the proposed citrus use in FL/152 review + proposed mitigations; I'm happy to receive those today.
We are expecting a call from FL this afternoon and can use that as an opportunity to obtain additional information from ahead of our next teleconference.

Thanks
Shaunta

From: Craig, Michael R. (CDC/OID/NCEZID) [mailto:bez7@cdc.gov]
Sent: Wednesday, March 02, 2016 12:13 PM
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Subject: RE: Follow-up: Streptomycin and Oxytetracycline pesticide requests pending with EPA

Yes, 16th works for me.

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Tel: 703.347.8961 | Fax: 703.305.6920
E-mail: hill.shaunta@epa.gov

Jean – could you please forward the materials to Ellen.

From: Harbottle, Heather </O=FDA/OU=FIRST ADMINISTRATIVE GROUP/CN=RECIPIENTS /CN=HHARBOTT>
To: Singh, Ruby
Sent: 5/16/2016 3:37:58 PM
Subject: FW: EPA - Pending antibiotic request for Streptomycin, request for a teleconference
Attachments: 1. Resistance Monitoring Protocol Draft 11-13-14.pdf; 2. 2014 Testing and Field Monitoring for Streptomycin Resistance under F....pdf; 3. 4921332-02-XX.PDF

Hey Ruby,
The file #3 that begins "4921…." Is the 152 assessment by the company that wants to be registered for this citrus greening use. The other two docs are some monitoring protocols to look and see if resistance is developing. They propose to conduct these studies and gather data concurrently, if I understand correctly. I'll send you their finalized review of the 152 in a separate email.
J H

From: Hill, Shaunta [mailto:Hill.Shaunta@epa.gov]
Sent: Wednesday, February 10, 2016 6:34 AM
To: Harbottle, Heather; Jennings, Susan
Cc: Gilbert, Jeffrey M
Subject: EPA - Pending antibiotic request for Streptomycin, request for a teleconference

Good Morning Heather and Jeff,
Please see the attached agenda and support files for our teleconference Wednesday – Feb 10, 2016 at 11 am.
The conference line information is noted on the agenda.

**Due to the file sizes, two emails will be sent.*

If you would not mind, could you please provide contact information and title for both you and Jeff.
Thank you

From: Harbottle, Heather [mailto:Heather.Harbottle@fda.hhs.gov]
Sent: Tuesday, February 09, 2016 4:58 PM
To: Hill, Shaunta <Hill.Shaunta@epa.gov>; Jennings, Susan <Jennings.Susan@epa.gov>
Cc: Gilbert, Jeffrey M <Jeff.Gilbert@fda.hhs.gov>
Subject: RE: EPA - Pending antibiotic request for Streptomycin, request for a teleconference

Hi Shaunta,
We'll be happy to call in. Is there a call in number and agenda yet for the teleconference tomorrow at 11am?
Thanks!
Heather

From: Hill, Shaunta [mailto:Hill.Shaunta@epa.gov]
Sent: Monday, February 08, 2016 12:16 PM
To: Harbottle, Heather; Jennings, Susan
Cc: Gilbert, Jeffrey M
Subject: RE: EPA - Pending antibiotic request for Streptomycin, request for a teleconference

Hello Heather,
We did meet during the IR-4 meeting. Happy to hear that you and Jeff will be joining our

discussion.
The meeting agenda will be finalized shortly and I will forward it along with several reference documents for our discussion.
In the meantime, I wanted to provide some background information on pesticide registrations.

The type of registrations permitted under FIFRA (i.e. Section 3 and Section 18) can be found here: http://www.epa.gov/pesticide-registration/types-registrations-under-fifra

Information on the general registration process can be found here: http://www.epa.gov/pesticide-registration/pesticide-registration-manual-chapter-1-overview-requirements-pesticide

I hope you find this initial information helpful.
If you have any questions, please let me know.

Regards,
++

Shaunta Hill-Hammond, Ph. D.
Plant Pathologist
U.S. EPA: Office of Chemical Safety and Pollution Prevention
Registration Division/Fungicide Branch (PYS)
1200 Pennsylvania Avenue, NW (7505P)
Washington, DC 20460

Tel: 703.347.8961 | Fax: 703.305.6920
E-mail: hill.shaunta@epa.gov
URL Address: www.epa.gov/pesticides

From: Harbottle, Heather [mailto:Heather.Harbottle@fda.hhs.gov]
Sent: Friday, February 05, 2016 8:35 AM
To: Hill, Shaunta <Hill.Shaunta@epa.gov>; Jennings, Susan <Jennings.Susan@epa.gov>
Cc: Gilbert, Jeffrey M <Jeff.Gilbert@fda.hhs.gov>
Subject: FW: EPA - Pending antibiotic request for Streptomycin, request for a teleconference
Importance: High

Good morning Ms. Hill and Ms. Jennings,

My name is Heather Harbottle and I believe we met during the IR-4 Bacterial Challenges Mini-Summit meeting "Understanding the ABCs (Awareness of Bacterial Challenges) with Antibiotics In Crops" in September of 2014. As you may remember, I delivered a presentation regarding FDA's use of GFI #152 due to our extensive use of this guidance assessing risk for the use of antimicrobials in food producing animals. I've been asked by Bill Flynn and my team leader, Dr. Jeff Gilbert, to get in touch with you regarding your email below. Dr. Gilbert and I would be happy to attend the teleconference on Wednesday, and provide any assistance with GFI #152 as it pertains to your application for streptomycin or any other antimicrobial.

Please let us know how we can be of help.

Best,

Heather Harbottle

From: Hill, Shaunta [mailto:Hill.Shaunta@epa.gov]
Sent: Thursday, February 04, 2016 9:59 AM
To: Flynn, William T
Cc: Jennings, Susan
Subject: EPA - Pending antibiotic request for Streptomycin, request for a teleconference

Hello Dr. William;

My name is Shaunta Hill and I am a Risk Assessor/Plant Pathologist with EPA's Office of Pesticide Programs – Registration Division.
I received your name from Dr. Jean Patel at CDC as a potential contact.

As EPA manages antibiotics for pesticidal use, we are interested in accessing the resistance risk potential along with human and environmental risks. We have previously worked with CDC and FDA (via David White) utilizing the FDA Guidance for Industry #152 for this purpose.

We have a number of applications currently pending and have scheduled a teleconference for **Wednesday Feb 10 at 11 am** to begin discussions.
I am hopefully that you are available to participate in this discussion as FDA input is valued. The primary application for consideration next week is Streptomycin sulfate use on grapefruit and tomatoes via FIFRA Section 3 Registration.

If you are available, I can provide additional background information in addition to our meeting agenda.
Should you have any questions, please let us know. I have cc'ed on this communication Susan Jennings, who serves as our Public Health Coordinator and is available to address questions on this meeting request as well.

Thank you for your time and I look forward to hearing from you.

Regards,
+++

Shaunta Hill-Hammond, Ph. D.
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Registration Division/Fungicide Branch (PYS)
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Washington, DC 20460

Tel: 703.347.8961 l Fax: 703.305.6920
E-mail: hill.shaunta@epa.gov
URL Address: www.epa.gov/pesticides

From:	Harbottle, Heather </O=FDA/OU=FIRST ADMINISTRATIVE GROUP/CN=RECIPIENTS /CN=HHARBOTT>
To:	Singh, Ruby
Sent:	5/16/2016 3:39:24 PM
Subject:	FW: EPA - Pending antibiotic request for Streptomycin, request for a teleconference
Attachments:	6. FL Citrus Greening Section 18 Antimicrobial Request petition and lett....pdf; 7. FDA 152 FireWall Resistance Risk Assessment HLB and Canker 10-19-15.pdf; 8. FDA 152, FireLine Resistance Risk Assessment, 10-2-15.pdf

Ok this one is the emergency exemption request (section 18) and two more 152s.... So they are requesting regular registration and also the emergency registration.

From: Hill, Shaunta [mailto:Hill.Shaunta@epa.gov]
Sent: Wednesday, February 10, 2016 6:34 AM
To: Harbottle, Heather; Jennings, Susan
Cc: Gilbert, Jeffrey M
Subject: EPA - Pending antibiotic request for Streptomycin, request for a teleconference

This is the second email for Wednesday's teleconference.
If you have any questions / trouble with the files, please let me know.
Thank you

Regards,
++

Shaunta Hill-Hammond, Ph. D.
Plant Pathologist
U.S. EPA: Office of Chemical Safety and Pollution Prevention
Registration Division/Fungicide Branch (PYS)
1200 Pennsylvania Avenue, NW (7505P)
Washington, DC 20460

Tel: 703.347.8961 | Fax: 703.305.6920
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Subject: FW: EPA - Pending antibiotic request for Streptomycin, request for a teleconference
Importance: High

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Tel: 703.347.8961 | Fax: 703.305.6920
E-mail: hill.shaunta@epa.gov
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OFFICE OF THE COMMISSIONER
(850) 617-7700

THE CAPITOL
400 SOUTH MONROE STREET
TALLAHASSEE, FLORIDA 32399-0800

FLORIDA DEPARTMENT OF AGRICULTURE AND CONSUMER SERVICES

COMMISSIONER ADAM H. PUTNAM

December 4, 2015

Debra Rate, Ph.D.
Acting Emergency Response Team Leader
U.S. Environmental Protection Agency
Office of Pesticide Programs (7505P)
Risk Integration, Minor Use and
Emergency Response Branch
Room S4900, One Potomac Yard
2777 Crystal Drive
Arlington, Virginia 22202

Dear Dr. Rate:

Enclosed is a FIFRA Section 18 specific exemption petition submitted on behalf of Florida Fruit and Vegetable Association (FFVA) for the use of FireWall™ 50 WP (streptomycin sulfate; EPA Reg. No. 80990-3), FireLine™ 17 WP (oxytetracycline hydrochloride; EPA Reg. No. 80990-1), and Mycoshield® (oxytetracycline calcium complex; EPA Reg. No. 55146-97) to control *Candidatus* Liberibacter asiaticus (*C*Las) bacterium in citrus.

Candidatus Liberibacter asiaticus, the bacterium causing citrus greening disease, has been documented in Florida citrus since 2005. Since its establishment, efforts to control the spread and progression of the disease have largely focused on removal of diseased trees, nutritional support, as well as rigorous efforts to control the Asian citrus psyllid, the vector for this disease. However, more recently, research efforts have shifted towards a focus on both ridding infected trees of the pathogen as well as slowing the progression of the disease through the use of antimicrobial agents.

The requested exemption stipulates that no more than 1.35 pounds streptomycin sulfate (2.07 pounds of FireWall) per acre per year and no more than 2.04 pounds oxytetracycline equivalent (potentially from FireLine and Mycoshield) per acre per year. Florida has over 388,000 acres of commercial citrus throughout the state. Additional details of the proposed use pattern are found within the narrative document of this petition.

The Department has reviewed and/or consulted with the affected agencies and determined that use of FireWall, FireLine and Mycoshield antimicrobials under the conditions of this proposed specific exemption will not pose a risk to endangered species (Department assessment to follow).

EPAREF2656-000664

Please send any correspondence on this request to: Mr. Charlie L. Clark, Environmental Administrator, Pesticide Registration Review Section, Bureau of Scientific Evaluation and Technical Assistance, Division of Agricultural Environmental Services, 3125 Conner Boulevard, Building #6, Tallahassee, Florida 32399-1650, Phone 850-617-7940, e-mail: Charlie.Clark@FreshFromFlorida.com.

Sincerely,

Adam H. Putnam
Commissioner of Agriculture

AHP/dd

Attachment

cc: Mr. Mike Joyner
Dr. Lisa Conti
Mr. Matt Joyner
Dr. Joseph Joyce
Mr. John Hoblick
Mr. Randy Dominy
Mr. Philip Beard
Dr. Fred Fishel
Mr. Daniel Botts
Mr. Michael Aerts
Dr. Michael Rogers
Dr. Harold Browning
Dr. Michelle S. Samuel-Foo
Mr. Anderson H. Rackley
Ms. Kelly Friend
Dr. Davis Daiker
Mr. Charlie Clark
Ms. Sarah Oglesby
Mr. Dale Dubberly
Mr. Neil Richmond
Ms. Jo Marie Cook
Ms. Patty Lucas
Mr. Tau Richardson
Mr. Tom Jerkins
Mr. Mark Trimmer
Mr. Bill Bewlay

EMERGENCY EXEMPTION REQUEST

(Specific Exemption)

FOR THE USE OF THE ANTIBIOTICS

FireWall™ 50WP Fungicide/Bactericide (streptomycin sulfate)

FireLine™ 17WP (oxytetracycline hydrochloride)

Mycoshield® (oxytetracycline calcium)

TO SUPPRESS

Huanglongbing (HLB) (*Candidatus* Liberibacter asiaticus)

and IMPROVE TREE HEALTH

ON

Citrus

IN FLORIDA

December 2, 2015

EPAREF2656-000667

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EPAREF2656-000668

CONTACT PERSON(S) AND QUALIFIED EXPERTS(S) (166.20(a)(1))

(i) The Contact Person for matters relating to the administration of this exemption:

Daniel A. Botts/Michael J. Aerts
Florida Fruit & Vegetable Association
800 Trafalgar Ct.; Suite 200
Post Office Box 948153
Maitland, FL 32794-8153
Phone: (321) 214-5200
Fax: (321) 214-0210
daniel.botts@ffva.com
mike.aerts@ffva.com

Charlie Clark, Environmental Admin.
FL Dept. of Ag and Consumer Services
Pesticide Registration Section
3125 Conner Blvd. (Bldg. 6)
Tallahassee, FL 32399-1650
Phone: (850) 617-7940
Fax: (850) 617-7949
charlie.clark@freshfromflorida.com

(ii) The contact people for matters relating to the technical aspects of this exemption:

For Florida, it has been agreed that questions relating to technical aspects in the field for this emergency exemption petition will work through the Florida Department of Agriculture and Consumer Services and the Emergency Response Team within EPA's OPP.

For other technical aspects related to this petition, the contact is:

Agrosource:
Mark Trimmer
Director; R&D
AgroSource, Inc.
9889 Wilkinson Road
Mazomanie, WI 53560
Mobile: 608-628-2654
Mark@TrimmerConsulting.com

Nufarm:
Bill Bewlay
Director, Business Development
Nufarm Americas, Inc.
4020 Aerial Center Parkway, Suite 101
Morrisville, NC 27560
(919) 379-2506
bill.bewlay@us.nufarm.com

DESCRIPTION OF PESTICIDE REQUESTED (166.20(a)(2))

a. Common Chemical Names (Active Ingredients):

Streptomycin Sulfate, Oxytetracycline Hydrochloride and Oxytetracycline Calcium

EPAREF2656-000669

Trade Names and EPA Registration Numbers:

FireWall™ 50WP Fungicide/Bactericide
EPA Registration Number: 80990-4

FireLine™ 17WP Fungicide/Bactericide
EPA Registration Number: 80990-1

Mycoshield®
EPA Registration Number: 55146-97

Formulation:

All products are Wettable Powders

Percent Active Ingredient:

FireWall™ 50WP:	65.8% Streptomycin Sulfate (equivalent to 50% streptomycin)
FireLine™ 17WP:	18.3% Oxytetracycline Hydrochloride (equivalent to 17% oxytetracycline)
Mycoshield®:	31.5% Oxytetracycline Calcium Complex (equivalent to 17% oxytetracycline)

Manufacturers:

FireWall™ and FireLine™:	AgroSource, Inc.
Mycoshield®:	Nufarm Americas, Inc.

b. Additional labeling: see Appendix D (FireLine ™ and FireWall™) and Appendix E (Mycoshield®) for the proposed Section 18 labels.

DESCRIPTION OF PROPOSED USE (166.20(a)(3))

(i) Site to be Treated:

Rationale for Multiple Active Ingredient Products:

The Citrus Research and Development Foundation, Inc., (CRDF), a Florida based independent grower research support organization was created and funded by grower assessments to guide the search for solutions to the recently introduced disease/vector complex Huanglongbing disease/Asian citrus psyllid. This research effort has proceeded across many fronts, one of which is the discovery and development of therapeutic treatments for infected trees. This program has directly participated in the funding of

projects with registrants of agricultural antibiotics to determine the role if any these compounds may provide in addressing this industry need. These projects were initiated over the past twenty-four months and have provided indications of value in maintaining the health and productive vigor in citrus trees that are infected with the pathogen.

Initial experimentation and experience gained in commercial citrus groves with this disease/complex suggests that multiple bactericide applications will be necessary in order to improve tree health and suppress the effects of Huanglongbing (HLB) disease season-long/year-round on infected citrus trees. The information developed independently by the two registrants in cooperation with the Citrus Research and Development Foundation over the past two years indicates a measure of suppression and overall increase in tree health in HLB-infected citrus trees. Each registrant developed their research package independently of the other's involvement and the resulting data indicates the three products have efficacy when used in a season long program targeted to the flush periods in citrus. The use patterns of the oxytetracycline products, while somewhat complementary, were not based on the same treatment regimes. This petition has attempted to consolidate use patterns across those treatment regimens and develop a package that would allow the flexibility of the treatments proposed in each individual package. It is important to note that the research program to refine and finalize final use patterns are on-going and will result in label expansion actions by each registrant. It must be recognized that while all of these products have activity on other citrus plant pathogens, the reason for this petition is the need for a therapeutic treatment to prolong the life and viability of trees infected with HLB.

Additionally, the further rationale supporting the use of multiple active ingredients for this particular Section 18 request include the following:

- The *Candidatus* Liberibacter asiaticus (*C*Las) bacterium is a difficult organism to work with, starting with the fact that this organism has never been successfully cultured in the laboratory. Its potential to develop resistance to antibacterial compounds applied for its control in the field is therefore unknown.

- Since *C*Las may develop resistance if treated with just a single bactericide product, an effective resistance management strategy must be part of any antibacterial HLB management program from the start.

- The heart of any effective resistance management strategy against *C*Las will be the use of at least two bacterial control agents, each having a unique mode of action against the pathogen.

- Based on their respective and unique modes of action, streptomycin sulfate is classified as a Group 25 fungicide; oxytetracycline is classified as a Group 41 fungicide according to the Fungicide Resistance Action Committee (FRAC).

EPAREF2656-000671

- The use of streptomycin and oxytetracycline in alternation will thus minimize any selection pressure on *C*Las for development of resistance to either streptomycin or oxytetracycline.

- Since both streptomycin and oxytetracycline are individually efficacious against *C*Las in HLB-infected citrus, attacking the situation with these multiple products in rotation constitutes an effective resistance management program for HLB management and tree health improvement, thereby ensuring the long-term efficacy of these products against the *C*Las pathogen.

- This resistance management program should also help in preventing development of resistance in non-target bacteria as well.

All citrus (statewide) is the site to be treated. The proposed crop spectrum to be treated is slightly different for the two formulations of oxytetracycline. The FireLine™ label and FireWall ™ label covers all of the Citrus Crop Group 10, whereas the Mycoshield® label is proposing use on Orange, Crop Subgroup 10-10A and Grapefruit, Crop Subgroup 10-10C. According to the latest figures available from the 2015 Citrus Reference Book (Florida Agricultural Statistics Service Citrus Summary, 2013 – 2014; February 2015), in 2014 there was a total of 515,147 acres of Florida commercial citrus acreage (452,364 acres oranges, 45,922 acres grapefruit, and 16,861 acres specialty citrus). In a subsequent report (September 17, 2015), The National Agricultural Statistics Service reported 126,613 acres of abandoned or untended citrus acreage. This acreage would be deducted from the above number resulting in potentially treated acreage of 388,534 acres. See Appendix A for Florida counties and acreages in citrus.

(ii) <u>Method of Application</u>:

Ground application only.

(iii) <u>Rates of Application (in terms of a.i. and product)</u>:

FireWall™ 50WP
0.45 pounds active ingredient (a.i.) per acre per application
0.69 pounds of formulated FireWall™ 50WP per acre per application
FireLine™ 17WP
0.27 pounds of active ingredient (a.i.) per acre per application
1.5 pounds of formulated FireLine™ 17WP per acre per application
Mycoshield®
0.255 pounds of active ingredient (a.i.) (oxytetracycline base) per acre per application
1.5 pounds of formulated Mycoshield® per acre per application

Rates of application for Mycoshield® are based on reaching a 200 ppm oxytetracycline (1.5 pounds of formulated product in 150 gallons of water)

concentration in a finished spray volume necessary to fully cover the foliage of the tree to be treated. Spray volume and use rates per acre can be scaled downward in smaller trees depending on the amounts of spray volume to provide full coverage.

Maximum Number of Applications:

FireWall™ 50WP
A maximum of 3 applications per year is proposed, totaling no more than 2.07 pounds of formulated FireWall™ 50WP per acre per year (1.35 pounds active ingredient).
Allow a minimum of 21 days between applications.

Fireline™ 17WP
A maximum of 3 applications of this formulation per year is proposed, totaling no more than 4.5 pounds of formulated FireLine™ 17WP per acre per year (0.81 pounds active ingredient).
Allow a minimum of 21 days between applications.

Mycoshield®
A maximum of 8 applications per year is proposed, totaling no more than 12 pounds of formulated Mycoshield® per acre per year (2.04 pounds oxytetracycline base). Mycoshield® would be labeled to suppress infections of HLB in foliage with applications beginning two weeks after the initiation of a new leaf flush. Closer spray intervals are conducive to better performance but limit the ability to use the product on multiple flushes. Wider spray intervals and fewer applications on a given flush may not be as effective but allows for more applications on successive flushes, especially in young small frame citrus trees.

(iv) Total Acreage (or other units) to be Treated:

During 2013-14, approximately 515,147 acres of citrus were grown in Florida. Of this acreage 388,534 acres remain under commercial management.

(v) Total Amount of Pesticide to be Used (in terms of a.i. and product):

FireWall™ 50WP
In an absolute worst-case scenario, 804,265 pounds of formulated FireWall™ 50WP Fungicide/Bactericide, or 695,448 pounds of streptomycin sulfate, would be needed. (388,534 acres X 0.69 pounds of formulated FireWall™ 50WP X 3 applications = 1,066,354 pounds FireWall™ 50WP Fungicide/Bactericide; 388,534 acres X 0.45 lbs. a.i. X 3 applications = 524,520 lbs. a.i. streptomycin sulfate).

FireLine™ 17WP
At the maximum, 1,748,403 pounds of FireLine™ 17WP or 314,712 pounds of oxytetracycline hydrochloride, would be needed. (388,534 acres X 1.5 pounds of formulated FireLine™ 17WP X 3 applications = 1,748,403 pounds FireLine™ 17WP; 388,534 acres X 0.27 pounds a.i. X 3 applications = 314,712 pounds of oxytetracycline hydrochloride).

Mycoshield®
The total amount of Mycoshield® that could be used under the specific exemption assuming all trees are treated the maximum number of recommended applications would be a total of 4,662,408 pounds of formulated Mycoshield® or 762,309 pounds of oxytetracycline calcium. (388,534 acres X 1.5 pounds of Mycoshield® X 8 applications = 4,662,408 pounds of Mycoshield®; 388,534 acres X 0.255 pounds oxytetracycline base X 8 applications = 762,309 pounds of oxytetracycline base). While the use of Mycoshield® is limited to citrus crop subgroups 10 A and 10 C, the members of crop subgroup 10B (limes and lemons) represent less than 2,000 acres of production in Florida (less than 2,550 lbs of active ingredient.

Note Oxytetracycline Formulations:

Across the two formulations of oxytetracycline, the total amount of the active ingredient oxytetracycline that would be allowed under the proposed use patterns included in this petition is equivalent to the maximum amount of active ingredient that could be applied per individual acre of treated citrus under the proposed Mycoshield® Section 18 label plus the amount adjusted for the three applications on Citrus Subgroup B, which is allowed on the proposed FireLine™ 17 Section 18 label (0.81lbs X 2,000 Acres of lemons and limes = 1,620 lbs). This is (762,309 lbs. – (2,550 lbs. (5 applications at .255 lbs.)) = 759,759 lbs. of oxytetracycline. The use across the two formulated products (on Citrus Subgoups 10 A and 10 C) would be additive over the season and capped at the maximum level of active ingredient per acre of 2.04 lbs. of oxytetracycline for Citrus Subgroups A & C and 0.81lbs. on Citrus Subgroup B. <u>We would encourage the Agency in their decision document to clearly state that the maximum amount of oxytetracycline per acre per season is capped so that if growers choose to use both products they do not exceed the maximum per acre use allowed.</u>

While the amounts of product that could be needed is projected above; it is highly probable that not all of the eligible acreage will be treated, and a portion of the treated acreage will be treated at lower use rates than the maximum rate because of smaller canopy size in the younger age classes of

trees. This will result in less material being used than the numbers projected above.

(vi) <u>Use Season (period of time for which use of chemical is requested)</u>:

Access would be needed by February 1, 2016, to coincide and overlap with the typical spring foliage flush emergence. Availability subsequent to the date of approval is requested and crucial over the ensuing 12 months, especially when considering the continued infection rates and subsequent tree losses resulting from HLB disease.

FireWall™ 50WP
FireWall™ 50WP will be applied to all varieties and cultivars included in the Citrus Crop Group 10. Make an initial application at initiation of spring flush to suppress HLB titer and disease symptoms. Make a second application mid-summer (not less than 21 days after first application). Make a third application in late summer to reduce the incidence of HLB-induced fruit drop and to further suppress HLB titer and disease symptoms (not less than 21 days after second application). Spray to near runoff. Applications of FireWall™ 50WP should be rotated with another bactericidal product having a different mode of action, to reduce risks of selecting for streptomycin-resistant organisms.

FireLine™ 17WP
FireLine™ 17WP will be applied to all varieties and cultivars included in the Citrus Crop Group 10. Make an initial application at initiation of spring flush to suppress HLB titer and disease symptoms. Make a second application mid-summer (not less than 21 days after first application). Make a third application in late summer to reduce the incidence of HLB-induced fruit drop and to further suppress HLB titer and disease symptoms (not less than 21 days after second application). Spray to near runoff.

Mycoshield®
The recommendation is to make 3 to 4 applications to growth flushes in the spring and fall. Applications to the spring flush could be initiated in February through April depending on the citrus variety and the severity of the winter. It may take until the end of May to complete the entire application program on the spring flush. Fall flushes would consist of periods of new growth initiating after September 1st.

Foliar applications of these antibiotics are not expected to cure systemic infections of HLB in the branches, trunks or roots of a diseased tree. Application flexibility is needed so growers can target periods of disease

suppression and relief of associated symptoms that best fit their overall production program.

(vii) <u>Additional Restrictions, User Precautions and Requirements, Qualifications of Applicators, etc.</u>:

All active ingredients will be applied in accordance with the proposed Section 18 label and all applicable provisions of the Section 3 registered labels. Examples of various restrictions, requirements and qualifications include but are not limited to:

FireWall™ 50WP

- A total of three (3) applications of FireWall™ 50WP may be made at no less than 21 day intervals.
- Do not apply at less than 40 days prior to harvest.
- Do not apply through irrigation systems or by aircraft.
- Do not apply more than 2.07 pounds of formulated FireWall™ 50WP (1.35 pounds active ingredient) per acre.
- Personal protective equipment for applicators and handlers includes:
  - Long sleeved shirt
  - Long pants
  - Chemical resistant gloves made of a waterproof material
  - Shoes plus socks
  - Protective eyewear
  - MSHA/NIOSH approved dust/mist respirator with any N, R, P or HE filter.
- Worker re-entry into treated areas during the restricted entry interval of 12 hours is not allowed. For early entry to treated areas that is permitted under the Worker Protection Standard and that involves contact with anything that has been treated, such as plants, soil or water, wear:
  - Coveralls over long-sleeved shirt and long pants
  - Chemical-resistant gloves made of a waterproof material
  - Shoes plus socks
  - Protective eyewear.
- Do not apply directly to water, to areas where surface water is present or to intertidal areas below the mean high water mark.
- Do not contaminate water by cleaning of equipment or disposal of equipment washwater.

- The FireWall™ 50WP label contains a CAUTION statement of hazard and this product is considered to be a "General Use" pesticide. As a non-restricted pesticide, farmers without private applicator certification,

farmers with private applicator certification, and licensed commercial applicators are allowed to apply FireWall™ 50WP.

FireLine™ 17WP

- A total of three (3) applications of FireLine™ 17WP may be made at no less than 21 day intervals.
- Do not apply at less than 40 days prior to harvest.
- Do not apply through irrigation systems or by aircraft.
- Do not apply more than 4.5 pounds of formulated FireLine™ 17WP (0.81 pounds active ingredient) per acre.
- Personal protective equipment for applicators and handlers includes:
    - Long sleeved shirt and long pants
    - Chemical resistant gloves made of a waterproof material
    - Shoes plus socks
    - Protective eyewear
    - Dust/mist filtering respirator (MSHA/NIOSH approval number prefix TC -21C) or a NIOSH approved respirator with any N , R, P or HE filter.
- Worker re-entry into treated areas during the restricted entry interval of 12 hours is not allowed. For early entry to treated areas that is permitted under the Worker Protection Standard and that involves contact with anything that has been treated, such as plants, soil or water, wear:
    - Coveralls over long-sleeved shirt and long pants
    - Chemical-resistant gloves made of a waterproof material
    - Shoes plus socks
    - Protective eyewear.
- Do not apply directly to water, to areas where surface water is present or to intertidal areas below the mean high water mark.
- Do not contaminate water by cleaning of equipment or disposal of equipment washwater.
- The FireLine™ 17WP label contains a CAUTION statement of hazard and this product is considered to be a "General Use" pesticide. As a non-restricted pesticide, farmers without private applicator certification, farmers with private applicator certification, and licensed commercial applicators are allowed to apply FireLine™ 17WP.

Mycoshield®

- A total of eight (8) applications of Mycoshield® may be made at no less than 21 day intervals.
- Do not apply at less than 21 days prior to harvest.
- Do not apply through irrigation systems or by aircraft.

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- Do not apply more than 12.0 pounds of formulated Mycoshield® (2.04 pounds oxytetracycline base) per acre.
- Personal protective equipment for applicators and handlers includes:
- Long sleeved shirt.
- Long pants.
- Chemical resistant gloves made of a waterproof material.
- Shoes plus socks.
- Protective eyewear.
- Dust/Mist filtering respirator (MSHA/NIOSH approval number prefix TC-21C) or a NIOSH approved respirator with any N, R, P or HE filter.
- Worker re-entry into treated areas during the restricted entry interval of 12 hours is not allowed. For early entry to treated areas that is permitted under the Worker Protection Standard and that involves contact with anything that has been treated, such as plants, soil or water, wear:
    - Coveralls over long-sleeved shirt and long pants
    - Chemical-resistant gloves made of a waterproof material
    - Shoes plus socks
    - Protective eyewear.
- Do not apply directly to water, to areas where surface water is present or to intertidal areas below the mean high water mark.
- Do not contaminate water by cleaning of equipment or disposal of equipment washwater.
- The Mycoshield® label contains a WARNING statement of hazard and this product is considered to be a "General Use" pesticide. As a non-restricted pesticide, farmers without private applicator certification, farmers with private applicator certification and licensed commercial applicators are allowed to apply Mycoshield®.

Other specific use directions to be followed are found on the proposed Section 18 labels and the Section 3 labels found in Appendices D and E.

ALTERNATIVE METHODS OF CONTROL (166.20(a)(4)):

(i) Detailed Explanation of Why Currently Registered Pesticides Are Not Available in Adequate Supply and/or Are Not Effective to Control the Emergency:

The Huanglongbing (HLB) disease/vector complex and its impact on the industry have been rapidly increasing since the disease was first identified in Florida in August of 2005. The fact that HLB was on the U.S. Department of Homeland Security's Select Agent List made field work next to impossible until that status was modified. As experience with the disease has progressed, it has become apparent that managing the disease at levels that

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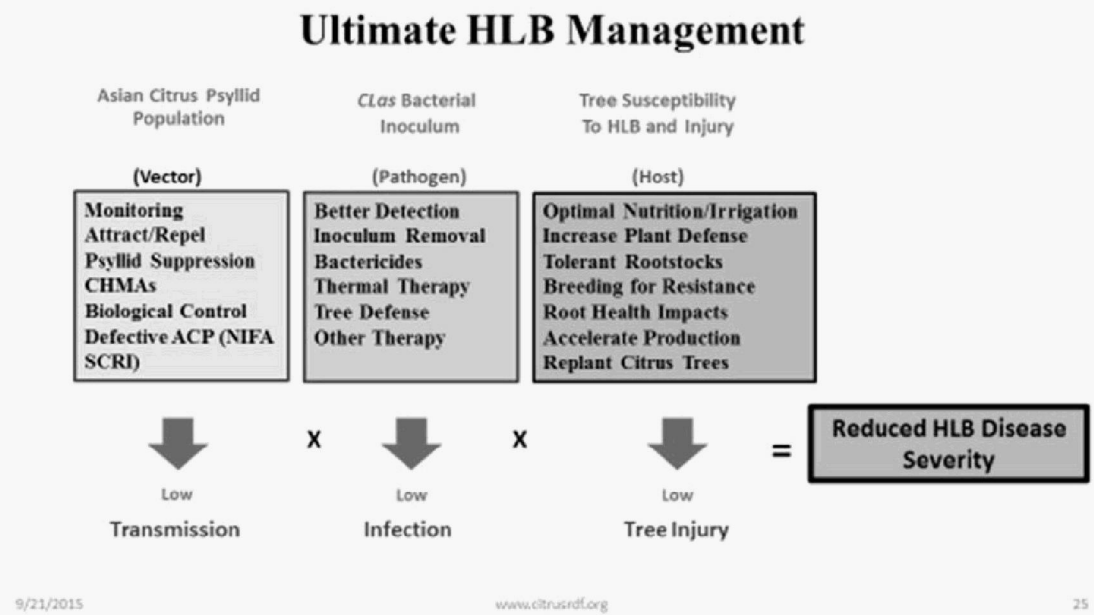
will allow continued commercial production in Florida depends on a multifaceted management strategy. This strategy includes the ability to replace non-productive trees with a realistic expectation that the newly planted replacement trees will have a reasonably productive life. Even with the complexities created by the lack of ability to culture the bacteria outside of the citrus vascular system and the digestive system of the insect, the industry has made significant strides in identifying the critical components of this management process.

From the beginning, there have been a range of approaches attempted to manage the devastation that HLB has caused to Florida citrus, and the pursuit of many parallel strategies continues. Challenges of managing HLB disease in Florida citrus are many and the application of tools that are available and emerging from research have yet to provide for a sustained leveling of disease impact or to restore tree health and productivity to trees infected with the pathogen. The graphic below highlights the breadth of effort underway in research to discover, test and deliver solutions to HLB, identifying the primary targets for intervention. Vector control, combined with therapy to reduce *C*Las titers (bacterial concentrations) in infected trees and ultimately, deployment of resistant or tolerant plant materials offers the balanced approach to disease management. Because of the absence of effective tools for bacterial therapy (the basis for this petition) and no proven plant resistance, the disease continues to impact all Florida growers and is discouraging the much-needed replanting to complement the current struggling tree inventory.



From the outset, it has been clear that vector control was tantamount to slow the spread of the disease, and many strategies were advanced to achieve this goal. Insecticidal suppression, biological control, attractants and repellants and other approaches have

been pursued, and as a result, Asian citrus psyllid (ACP) populations are well below initial levels. Similarly, as *C*Las infection spread and the numbers of infected trees grew, expansion of ACP control was necessary to protect new plants in existing groves and new plantings from becoming infected. Soil-applied neonicotinoid insecticides play a major role in protecting young trees during critical periods as they grow through the first 5 years, and these insecticides become more important as the disease reservoirs of inoculum and vector populations continue to expand. ACP suppression remains a critical component of HLB management with research and grower experience continuing to demonstrate the value of this segment of HLB management.

Florida citrus growers realized early that sustaining plant health through horticultural practices was an important response to onset and advancement of HLB disease. While trees possess considerable resilience in response to stresses, a chronically declining tree loses much of its resilience, and therefore must be managed more carefully. "Just-in-time inputs" or "spoon-feeding" trees showing advanced HLB symptoms with irrigation and fertilization can dampen limitations of compromised root systems, and cultural practices have been modified to more intensively manage tree health. In addition, plant growth regulators are being evaluated and used in an effort to assist in phloem regeneration and to limit pre-harvest fruit drop associated with HLB decline. Other cultural practices are being investigated to sustain health and productivity of infected trees and perhaps prolong productive life of these trees. Some of these same practices of intensive management are likewise being applied to newly planted trees to meet the goal of accelerating tree growth and maturity, thereby allowing for economic return to growers before HLB-induced tree decline commences. However, consistent success in this effort remains elusive.

Neither vector suppression nor cultural practices directly impact the bacterial pathogen, *C*Las, which is the target of the intervention proposed in this petition.

The goal of reducing *C*Las titer in infected trees has proven quite challenging, and relatively little progress has been made in this arena. The location of the pathogen within the plant's vascular system, difficulty of early detection of infection in citrus plants, and the inability of researchers to work with cultures of the bacteria *C*Las have limited development of *C*Las therapies to two strategies.

The first of these strategies is application of thermal therapy, where external heat is applied actively or passively to infected trees to differentially cause bacterial mortality in phloem tissues, while not harming the host plant tissues. The differential time versus temperature requirements to achieve this goal are being pursued through research and field experimentation on commercial farms.

The alternative to thermal therapy is the application of chemical therapy, wherein bactericidal chemicals are applied to trees to reduce *C*Las bacterial titer. This approach has been a priority focus for industry research efforts and extensive investment in evaluating efficacy, dose response, phytotoxicity and other parameters important to

development of a therapy tool. Chemical therapy encompasses a range of chemistries that correspond to various regulatory pathways, from conventional agricultural antibiotics to biopesticides to new active ingredients. Chemistries that fall within currently registered pesticides, 25(b) exempt list, or biopesticides offer the shorter term opportunities and these are being pursued aggressively while longer term new active ingredients are developed. Our strategy has focused most aggressively on agricultural antibiotics as these products offer an opportunity for label expansion from other U.S. crop uses as bactericides, and for which there is a broad pool of supporting data.

Processes in place to evaluate chemical therapy candidates include:

- A comprehensive laboratory bioassay system progressing from a high throughput surrogate bacterial assay to whole plant greenhouse assays;
- A range of field research spanning single plant initial trials to large scale commercial trials conducted in concert with registrants;
- Efficacy as a function of a.i., dose, timing, application method and disease intensity has been evaluated, as well as phytotoxicity, movement within the plant, and residues in plant parts.

Finally, several long-term lines of technology are being developed to identify and move the genetic components necessary to convey resistance into horticulturally important citrus cultivars. Field trials have been initiated to further investigate the potential for this to serve as a long-term means of restoring the viability of the industry. But, results are still expected to be years off.

All of this work in the state of Florida is being coordinated through the Citrus Research and Development Foundation (CRDF). This program of research to develop and deliver HLB solutions is also coordinated with existing national and international programs through USDA ARS, other research institutions, and, industry associations in Texas and California.

(ii) Alternative Control Practices:

Alternative *C*Las therapy/suppression practices are outlined above and are restricted at present to thermal therapy and chemical therapy. While there are other approaches mentioned above for vector or plant health management, none of these address reducing *C*Las titer in infected trees, and these tools are not likely to affect decline of infected trees.

Thermal therapy:

Some success has been observed with application of passive solar energy or active steam heat to young trees. These field demonstrations and trials have been evolving since the

spring of 2014, when proof of concept was completed with solarization inside single-tree tents. Early attempts with both passive and active thermal treatment resulted in severe tree injury or actual tree death, leading to subsequent investigations to define time/temperature relationships and methods of delivery to achieve the differential thermal effects on bacteria while preventing tree injury. At present, all systems operating in the field to advance this approach are designed to treat individual trees up to a maximum height of about 3 meters. Results appear most predictable when trees are in early stage in infection and disease onset. While delivery systems and time/temperature characteristics are being resolved, predictability of response and expected duration of effects are in early stages of evaluation. Practical limitations of the number of trees that can be treated with thermal therapy and the expected outcomes in balancing bacterial titer reduction with increasing injury to leaves, limbs and fruit on treated trees are being evaluated in small-scale field trials in Florida. Research and commercialization funding is encouraging innovation to solve issues of practical application of this *C*Las suppression strategy, but progress is slow at present. It is anticipated that this approach will emerge on a commercial scale as a tool for managing early infection that will perhaps be limited to young (small) trees.

Chemical Therapy of *C*Las:

Chemical therapy of *C*Las is under intensive investigation in Florida citrus, with relatively few candidate materials advanced to commercial use or demonstrated effectiveness. The only antibiotics available for use in the agricultural sector include streptomycin, oxytetracycline and kasugamycin. Among the groups of chemistries under consideration, the bactericides labelled for use in other crops are the front-runners in terms of available data and performance testing in Florida citrus. These are the subjects for this Emergency Exemption petition.

Alternatives available for field use against *C*Las are few. *C*Las bioassay and field trials are being conducted on the biopesticides that are labelled for pest or disease control in citrus to determine how effective these materials might be under current field use patterns. Field research is ongoing, but results that could indicate a clear effect are not yet available. Optimism around these products exists but none of these materials are currently considered as demonstrable *C*Las therapy.

Other alternative chemistries that are being evaluated in Florida citrus for HLB suppression or tree health management include products based on plant essential oils. Some of these oils appear on the EPA 25(b) exempt list. Several products containing plant essential oils are available in Florida [e.g., Thymeguard (AgroResearch), and Ecotrol Plus (Keyplex®)]. These products are being field evaluated by growers to determine their impact on HLB through foliar application.

Field trials are underway to quantify the impact of these potential tools, but it is too early to have meaningful results. Similarly, field evaluations by Florida growers in conventional and organic citrus blocks have failed to demonstrate a measurable effect of these plant

essential oils. While these tools may complement the bactericides being considered in this petition, there is limited evidence for their effectiveness in reversing HLB.

EFFECTIVENESS OF USE PROPOSED UNDER SECTION 18 (166.20(a)(5)) (166.20(a)(5))

FireWall™ 50WP and FireLine™ 17WP

To assess the potential management of HLB disease, foliar applications of two bactericides, streptomycin sulfate and oxytetracycline hydrochloride were applied to commercially-grown grapefruit and oranges at 17 Florida field test locations in 2014 (year 1) and 2015 (year 2). Trials were located in the Indian River, the Central Ridge and the Peace River regions of Florida's citrus industry. Prior to treatment applications, all trees at each location were confirmed to test "positive" for HLB, based on PCR (polymerase chain reaction) analysis. Treatment effects for streptomycin and oxytetracycline applications were determined by quarterly DNA titer assays of the bacterium *Candidatus* Liberibacter asiaticus present in leaf samples collected from each treatment plot. In addition, multiple assessments of tree health were made, including improvement in tree canopy density (e.g. health), increased tree height and reductions in leaf drop, fruit drop, visual HLB symptoms, branch dieback and increases in fruit load in treated versus untreated trees. Foliar applications with streptomycin or oxytetracycline to grapefruit and orange trees in year-1 resulted in a statistically significant reduction ($p < 0.05$) in *C*Las titer, and this remained evident 4 to 5 months after the last application of streptomycin or oxytetracycline. In addition, significant improvements ($p < 0.05$) in leaf drop, fruit drop, visual HLB symptoms, and visual tree health, were noted in treated year-1 trees. Significant treatment effects ($p < 0.05$) were also recorded for these same parameters plus tree height in year-2. Results from these trials showed that foliar applications of streptomycin and oxytetracycline bactericides to commercially grown citrus significantly reduces titer for *C*Las in HLB-infected trees, and results in significant improvements to overall tree health. These field evaluations serve to illustrate that the reduction in *C*Las titer from the PCR results has correlation to healthier citrus trees in a production grove environment.

Mycoshield®

Mycoshield® oxytetracycline calcium complex was first registered in 1979 for control of fire blight (*Erwinia amylovora*) of pear and bacterial spot (*Xanthomonas arboricola* pv. *pruni*) of peach. Apple (fire blight) and nectarine (bacterial spot) were added to the label in later years. Oxytetracycline hydrochloride was first approved for agricultural use in 2004. EPA has determined that oxytetracycline calcium complex and oxytetracycline hydrochloride rapidly convert to oxytetracycline when added to water and "both OTC calcium complex and OTC-HCL will be mainly introduced into the environment as OTC." Thus, it was determined that environmental fate data for OTC calcium complex and OTC-

HCL are interchangeable. Disease control with the two forms is expected to be equivalent because the spray deposits would be oxytetracycline.

Oxytetracycline is produced naturally by *Streptomyces rimosus*. Commercial production of Mycoshield® is achieved by fermentation of the natural organism. This is followed by an extraction and concentration process to obtain a manufacturing concentrate that is used to make the final end product. OTC is a reversible bacteriostat that inhibits protein synthesis at the ribosome. Susceptible bacteria may resume development if the exposure period is inadequate for action by a secondary mortality factor such as senescence, attempted cell division, environmental stress or a host plant response.

Potted seedlings of various citrus cultivars were sprayed to run off with daily foliar applications of oxytetracycline at 100 ppm in a 1975 report (A. L. Martinez, 1975). A majority of the plants demonstrated partial recovery with obvious improvements in color and shoot production. However, none of the plants were completely cured. Injections of tetracycline to Sakkan orange and Fuju mandarin at 500 to 1000 ppm were effective at reducing disease symptoms and preserving higher yields in a 1991 article (K. Chung and W. Zhisheng, 1991). The trees were not cured and growth of the disease was evident one year later. Injection of tetracycline resulted in phytotoxic effects such as rotten tissue around the injection points and leaf drop. Oxytetracycline was not considered to be of value in the early stages of the Florida epidemic because of the inability to cure infected trees.

The following characteristics are required for bactericides to make definitive claims for direct suppressive activity on HLB and have practical utility for use in the field:

1. **Proven activity on *Liberibacter spp.* in culture**. It must inhibit *Candidatus* Liberbacter crescens, the closest cultured relative of *Candidatus* Liberibacter asiaticus, at low concentrations. Oxytetracycline strongly inhibits *Candidatus* Liberbacter crescens culture growth by more than 90 percent at a concentration of 0.54 µM, a level suitable for field use. Thus, it is believed that oxytetracycline can inhibit *Candidatus* Liberbacter asiaticus.

2. **Phloem mobility**. The chemical structure of oxytetracycline suggests that it can penetrate the phloem where the causal agent, *Candidatus* Liberibacter asiaticus, resides in the tree.

3. **Excellent crop safety**. Mycoshield® applied twice weekly to citrus at 1000 ppm for 12 weeks (24 total applications) did not cause noticeable injury in a 2013 field trial by the University of Florida's Dr. Eric Triplett (personal communication).

Zebra chip disease is caused by *Candidatus* Liberibacter solanacearum, a very close relative of *Candidatus* Liberbacter asiaticus. As in HLB disease, the *Liberibacter* pathogen resides in the phloem after having been vectored by a phloem-feeding insect (potato psyllid). Testing bactericides against zebra chip disease on tomato or potato generates

results much faster than can be obtained on citrus. Symptoms on tomato appear in 10 days but can take many months on citrus. Disease suppression through the use of an effective bactericide can be observed in less than three weeks in tomato but can take many months on citrus.

Zebra chip is not endemic to Florida, but laboratory and field research can be conducted in south Texas where the disease and potato psyllid are widely established. Dr. Erik Mirkov (Texas A&M AgriLife Research) has shown in laboratory studies that oxytetracycline effectively manages the symptoms of Zebra chip disease on tomato and dramatically reduces the number of bacteria residing in the plant (data in preparation for publication). Dr. Manuel Campos (Texas A&M AgriLife Research) conducted a field trial on potato in 2015. Five weekly applications of Mycoshield® at 200 ppm resulted in 13 percent infected tubers as compared to 90 percent in the untreated. This study demonstrated that oxytetracycline can reduce disease caused by a phloem-limited pathogen very closely related to *Candidatus* Liberbacter asiaticus.

Nufarm conducted experimental field trials in 2014 and 2015 (Better Crops, LLC, 2014 / 2015) evaluating the suppressive activity of Mycoshield® foliar sprays against HLB in Florida groves with HLB symptoms. This was a commercial grapefruit grove with 7 – 10 year old trees.

In 2014, the treatment list was based on anecdotal information suggesting that a combination of a bactericide with a strong penetrant (Pentra-Bark®) plus fertilizers would provide the best results. Unfortunately, the treatments with Pentra-Bark®/fertilizer combinations (with or without a bactericide) resulted in phytotoxic effects in the form of severe leaf and fruit drop. Although 2014 growth information was confounded by the crop injury, qPCR data demonstrated that oxytetracycline foliar applications suppressed the incidence of HLB infection in new growth. Samples of mature foliage collected prior to the initiation of the program revealed an infection incidence of 75 – 100 percent throughout the study area. Samples of mature foliage collected after the treatment program (4 applications at 3 week intervals) had the same incidence of infection.

However, samples of new foliage that was flushing during the treatment period showed that all Mycoshield® foliar treatments (treatments 6 – 12) only had an infection incidence of 25 – 50 percent. The untreated, fertilizer + Pentra-Bark® alone, Agri-Mycin® 17 streptomycin (with and without Pentra-Bark®) and Mycoshield® trunk spray had an infection incidence of 50 – 75 percent.

Table 1: Mycoshield® HLB Foliar Suppression - Grapefruit - St. Lucie W 2014 Percent of Plots Positive for HLB / Old vs. New Foliage

Treatment	% Old Infect 7-27	% Old Infect 10-29	% New Infect 10-29
Untreated	75	75	75
Fertilizer (F) + Pentra-Bark® (P)	75	75	50
Agri-Mycin® Low Vol (AL)	100	100	50
AL + P	100	100	75
Mycoshield® + P Trunk	75	75	50
Mycoshield® Low Vol (ML)	100	100	25
ML + P	75	75	50
Mycoshield® High Vol (MH) + P	75	75	25
ML + F + P	100	100	25
MH + F + P	100	100	25
MH + RTREX Plus	100	100	25
MH + KeyPlex® 1400 DP	100	100	25

Antibiotic Foliar and Trunk Applications: 7-27, 8-15, 9-12, 10-11
Fertilizer Foliar Application: 7-27, 9-12
Fertilizer: 1 gal chelated iron + 5 lb. zinc sulfate + 5 lb. manganese sulfate / A
Agri-Mycin® 17 and Mycoshield® Low Vol: 1.5 lb. product in 100 GPA
Mycoshield® High Vol: 1.5 lb. product in 150 GPA
Mycoshield® Trunk: 1.5 lb. in 12.5 GPA @ approximately 8 oz./tree
Pentra-Bark®: Applied at 0.5% v/v foliar; 2.5% v/v trunk
Infection Incidence: % of plots testing positive for HLB based on PCR of old or young foliage

Table 2: Mycoshield® HLB Foliar Suppression - Grapefruit - St. Lucie W 2014 Percent of Tree Canopy a Contiguous Leaf Wall

Treatment	% leaf Wall Area 3-31-2015
Untreated	49 b
Fertilizer (F) + Pentra-Bark® (P)	48 b
Agri-Mycin® Low Vol (AL)	53 ab
AL + P	67 a
Mycoshield® + P Trunk	59 ab
Mycoshield® Low Vol (ML)	69 a
ML + P	67 a
Mycoshield® High Vol (MH) + P	71 a
ML + F + P	63 ab
MH + F + P	64 ab
MH + RTREX Plus	58 ab
MH + KeyPlex® 1400 DP	58 ab

Percent Leaf Wall: Visual assessment of canopy fullness averaged for 4 angles of perspective on each tree.

The 2014 study area recovered from the phytotoxicity and increased spring growth of the new canopy in 2015 was evident in all oxytetracycline foliar treatments relative to the untreated (9 – 22% denser canopy than the untreated). Several of the treatments were significantly superior to the untreated (5% probability level).

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Table 3: Mycoshield® HLB Foliar Suppression /Grapefruit - St. Lucie W 2015

Treatment	Vigor Rating 7-21-2015
Untreated	5.2 c
Mycoshield® + Pentra-Bark® Trunk	5.5 bc
Phostrol® 4.5pt/100 gal	5.5 bc
Mycoshield® LV	5.6 bc
Mycoshield® HV	6.8 abc
Mycoshield® + Phostrol® LV	6.3 abc
Mycoshield® + Tactic® 0.125% LV	6.7 abc
Mycoshield® + Tactic® 0.125% HV	6.2 abc
Mycoshield® + Tactic® 0.125% LV 4 appl*	6.8 abc
Mycoshield® + Dyne-Amic® 0.25% LV	5.7 bc
Mycoshield® + Dyne-Amic® 0.25% HV	6.2 abc
Mycoshield® + LI 700 0.25% LV	7.1 ab
Mycoshield® + LI 700 0.25% LV	7.7 a

Three applications to spring 2015 flush @ 2 week intervals
* A 4th application made 6 days after the 3rd
Mycoshield® Low Vol: 1.0 lb. product in 100 GPA
Phostrol® Low Vol: 4.5 pints in 100 GPA
Mycoshield® High Vol: 1.5 lb. product in 150 GPA
Mycoshield® Trunk: 1.5 lb. in 12.5 GPA @ approximately 8 ounces per tree
Pentra-Bark®: Applied at 0.5% v/v foliar; 2.5% v/v trunk
Tree Vigor Rating: 0 = dead; 10 = completely healthy growth

The 2015 grapefruit study was established on different trees. Application timing focused on periods of new growth flush in the spring, summer and fall. Periods of new growth are the optimal times for infection by *C*Las and it was expected that phloem penetration of oxytetracycline would occur at a greater concentration in newer foliage.
Many of the treatments involved the identification of additives that would improve performance without causing crop injury and the comparison of two spray volumes (100 and 150 gal/acre). Most treatments involved three applications at two week intervals initiated at a flush of new growth. Approximately six weeks after flush initiation, the foliage hardens, becomes less attractive to psyllid feeding and is less amenable to the penetration of oxytetracycline. One tank mix treatment of Mycoshield® + Tactic included a fourth spray applied six days after the third application. A trunk spray of Mycoshield® + Pentra-Bark® was added as a comparison with the foliar sprays which were applied to the point of runoff. Mid-season tree vigor ratings (0 – 10 scale) showed that all oxytetracycline foliar treatments were numerically higher than the untreated, trunk spray and Phostrol® alone. The mixture of Mycoshield® + LI 700 at 100 and 150 gal/acre was significantly superior to the untreated (5% probability level). Oxytetracycline degrades quicker at a neutral pH than under acidic conditions. LI 700 is an acidifying penetrating surfactant which may be stabilizing the applied residues and extending the period for leaf absorption.

Leaves were collected from selected treatments in the 2015 grapefruit trial and forwarded to Dr. Xiaoan Sun (Florida Department of Agriculture and Consumer Services,

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Division of Plant Industry) for residue analysis. Dr. Sun uses a method that has a lower limit of quantification (1 ppm). Values lower than this may represent false detects. The analysis proved that oxytetracycline penetrated the foliage and was still detectable in the single treatment that was collected four days after application. As predicted the residues were higher in young leaves than old leaves. However, oxytetracycline was not found at the limit of quantification in leaves at 10 days after application. The grapefruit leaf residue analysis supports that the application needs to be less than 10 days to prevent HLB bacteria from recovering and resuming growth.

Table 4: Mycoshield® - Grapefruit Leaf Residues 2015

Treatment	Additive	# Appl	Last Appl	Sampled	Foliage Residues (ppm)	
					Mature	New
Untreated	none	0	NA	22 May	ND – all Reps	ND, 0.5
Mycoshield® Foliar 1.0 lb./100 GPA	none	3	12 May	22 May	ND – all Reps	ND, 0.5
Mycoshield® Foliar 1.5 lb./100 GPA	none	3	12 May	22 May	ND – all Reps	ND, 0.7
Phostrol® Foliar 4.5 pt./100 GPA	none	3	12 May	22 May	ND – all Reps	ND – all Reps
Mycoshield® + Phostrol® /100 GPA	none	3	12 May	22 May	ND – all Reps	ND – all Reps
Mycoshield® Foliar 1.0 lb./100 GPA	Tactic	3	12 May	22 May	ND – all Reps	ND – all Reps
Mycoshield® Foliar 1.0 lb./100 GPA	Tactic	4	18 May	22 May	1.4 ,0.9, 0.6, 0.8	2.9, 0.8, 1.6, 0.8
Mycoshield® Foliar 1.0 lb./100 GPA	LI 700	3	12 May	22 May	ND – all Reps	ND – all Reps
Mycoshield® Foliar 1.0 lb./100 GPA	Dyne-Amic®	3	12 May	22 May	ND – all Reps	ND – all Reps

Comparison of oxytetracycline residues in mature and new flush foliage collected from the same trees.
Residues determined by *Bacillus subtilis* bioassay.
Leaf samples collected by John Curtis, Better Crops, LLC.
Leaf analysis conducted by Dr. Xiaoan Sun, FDACS, Div. of Plant Industry.

Table 5: Mycoshield® - Orange Leaf Residues 2015

Treatment	Additive	# Appl	Last Appl	Sampled	Foliage Residues (ppm)	
					Mature	New
Untreated	none	0	NA	19 Aug	ND	ND
Untreated	none	0	NA	22 Aug	ND	ND
Mycoshield® Foliar 1.5 lb./150 GPA	none	1	18 Aug	19 Aug	3.2	7.3
Mycoshield® Foliar 1.5 lb./150 GPA	none	1	18 Aug	22Aug	ND	ND

Comparison of oxytetracycline residues in mature and new flush foliage collected from the same trees.
Residues determined by *Bacillus subtilis* bioassay.
Leaf samples collected by Henry Younce, KAC Agricultural Research, Inc.
Leaf analysis conducted by Dr. Xiaoan Sun, Florida Department of Agriculture and Consumer Services, Div. of Plant Industry

Similar results were obtained from a residue analysis of treated orange (Hamlin) foliage from another location. One day after application, the oxytetracycline residue concentration in new flush foliage was 7.3 ppm, which exceeded the concentration in mature leaves by more than 2X. At the orange site, residues were not detected in foliage at four days after application

Based on this information then, the following use instructions are proposed for the specific exemption:

- A use concentration of 200 ppm that provides disease suppression in field trials and is consistent with the current maximum use concentration on the Mycoshield® label.

- Full coverage foliar application to the point of run-off. Oxytetracycline residues are rapidly degraded and inactivated in the soil. High volume applications that result in the run-off of excess material would be of no performance value.

- Testing the crop safety of tank mixtures to avoid potential phytotoxicity issues.

- Targeting applications to periods of new leaf flushes. This is supported by disease suppression results, leaf residue analysis and the infection properties of HLB.

- Apply at 21 day intervals. Although there were distinct benefits with 2- and 3-week intervals in 2014 and 2015 field trials, there was room for improvement. As a bacteriostat, the activity of oxytetracycline is improved by extended intervals of exposure. Residues were not detected in foliage at 10 days after application in the grapefruit trial and at four days after application in the orange trial. Applications at 3 – 7 day can be made for labeled use for control of fire blight on apples and pears.

- Use in combination with an Asian citrus psyllid management programs recommended by local experts. Imperfect vector control and suppression of HLB would be complementary strategies.

- Studies (Xia, 2012) have shown that high summer temperatures reduce the HLB levels in infected trees and in the psyllid. Thus, this emergency exemption request recommends targeting spring and fall flushes with oxytetracycline applications when the greatest benefit is expected. The exception would be a grower that intends to use oxytetracycline in combination with vector control to delay the infection of newly planted trees. In this situation, all flushes would need to be targeted with both technologies. Additional research is needed to investigate the use of oxytetracycline in a preventative program and large treatment areas are needed to optimize the activity of the vector control component. The expanded treatment acreage allowed under this emergency exemption request will enable the investigation of large area HLB prevention programs.

DISCUSSION OF RESIDUES IN FOOD (166.20(a)(6)) (166.20(a)(6))

FireWall™ 50WP and FireLine™ 17WP

AgroSource, Inc. and the IR-4 Project have performed Magnitude of Residue studies for streptomycin sulfate and oxytetracycline in/on citrus commodities. Field residue studies have been conducted and this information has been submitted to the Agency or is being

submitted to the Agency. Dietary and drinking water exposure and risk assessment with the current crop uses plus citrus have been performed using DEEM-FCID version 4.02 and citrus residue data from recent citrus field studies treated with three foliar applications at the proposed Section 18 label rates of both streptomycin and oxytetracycline each application. Based on available information, a temporary streptomycin tolerance of 0.5 ppm and a temporary oxytetracycline tolerance of 0.1 ppm on citrus are proposed.

For the streptomycin dried pulp fraction, the proposed tolerance will be 3.5 ppm and for the oil and juice fractions the proposed tolerance is 0.005 ppm (50% of the LOQ).

For oxytetracycline, no residues (LOQ=0.01 ppm) were found in whole fruit, orange peel, juice or dried pulp in crop residue trials. Residues of oxytetracycline in orange oil ranged from ND (<0.002 ppm) to <LOQ (0.01 ppm). Therefore, the NAFTA MRL of 0.01 ppm on the citrus fruit group 10-10 is proposed as the tolerance.

The summary of the residue data and the corresponding risk assessments to support the use of FireWall ™ and FireLine ™ for on citrus is included in the Appendix D – 3 and D – 4)

Mycoshield®

A GLP residue study on citrus fruit sponsored by Nufarm Americas Inc. was initiated in March 2015 to support a tolerance petition and registration application for the use of Mycoshield® on the Citrus Fruit Crop Group 10-10 commodities. The study is expected to be completed by the end of June 2016. Residue data are currently available for several of the field trials and include data for raw agricultural commodities and processed fractions. Based on available data, Nufarm is proposing the establishment of time-limited tolerances for residues of oxytetracycline in or on orange, Crop Subgroup 10-10A, at 0.4 ppm and grapefruit, Crop Subgroup 10-10C, at 0.4 ppm. A summary of analytical results is provided in the Appendix E - 3.

The proposed time-limited tolerances for orange and grapefruit commodities are consistent with the tolerances of 0.35 ppm already established for apples, pears and peaches. The processing study was conducted at the exaggerated rate of 5 times the proposed application rate of 1.5 pounds Mycoshield®/acre (7.5 lb. Mycoshield®/acre). No detectable residues were found in orange juice. Residues in whole oranges and grapefruit were approximately 0.2 and 0.02 ppm, respectively.

To mitigate the small dietary risk posed by the specific exemption use on Florida orange and grapefruit crop subgroups 10-10A and 10-10C, a maximum of 8 applications per year and a maximum annual rate of 12 pounds of Mycoshield® per acre are proposed (compared to the 12 applications and the total rate of 21 pounds of Mycoshield® per acre used for the conduct of the residue study on citrus). In addition, a retreatment interval of 21 days is proposed instead of the 2-day retreatment interval used in the residue

trials. With these risk mitigation measures in place, it is very unlikely that any residues detected in treated citrus commodities will exceed the proposed time-limited tolerances for oxytetracycline in/on orange and grapefruit crop subgroups 10-10A and 10-10C. The incremental risk associated with the Section 18 use is therefore expected to be below the Agency's level of concern.

The summary of the residue data and the corresponding risk assessments to support the use of Mycoshield on citrus subgroup 10(A) and 10(C) is included in the Appendix E – 3 and E – 4)

Proposed Time Limited Tolerance

It is anticipated that a single time limited tolerance would be set for the use of Oxytetracycline under the Section 18. As a result of the status of the supporting data across both registrants we would propose the following:

- Fruit, citrus, subgroup 10-10A at 0.4 ppm (the highest of the tolerance level needed for both FireLine 17WP and Mycoshield)
- Fruit, citrus, subgroup 10-10B at 0.1 ppm (needed to cover anticipated residues resulting from the use of FireLine 17WP only)
- Fruit, citrus, subgroup 10-10C at 0.4 ppm (the highest of the tolerance level needed for both FireLine 17WP and Mycoshield)

DISCUSSION OF RISK INFORMATION (166.20(a)(7))

Description of application sites, including proximity to residential areas, aquatic systems, endangered or threatened species habitats, soil types, etc.:

FireWall™ 50WP and FireLine™ 17WP

FireWall™ 50WP and FireLine™ 17WP will only be applied to commercial citrus groves. These groves are typical of those found in Florida. Commercial groves are intensive and no unreasonable risks to human health, endangered or threatened species, beneficial organisms, or the environment are expected from the proposed use of this product.

Also included in the Appendix is an executive summary of work done in association with FDA requirements #152, Resistance Risk Assessment for Foliar Applications of FireWall™ and FireLine™ to citrus crops. With integration of the effective resistance management options, this situation does not significantly change the existing Qualitative Risk Assessment for the emergence of streptomycin or oxytetracycline resistance among clinical pathogenic bacteria. Since this proposed new use of streptomycin and oxytetracycline on citrus crops to improve tree health

and manage HLB is unlikely to represent a source for potential emergence of streptomycin or oxytetracycline resistance among clinical pathogens, approval of the proposed new use of streptomycin and oxytetracycline on citrus crops is believed to be in the public interest.

Mycoshield®

Mycoshield® will be applied to commercial orange and grapefruit plantings, including all citrus fruit belonging to the citrus crop subgroups 10-10A and 10-10C (Calamondin; citron; citrus hybrids; grapefruit; Japanese summer grapefruit; Mediterranean mandarin; orange (sour); orange (sweet); pummelo; satsuma mandarin; tachibana orange; tangelo; tangerine (mandarin); tangor; trifoliate orange; uniq fruit; cultivars, varieties, and/or hybrids of these). Use under the Section 18 will occur in all areas of the state with commercial citrus groves.

Possible risks posed by use:

FireWall™ 50WP and FireLine™ 17WP

FireWall™ 50WP Fungicide/Bactericide and FireLine™ 17WP Fungicide/Bactericide are approved products registered by the U.S. Environmental Protection Agency that have been used in the field for more than 40 years. Possible risks were evaluated during Section 3 registration and reregistration processes for both compounds. FireWall™ is currently registered for use on crops such as beans, celery, peppers, potatoes, tomatoes, apples and pears, and FireLine™ is currently registered for use on crops such as apples, pears, peaches and nectarines. No unreasonable adverse effects to man or the environment are anticipated with this proposed use of three applications of streptomycin and three applications of oxytetracycline to Florida citrus. Additional information for FireWall™ and FireLine™ on these subjects can be obtained from Taw Richardson with AgroSource. His phone number is (908) 215-3500.

Facts associated with the potential for increasing the risk of human resistance to streptomycin and oxytetracycline have also been addressed in the TRED for oxytetracycline and the R.E.D. Facts publications for streptomycin, streptomycin sulfate and oxytetracycline. The streptomycin R.E.D. EPA report says that "regarding the problem of drug resistance, EPA has no data indicating that streptomycin residues remaining in the food supply have a significant or even a measurable potential for increasing human resistance to that drug." The Regulatory Conclusion of that same publication says that "all currently registered pesticide products containing streptomycin or streptomycin sulfate as the active ingredient are not likely to cause unreasonable adverse effects in people or the environment." The TRED for streptomycin says that "antibiotic resistance from pesticidal use of streptomycin is unlikely to result directly from dietary residues of streptomycin because dietary residues are very low. The drug dose is 3,000 times greater than the estimated pesticidal dietary exposure. The small dose from

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(streptomycin) pesticidal exposure would not be expected to select for resistant bacteria because very few bacteria would be killed by this small dose."

The streptomycin FDA #152 study summary paper notes that "streptomycin has been safely and effectively used in plant agriculture since 1955, yet a direct connection to the emergence of streptomycin resistance among clinical pathogens as a consequence of this use pattern remains undocumented. EPA has previously determined that the dietary exposure to streptomycin is below its level of concern. The use of streptomycin to manage HLB in commercially grown citrus crops does not increase the chronic aggregate exposure to a level of concern, since the combined aggregate residential and chronic dietary exposure to all agricultural applications of streptomycin, including the proposed us of streptomycin on citrus crops is 2,491 times less than the No Observed Adverse Effects Level (NOAEL) for the total U.S. population and 719 times less than the NOAEL for the most affected population subgroup, non-nursing infants. Dietary intake of streptomycin does not constitute a source of selection pressure for streptomycin resistance among enteric gut flora, since the dietary exposure from streptomycin applications to plant agriculture is so low and oral absorption for streptomycin is extremely low (<1%). Recent studies have revealed streptomycin-resistant isolates of many plant pathogenic bacteria exist as stable populations in the environment, even where streptomycin has never been applied, giving indication that factors other than streptomycin applications in the field influence the emergence of streptomycin resistance among plant pathogenic bacteria."

Similarly, the R.E.D. publication for oxytetracycline says that the "use of the active ingredients hydroxytetracycline monohydrochloride and oxytetracycline calcium in accordance with approved labeling will not result in unreasonable adverse effects to human health or the environment." Facts pertaining to risks have also been addressed in association with the potential for increasing the risk of human resistance to oxytetracycline in EPA's TRED for oxytetracycline, as well as the FDA #152 assessment. The EPA oxytetracycline TRED concluded that "because anticipated dietary residues are extremely low, it is unlikely that antibiotic resistance from pesticidal use of oxytetracycline would result from food exposure," and "the drug dose is 50,000 times greater than the estimated pesticidal dietary exposure (25 mg/kg/day dose divided by maximum aggregate dietary exposure of 0.000473 mg/kg/day). The small dose from pesticidal exposure would not be expected to select for resistant bacteria because very few bacteria would be killed by this small dose." In the latest oxytetracycline dietary risk assessment, the drug dose is nearly 82,000 times greater than the estimated pesticidal dietary exposure [25 mg/kg/day dose divided by maximum aggregate dietary exposure of 0.000305 mg/kg/day for non-nursing infants (the highest population sub-group)]. Therefore, anticipated dietary residues of oxytetracycline are extremely low, and it is also unlikely that antibiotic resistance from the pesticidal use of oxytetracycline would result from food exposure.

The AgroSource oxytetracycline FDA #152 study summary paper notes that "oxytetracycline has been safely and effectively used in plant agriculture for more than 40 years yet a connection to the emergence of oxytetracycline resistance among clinical pathogens remains undocumented. EPA has previously determined that dietary exposure to oxytetracycline is below its level of concern. The use of oxytetracycline to combat HLB in citrus crops does not significantly increase the chronic aggregate exposure to oxytetracycline. Dietary intake of oxytetracycline is not expected to constitute a source of selection pressure for oxytetracycline resistance among enteric gut flora since the combined aggregate residential and chronic dietary exposure to all agricultural applications of oxytetracycline, including the proposed us of oxytetracycline on citrus crops, by non-nursing infants is 164 times less than the NOAEL, and approximately 82,000 times less than the commonly prescribed therapeutic dose for this most affected population subgroup."

As a condition of the approval of a Section 18 exemption for the use of FireWall™ 50WP for the management of citrus canker (*Xanthomonas citri* pv. *citri*) on commercially-grown grapefruit in Florida, field studies were conducted during the 2014 season designed to detect potential development of streptomycin resistance in the culturable microbial communities from both phyllosphere and rhizosphere zones of FireWall™ 50WP treated (tested) and untreated (control) trees. Two commercial grapefruit grower cooperators provided a total of five unique test sites, all located within the Indian River Citrus growing region of southeastern Florida. No test site had previously received any treatments with streptomycin or streptomycin-based products. FireWall™ 50WP was applied to the test sites following the Section 18 label directions. Samples for culturable bacteria (as found in soils from beneath each tree and leaves taken from each tree) were collected at four dates beginning in August 2014 (T0) and ending in December 2014 (T3). Samples from all FireWall™ 50WP treated and corresponding untreated plots were analyzed for evidence of streptomycin-resistant bacteria. When the data were analyzed across all five test sites, results indicated no consistent and significant change ($p=0.05$) in phyllosphere or rhizosphere microbial populations. More importantly, results revealed no evidence for development of streptomycin resistance among bacterial populations resident in FireWall™ 50WP treated grapefruit trees or soils in response to the use of FireWall™ 50WP on Florida grapefruit for management of citrus canker.

Mycoshield®

Mycoshield® is currently registered for use on apples, pears, peaches and nectarines. Occupational exposure and risk are not expected to exceed the Agency's level of concern since airblast application at the same maximum rate of 1.5 pounds of formulated product per acre per application is already registered for peaches, nectarines and apples. EPA stated in the 2008 Health Effects Division (HED) Scoping Document for Registration Review of oxytetracycline that an

occupational assessment was not needed because of the low level of exposure anticipated from application of oxytetracycline products and the personal protective equipment required by the Section 3 label that includes protective clothing, chemical-resistant gloves, protective eyewear and a respirator. The occupational exposure and risk associated with the proposed Section 18 use on Florida citrus is therefore expected to be well below the Agency's level of concern.

The proposed time-limited tolerances of 0.4 ppm for residues of oxytetracycline in or on orange, Crop Subgroup 10-10A, and grapefruit, Crop Subgroup 10-10C, are based on data available to date from the ongoing magnitude of residue study (included in the Appendix E). Twelve foliar airblast applications of Mycoshield® were made at the maximum use rate of 1.5 pounds of formulated product per acre per application with a 2-day retreatment interval plus two trunk applications of Mycoshield® at 1.5 pounds of formulated product per acre per application. This resulted in a total application rate of 21 pounds of formulated product/acre (3.57 lb. oxytetracycline/acre) whereas the proposed Section 18 label limits application to 12 pounds of formulated product/acre (2.04 lb. oxytetracycline/acre) total per year.

In the 2008 EPA Health Effects Division's Scoping Document for Registration Review of oxytetracycline, EPA concluded that expected dietary (food and water) risk for the U.S. population and all subpopulations was conservative and below the level of concern. Acute dietary exposure was not estimated because no acute toxicity was identified in any of the relevant studies in the oxytetracycline database. As a result, EPA determined that acute dietary risks are not of concern.

In order to investigate potential exposure and risk associated with the proposed Section 18 use on Florida citrus, Nufarm sponsored a chronic aggregate dietary assessment for currently registered uses of oxytetracycline and the proposed use on citrus in Florida. The available data from Nufarm's residue study on citrus were used to assess dietary exposure. The resulting chronic risk estimates are not of concern for any population assessed. Based on this assessment, there are no dietary exposure issues that would preclude the specific exemption use on citrus trees in Florida. Since there is no residential use of oxytetracycline, an assessment that aggregates more than food plus water is not needed.

A drinking water exposure assessment was also conducted for currently registered uses of Mycoshield® and the proposed Section 18 use on Florida citrus trees. The resulting drinking water concentrations were used in the dietary risk assessment. Concentrations were calculated to be very low or practically non-existent (report included in the aggregate dietary risk assessment). The impact of the Section 18 use on the ecological risk is not expected to exceed the Agency's level of concern. Oxytetracycline residues degrade rapidly in citrus foliage. As discussed in the section "Effectiveness of Proposed Use under Section 18", leaf residue analysis has shown that oxytetracycline residues were no longer detectable in foliage 10 days

after application to a grapefruit location and 4 days after application to an orange site.

Nufarm has responded to Data Call-In notices issued for the TRED and Registration Review of Oxytetracycline. Several studies including environmental fate and ecotoxicology studies were conducted to support the continued registration of Mycoshield®. Most of these studies have already been submitted to the EPA or will be submitted in the near future.

Regarding the potential for resistance development, it is unlikely that antibiotic resistance from pesticidal use of oxytetracycline would result from food exposure. Anticipated dietary residues for existing agricultural uses of oxytetracycline and the proposed Section 18 for Florida citrus are extremely low (conservatively estimated at 0.000076 mg/kg/day for the general U.S. population). The maximum aggregate dietary exposure calculated is very small when compared to pharmaceutical or veterinary doses. The small dose from pesticidal exposure would not be expected to select for resistant bacteria because very few bacteria would be killed by this small dose. An assessment of the potential for antibiotic resistance to develop as a result of the use of Mycoshield® on citrus was conducted following FDA Guidance #152 and is included in Appendix E-4. Additional information for Mycoshield® on these subjects can be obtained from Bill Bewlay with Nufarm.

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Proposals to mitigate risks:

Existing use restrictions already listed on both the streptomycin and oxytetracycline labels will further reduce risk. These label restrictions include: do not apply directly to water, or to areas where surface water is present, or to intertidal areas below the mean high watermark; do not contaminate water when disposing of equipment wash water; do not apply by aircraft; do not apply these products through any type of irrigation system; and, only three applications of streptomycin and three applications of oxytetracycline are allowed per season. Current labeling directives are sufficient to mitigate any potential risks. Full reports of tests and investigations made with respect to the safety of streptomycin and oxytetracycline, including all information pertaining to the methods and controls used in conducting these tests and investigations have been submitted and reviewed by the Agency.

The enforcement analytical methods for both products are available to monitor residues of streptomycin and oxytetracycline in citrus.

FQPA INFORMATION (OCTOBER 24, 1996 EPA LETTER)

EPA requested that additional information be submitted with Emergency Exemption requests to address new risk considerations associated with requirements of the Food Quality Protection Act. This information has been provided to the Agency. Since these products are approved for other Section 3 registrations an initial FQPA review has already occurred.

COORDINATION WITH OTHER AFFECTED FEDERAL, STATE, AND LOCAL AGENCIES (166.20(a)(8))

As EPA's state lead agency, the Florida Department of Agriculture and Consumer Services should provide this information.

NOTIFICATION OF REGISTRANT (166.20(a)(9))

AgroSource, Inc. and Nufarm Americas Inc. have been notified of this request. The companies are supportive of this emergency exemption petition (see the Appendix for registrant support letters).

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DESCRIPTION OF ENFORCEMENT PROGRAM (166.20(a)(10))

As EPA's state lead agency, the Florida Department of Agriculture and Consumer Services should provide this information.

REPEAT USES (166.20(a)(11))

This is the first request for the use of each of the requested products, streptomycin and oxytetracycline on citrus by Florida for management of HLB and improvement of overall citrus tree health. The use of antibiotics under this Emergency Exemption Request will suppress HLB in new growth but will not cure the infection in the branches, trunk and roots. The reservoir of bacteria in the lower portions of the tree is a source for constant reinfection. Even new plantings are subjected to continuous pressure from 'hot' psyllids. A Section 18 Emergency Use Exemption would be needed until the Section 3 registrations are obtained.

PROGRESS TOWARD REGISTRATION (166.25(b)(2)(ii))

FireWall™ 50WP and FireLine™ 17WP

AgroSource, in conjunction with the IR-4 Project, continues to make progress toward new registrations for the use of streptomycin and oxytetracycline on the citrus crop group and a variety of other crops. The company is preparing or has prepared and submitted the necessary documentation for a Section 3 registration for citrus. The application to amend the Section 3 label for streptomycin has been submitted to EPA (Decision Number: 486863) and a Pesticide Registration Improvement Extension Act (PRIA) due date of 05/04/2015 had been assigned. EPA subsequently decided to require that this request go through a "public participation process". As part of preparation for this process, EPA issued a deficiency letter to AgroSource (to provide more benefits information) and both parties "mutually agreed" on a new PRIA date of June 2016. Subsequently, the new submission goal for oxytetracycline on citrus is now October 1st, 2015 and for streptomycin the new citrus submission goal is November 1st, 2015.

Mycoshield®

A GLP residue study on citrus fruit sponsored by Nufarm Americas Inc. was initiated in March 2015 to support the registration of Mycoshield® on the Citrus Fruit Crop Group 10-10. The study is expected to be completed by the end of June 2016. It will then be submitted to the EPA in support of a tolerance petition and Section 3 registration application. Nufarm anticipates submitting the application by August 1st, 2016. Assuming a timeline of 15 months for the EPA review, the registration could possibly be granted by the end of November 2017.

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Nufarm is the basic registrant for Oxytetracycline Calcium and is responding to Data Call-In notices issued for the TRED and the Registration Review of Oxytetracycline. Several studies were required including environmental fate and ecotoxicology studies that also support the Registration Review of Oxytetracycline Hydrochloride (Appendix E-5).

NAME OF PEST (166.20(b)(1))

Scientific Name:

Candidatus Liberibacter asiaticus (*C*Las)

Common Name:

Disease:
Huanglongbing (HLB) or Citrus Greening or Yellow Dragon Disease

Vector:
Asian Citrus Psyllid (ACP) (*Diaphorina citri* Kuwayama)

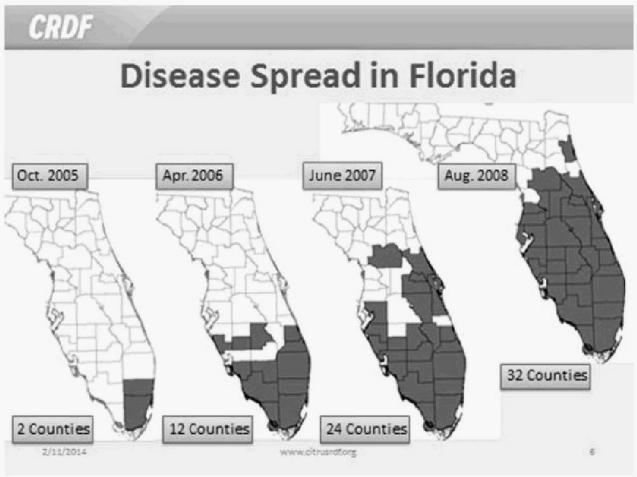
DISCUSSION OF THE EMERGENCY CONDITION (166.20(b)(2))

Citrus huanglongbing has been known in China for more than 100 years. In 1929, a disease with similar symptoms appeared in South Africa and was named 'yellow branch' in Western Transvaal and 'greening' in Eastern Transvaal. The agent associated with the disease was transmitted by graft-inoculation from citrus to citrus for the first time by Lin in China in 1956. This work remained unknown outside China; McLean and Oberholzer demonstrated independently that South African greening was graft-transmissible. Because 'huanglongbing' was the name used in the paper describing graft-transmission of the agent for the first time, it has priority over other names and has been unanimously adopted as the official name of the disease by the International Organization of Citrus Virologists (IOCV) at the 12th Congress of IOCV, Fuzhou, China, 1995.

In the 1960s, the agent was shown to be transmitted by two insects: the African citrus psyllid *Trioza erytreae* in Africa and the Asian citrus psyllid *Diaphorina citri* in Asia.

Symptoms of HLB were reported in Sao Paulo state in Brazil in 2004. Then, in 2005, HLB, was found to be present in Florida. This disease is caused by the pathogen *Candidatus* Liberibacter asiaticus and is spread by the Asian citrus psyllid (*Diaphorina citri* Kuwayama), which is an invasive pest to Florida, first discovered in 1998. HLB is considered to be the most serious disease of citrus worldwide and has greatly limited commercial production of citrus in countries where it is present. Since its discovery in Florida, this disease has rapidly spread throughout citrus production area to all

commercial production areas in the state. The graphic below illustrates the rapidity with which HLB invaded Florida commercial citrus counties:



(Source: CRDF Presentation to EPA, February 5, 2014)

HLB is a prime example of how an unintentional, but illegal, plant introduction into a country can cause multi-billion dollar crop losses, unemployment and industry-wide financial strain. The HLB bacterium lives in the vascular system component (phloem) that conducts synthesized food materials from the tree to the roots. Like the human blood vessels, a blockage of these vascular system conducting tissues by any foreign substance produces deleterious effect. The presence of *C*Las in the phloem prevents the tree from effectively transporting water, nutrients and minerals between the leaves, fruit and the roots in the ground, thereby driving the tree into decline. Since this disease's appearance, citrus production has been compromised with the loss of millions of trees, and HLB has subsequently been detected in every county with commercial citrus and in residential dooryard citrus as well. Trees infected with HLB will continuously decline and eventually die, even when incorporating all management options available to the industry at this time. The HLB-causing bacterium found in Florida is the Asian species that occurs in warm low altitude areas. HLB survives and multiplies within the psyllid vector throughout the psyllid's lifetime. The psyllid was first found in Florida in June 1998.

The severity of HLB and declining tree health far exceeds that of any previously known citrus disease, and all citrus species and their hybrids are confirmed to be affected by HLB. Infected trees first produce leaf symptoms; typically leaf yellowing on one or more branches, then leaves develop a blotchy (irregular spotted) appearance with grades of color. Infected trees typically also show symptoms that resemble micronutrient deficiency, especially, zinc and manganese. Fruit set becomes thin, fruit appear lopsided, the lopsided fruit may contain aborted seeds, and juice quality is unacceptable.

Impacts from HLB are numerous. On infected trees fruit are few in number, small, lopsided with a curved central core, and they fail to color properly, remaining green at the stylar end (hence the name "greening"). Excessive fruit drop occurs prematurely on

afflicted trees, and this has been reported in the past three harvest seasons in Florida to exceed 10 percent per season across all varieties. Even if fruit remain on the tree until harvest, the fruit are undersized and contain bitter juice, rendering it of reduced economic value. From a fruit size standpoint, HLB-infected trees have a significantly greater portion of fruit in smaller size categories compared to healthy trees (more than 95% of symptomatic fruit are less than 2.25 inches in diameter). Total juice volume produced is less from HLB-positive trees because of the smaller fruit size as well. Extensive research has been done to characterize the off-flavors associated with HLB-infected trees, highlighting both the general brix/acid ratio impacts as well as the components that contribute to flavor. This work is presented in detail by Baldwin, et al. 2010, Ikpechukwu et. al, 2011, Plotto et. al., 2013 and Massenti et. al. 2015.

HLB disease and the lack of any tree health improvement antibiotic has already pushed untold numbers of farmers out of the industry. Between 2004 and 2014, the amount of Florida land planted with citrus shrunk by nearly one-third, from 748,555 acres down to 515,147 acres (USDA, FASS). During that same timeframe, overall citrus production in the state dropped from 292 million boxes of fruit down to 124 million boxes (a 58% reduction). Average orange yields sunk from 428 boxes per acre in 2004 down to 250 boxes an acre in 2014 (a 42% reduction), despite the higher-density new plantings of orange trees, almost solely resulting from HLB infection.

Also contributing to the situation (and the continued higher grove maintenance costs) are Asian citrus psyllid management requirements. Since the psyllid's discovery, annual production costs have more than doubled. The majority of these increased costs are derived from psyllid management requirements and the necessary modified cultural practices. Psyllid management is an absolute necessity with respect to controlling HLB spread; the threshold for psyllid treatment has become "less than zero" in the industry. A high proportion of psyllids are now infected with the bacteria and capable of transmitting the disease. Florida citrus growers are currently spending more than $240 million a year on insecticides directed solely to manage psyllids, which is about 30 percent more than they were spending in 2004, even though they're farming about 30 percent less land and yielding half as much fruit.

Citrus production and research experts believe that looking forward, the pursuit of interventions to reduce Asian citrus psyllid populations, reducing HLB bacterial populations within infected trees, and promotion of optimal tree health in the presence of HLB are the keys to the citrus industry's sustainability. The industry to this point has pursued a three-pronged approach to combating HLB, focusing on interventions on the three components of the disease pathosystem. The first component involves managing the psyllid. The second is understanding the bacterium itself, with the goal of hopefully neutralizing impact on psyllids or trees. Access to antibiotic materials such as streptomycin and oxytetracycline is vital to induce the improvement of tree health and subsequently keep trees viable until these other HLB management approaches can be developed. The third component is to breed new citrus trees that will hopefully tolerate or resist infection.

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HLB is truly a limiting factor for citrus production. In the attempt to improve tree health to the degree possible, cultural practices such as foliar micronutrient sprays are employed once HLB infects a tree, but these effects are short-lived and certainly will not sustain the industry. HLB is already directly responsible for the loss of thousands of acres of Florida citrus trees. An emergency exemption involving multiple antibacterial strategies that enables improved fruit production must be gained in order to counter the impact of this bacterium/vector complex that is threatening the short- and long-term viability of the state's $7 billion citrus industry. Without such antibiotic access and without anything else changing, within five to eight years of becoming infected, diseased trees will no longer be economically productive.

Limitations on replanting to replace declining tree inventories have made it critical to extend the productive life of the more than sixty million mature citrus trees in commercial groves. Continued production from this inventory of mature (infected) trees while new trees come on line is the process by which the Florida citrus industry can avoid failure and loss of critical nursery, production, harvesting, processing, packing and marketing infrastructure.

HLB infection rates in new plantings

Groves ~2 years of age (2014)

Psyllid pressure	HLB infection range	Average infection rate	# of groves
1 - low	0 – 4.05%	1.02%	20
2 – medium	1.73 – 65.6%	17.7%	20
3 - high	0 – 36.9%	20.96%	21

The graphic above emphasizes the point that despite ACP management programs, new plantings are still becoming infected and these would be primary targets for bactericide treatment.

Biology of *C*Las and Disease Onset/Progression

The complicated biology of HLB and the interactions between vector, pathogen and host citrus plant make development of solutions challenging. Following inoculation of *C*Las into uninfected citrus trees, a period of latency follows during which time there is no

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evidence of infection. Early symptom development is manifested through mottled foliage, followed progressively by smaller and narrower leaves, reduced mature fruit size and thinning of canopies. Chronic symptoms include limb dieback, fruit yield and quality reduction, and pre-harvest shedding of mature fruit. The time period of this disease progression varies with tree age and inoculum pressure, but generally in mature trees chronic decline appears within three to four years of initial infection.

New information on Root Impacts

Research reported over the past three years (Graham et. al., 2012, Johnson et. al., 2014, and Graham and Morgan 2015) has revealed that *C*Las infection of citrus involves early movement of bacteria to root systems, where direct impacts on root health result. Root systems of infected trees have relatively fewer feeder root densities, diminishing water and nutrient uptake efficiencies and exposing diseased trees to additional stress. Further evidence from field research has demonstrated that HLB-infected trees are susceptible to lower populations of Phytophthora propagules than healthy trees, indicating that HLB infection allows soil diseases to overcome or break rootstock tolerance.

Significant economic loss has been experienced through lower fruit quality and smaller fruit size as described below, and proposed bacterial therapies have the potential to improve this aspect of the disease as root systems are restored. Strategies that address reduction in *C*Las titers in infected plants are few, but focus on reduction of bacterial levels early in disease development.

While research continues to further elucidate the impacts of early migration of *C*Las into root systems, it has become necessary for growers to apply additional treatments for Phytophthora, root weevils and other soil stressors. It is expected that this root health compromise will also impact the ability of citrus trees to respond to weather disruptions like freeze events or sustained heavy rainfall.

<u>Non-Routine Emergency Situation:</u>

The rapid decline of HLB-infected mature citrus trees as evidenced by reduction in fruit size and quality and with the dramatic increase of fruit drop as fruit reaches harvest maturity.

Dr. Ariel Singerman of the University of Florida, IFAS, Citrus Research and Education Center has updated grower estimates of the spread of HLB in Florida and its impacts on production. This study is included in the Appendix and is posted at http://www.crec.ifas.ufl.edu/extension/economics/. Here are highlights regarding HLB incidence in Florida:

- 57 percent of growers surveyed report that 100 percent of their groves were infected, while 24 percent and 13 percent reported 80-99 percent and 60-80 percent infection, respectively.

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- On a tree-by-tree basis, 15 percent reported 100 percent of their trees were infected, while 49 percent and 21 percent reported 80-99 percent and 60-80 percent tree infection rates, respectively.

- 80 percent of respondents reports yield losses in the range of 20-60 percent, with 13 percent of respondents reporting more than 60 percent yield loss.

These estimates reinforce official crop production figures from USDA/FASS reported elsewhere in this petition and highlight the level of impact on individual growers as the disease decline continues.

DISCUSSION OF ECONOMIC LOSS (166.20(b)(4))

The damage resulting from HLB infection is considerable. Diseased trees decline, yields are reduced, and fruit quality is affected. As the disease severity increases, yield is reduced through a combination of smaller crop set, preharvest fruit drop from affected branches and smaller fruit size. The yield reduction can reach 30 to 100 percent, depending on proportion of affected canopy. This level of disease progression makes the grove economically nonviable 7 to 10 years after planting. As disease severity increases, the percentage of affected fruit increases, reaching more than 40 percent. The affected fruit are smaller, lighter, very acidic, with reduced Brix, ratio, percentage of juice and soluble solids per box, and juice quality is negatively impacted. Millions of citrus trees in Florida have been affected by HLB and subsequently destroyed. The last projected value that has been established as a direct cost of HLB to Florida's citrus industry is around $300 million annually.

The loss of production is felt by more people than just the famers that grow citrus. As production declines, packing houses do not run, box makers do not sell their products, shipping companies do not operate, etc.

Dr. Ariel Singerman, Assistant Professor of Agricultural Economics at the University of Florida, IFAS, Citrus Research and Education Center, has recently evaluated the impact of HLB on citrus production costs across the three general production regions of the state. His work is posted on http://www.crec.ifas.ufl.edu/extension/economics/.
Below is a summary of Dr. Singerman' s findings from citrus production operations in the three regions:

Central Florida (Ridge) Cost of Production for Processed Oranges:

The Table below shows total costs growers incurred for 2014-15, which includes cultural costs, tree replacement plus other costs such as management, regulatory and opportunity costs. The total cost of production for processed oranges for 2014-15 is reported to be $2,282.19 per acre. Contributions to cultural operations include foliar

sprays at $705.30 per acre; Citrus Health Management Area (CHMA) sprays $56.65 per acre; fertilizer expense at $469.80, and weed control at $246.31. With thinner tree canopies and open spots where HLB has caused tree death, even weed management costs have escalated. This can be compared to production costs averaging $700-800 per acre prior to HLB.

Table 6: Total Costs of Production per Acre for Processed Oranges in Central Florida (Ridge), 2014/15.

Total Cultural Costs with Tree Replacement		1819.74
Other Costs	Interest on Operating (Cultural) Costs	90.99
	Management Cost	81.75
	Property Tax/Water Management Assessment	35.37
	Interest on Average Capital Investment	254.34
Total Other Costs		462.45
Total Costs		**2282.19**

Southwest Florida Cost of Production for Processed Oranges:

Similarly, costs for production of oranges in southwest Florida continue to climb, in the Table below excerpted from this section of the Singerman report. In this case, foliar sprays average $666 per acre plus $20.55 for CHMA sprays. Fertilizer costs were $486.90 per acre, and weed control averaged $248.19. The total cultural operations costs of $1,998.10 per acre are more than double those experienced prior to HLB impact.

Table 7: Total Costs of Production per Acre for Processed Oranges in Southwest Florida, 2014/15

Total Cultural Costs		1998.10
Other Costs	Interest on Operating (Cultural) Costs	99.91
	Management Cost	63.34
	Property Tax/Water Management Assessment	28.73
	Interest on Average Capital Investment	254.34
Total Other Costs		446.31
Total Costs		**2444.41**

Indian River Cost of Production for Fresh Grapefruit:

In the case of the Florida's premier production area for fresh grapefruit, the Indian River, the production costs mirror the increases observed in the other regions for processed

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oranges, but are magnified due to the need for fresh fruit quality and its impacts on production costs. The Table below from the Indian River portion of the report indicates a total of $2,478.61 cultural costs for 2014-15 and an overall per acre average production cost of $3,073.38 per acre. Relevant operational costs are $1,300.40 per acre for foliar sprays and $14.75 for coordinated sprays (CHMA); fertilizer costs average $452.55 per acre and weed control averaged $190.60 per acre. This compares to fresh fruit production costs prior to HLB that averaged $1,000-1,200 per acre per year.

Table 8: Total Costs of Production per Acre for Fresh Market Grapefruit Grown in Indian River, 2014/15.

Total Cultural Costs with Tree Replacement		2478.61
Other Costs	Interest on Operating (Cultural) Costs	123.93
	Management Cost	75.00
	Property Tax/Water Management Tax	18.50
	Fly protocol	16.00
	Water Drainage District Assessment	107.00
	Interest on Average Capital Investment	254.34
Total Other Costs		594.77
Total Grower Costs		**3073.38**

Integrating the increased production costs for Florida citrus with statewide declines in per-acre yields illustrates the emergency status and the business failure that is being witnessed in Florida. Small- and medium-sized operations are economically abandoning blocks of citrus which have fallen below break-even levels for several consecutive years, reducing any further losses associated with continued investment in the face of continuing decline in production. An option considered by some is reduction in inputs to offset smaller crop size and quality. Experience over recent years indicates that this pull-back in intensity of management of tree health accelerates the disease decline and only hastens economic abandonment. At the same time, these unmanaged groves become a source for inoculum for the pathogen and reservoir for the vector ACP.

Large citrus operations in Florida are facing similar decisions on the declining return or loss due to HLB, and are risk assessing individual blocks each year to determine where investments are warranted. They, too, are removing groves that have fallen below economic return thresholds from active management.

This scenario also is not favorably affecting growers' interest in replanting, as the uncertainties of being able to sustain production on new trees is influenced heavily by their experience with standing groves. Data on declines in nursery tree production in the past year attests to this uncertainty, despite availability of industry and other incentive programs to replant. The health of Florida's citrus industry is usually mirrored in nursery production. As industry production falls or fruit prices weaken, citrus nursery tree orders suffer. A total of 54 citrus nurseries propagated 4,438,128 trees in 2014-15, which is a decrease (5.8%) from last year. Nursery activity was strong for several new nurseries

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that began producing trees this year; 6 new nurseries accounted for over 5 percent of the total nursery propagations. Existing nurseries mostly saw a decline in budding and tree orders. A total of 33 nurseries had reduced production from the previous year and only 15 saw an increase. Overall, tree production based on reports decreased by 274,311 trees. Taking into account that six new nurseries contributed to the production figures, it signified a downward trend for most nurseries. (FDACS Budwood Certification Program, Annual Report 2014-15).

The Economic Impact of HLB on the Florida Citrus Industry:

As described in a recent publication, this disease and the resulting loss of production cost the industry over $7 billion in lost revenue by 2012 (Hodges A.W., Spreen T. H., 2012). This loss of production translates to more than 8,000 lost jobs over the same five-year period. As trees succumb to the effects of the disease, the industry is faced with the challenge of replanting groves to replace the lost production. Although these figures have not been formally updated, the losses have risen considerably since this analysis was published.

Economic Effects of HLB in Florida:

Florida's iconic citrus industry is an essential part of the economy of Florida, especially in the 28 central and southern counties of Florida where citrus is grown and processed. The most recent study before HLB became endemic put the overall economic impact at $8.91 billion and provision of 75,827 jobs.

However, in 2012 economists calculated that over $4.5 billion in economic impact had been lost because of the effects of HLB on the Florida orange juice industry for the period 2006 to 2010. The report details the category of losses, i.e., direct economic impacts, indirect economic impacts and induced impacts. On average, Florida's economy suffered with the loss of $908.2 million dollars each year, and 8,257 permanent jobs.

These losses are mainly because of the reduced production of Florida oranges versus a scenario without the effects of HLB in the citrus growing environment. Losing orange production is exacerbated by further losses of the value-added segment of the industry, that is fruit processing, juice manufacturing, and juice packaging and distribution. Since most of the orange juice sold in the United States is produced solely in Florida, this becomes a loss of economic benefits for Florida residents.

As the disease progresses, more losses are expected each year. An estimate of the most current losses are explained by looking at Florida citrus production statistics over the period prior to first detection of HLB in Florida (1996-1997 through 2005-2006) and the decline in production experienced in the recent three years as a result of both accumulation of disease across the state as well as the cumulative decline due to multi-year chronic HLB infection (Table 9).

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Table 9: Florida Citrus Production Statistics during the Period 1996-1997 through 2013-2014.

Crop Production by Fruit Type 1996-1997 through 2014-2015				
Crop Year	**Oranges**	**Grapefruit**	**Other Citrus**	**Total**
	(1,000 Boxes)			
1996-1997	226,200	55,800	13,315	295,315
1997-1998	244,000	49,550	10,900	304,450
1998-1999	186,000	47,050	10,115	243,165
1999-2000	233,000	53,400	12,030	298,430
2000-2001	223,300	46,000	9,505	278,805
2001-2002	230,000	46,700	10,565	287,265
2002-2003	203,000	38,700	9,305	251,005
2003-2004	242,000	40,900	8,900	291,800
2004-2005	149,800	12,800	6,650	169,250
2005-2006	147,700	19,300	7,600	174,600
2006-2007	129,000	27,200	5,850	162,050
2007-2008	170,200	26,600	7,000	203,800
2008-2009	162,500	21,700	5,000	189,200
2009-2010	133,700	20,300	5,350	159,350
2010-2011	140,500	19,750	5,800	166,050
2011-2012	146,600	18,850	5,440	170,890
2012-2013	133,600	18,350	4,280	156,230
2013-2014	115,000	16,500	4,400	135,900
2014-2015	96,700	12,950	2,980	112,630

Source: USDA, National Agricultural Statistics Service, FASS, Florida Citrus Statistics. 2011-2012, published February 12, 2013. Data for crop years 2012-2013 and estimates for 2013-2014 provided by USDA, NASS, FASS, Citrus Forecast, January 10, 2014. 2014-15 July 10, 201 Final Forecast for Season.

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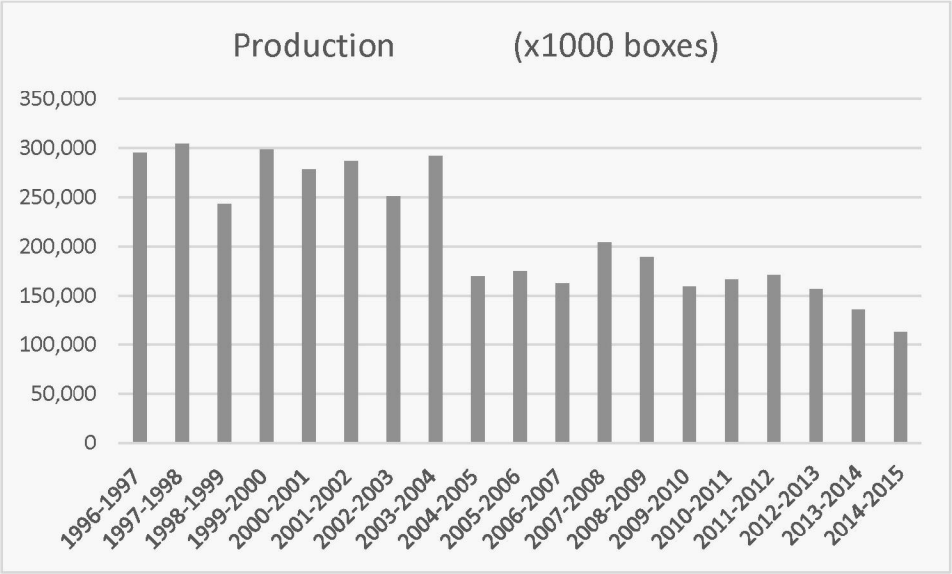

Note: The above graph depicts the data in the table for total production, all varieties, and is included as an alternative data presentation, or to be used elsewhere in the petition.

Losses have now reached levels that annual citrus production is less than half of what it was as recently as 2003-2004. The decrease in fruit in successive harvests over the past three seasons is shown here:

2010-2011 to 2011-2012		**9%**
2012-2013 to 2013-2014		**11%**
2013-2014 to 2014-2015		**17%**
Net loss (3 years)	**=**	**34%**

With the rapid spread of HLB disease, and the increasing infection rates within standing groves, the situation that we are experiencing now in Florida is a combination of:

- Widespread infection of citrus trees throughout the growing region of Florida.
- Heavy inoculum in infected trees available for acquisition by the vector, ACP. Recent samples indicate up to 100 percent of field-collected ACP are positive for *C*Las, the pathogen.
- Limited removal of infected trees means that local spread can be rapid if psyllids are not managed effectively. With high rates of infection within a block, tree removal is not practical.

- The accumulation of years of progressive infection by *C*Las means that a higher percentage of trees are beginning to show chronic infection, including more widespread symptoms within trees, thinner canopies and impaired root systems.

- These factors all contribute to the reduced fruit production (yield), even though the official acreage of citrus plantings has not declined significantly in the last few years. And,

- Fruit quality is declining, in size, flavor and maturity.

Thus, the productive population of mature trees is declining in health and productivity, and will likely continue to do so without effective therapeutics, which currently are not available. In addition, new citrus trees that are either inter-planted in existing groves of mature trees or planted solid in new blocks are at high risk to infection via the ACP vector bringing inoculum from *C*Las reservoirs. It is these new trees that will provide the ability for economic production of citrus to continue, and the confidence to replant is, at present, limited by early and fatal infection of young trees by *C*Las through psyllid transmission. Trees in the first 4-5 years of growth are particularly vulnerable since they grow new flush off-cycle when other trees are not producing new leaves. This makes them more attractive to ACP colonization and vulnerable to disease transmission.

The importance of management of HLB in Florida citrus is reduced to two major considerations. The first is to delay further health decline in existing mature trees that will further erode production. Second, and more vital, is the ability to manage ACP populations in young plants, thereby providing confidence to growers to replant. Both of these considerations could be positively impacted by availability of effective bactericides.

Consideration of Expected Economic Benefits of Improved HLB Management, Particularly Through Availability of Bactericides

This overview adds insights by attempting to quantify potential economic benefits to Florida if research efforts change the trajectory of any one of several factors that affect the economic impact of citrus production (specifically oranges) in the state. The initial overview focuses on the various aspects of production, such as acreage, yields, fruit loss to drop and quality reduction and other measures of decline due to HLB that would be expected to show improvement with implementation of an effective bactericidal program, as well as the trends in replanting, which likewise would be expected to improve as bactericidal therapy is made available.

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To understand the economics of expected response to exposure of HLB-infected trees to a time course of one or more bactericidal treatments, it is important to outline the disease progression associated with this disease and to determine which aspects of the disease impact would be improved through treatment. As stated earlier in this petition, infection of citrus by *C*Las is initially invisible, followed in a multi-year time course by a series of symptoms and injury which begin as foliar mottling and chlorosis and progressing to reduction in canopy density, and leaf size, and overall appearance of decline in one or more branches of the infected tree. General decline reflects root injury and limited movement of plant products through the impaired vascular system. With time, the appearance of small fruit, further thinning of canopies, and leaf and premature fruit drop signal more advanced imbalance in the tree. Leaf symptoms also include general chlorosis (yellowing) and their noticeable appearance as thinned canopies, with bare patches within the canopy of chronically infected trees. These advanced symptoms, and the continued decline to death of chronically infected trees, may not appear for several years following infection, or even following first visual symptoms. The general decline is symptomatic of the breakdown of several plant systems, including roots (lower feeder root density), reduced vascular movement (phloem plugging) of nutrients from sources to areas of need (leaves to roots, roots to developing fruit, etc.), and impaired photosynthesis due to canopy loss.

Thus, in evaluating the expected response to treatment of *C*Las in infected trees, the forgoing description also defines the measures necessary to determine stabilization or recovery from disease symptoms. Expected changes in the following parameters can be predicted from previous research on epidemiology of HLB in citrus and are the metrics associated with field evaluation of therapies as pursued by the registrants of the candidate bactericides.

- Reduction in *C*Las titer in infected trees following bactericidal regimen: The first measurable impact of bactericidal treatment would be expected to be reduction in bacterial titer in infected tissues. This is best measured at present using qPCR, and the numerical scale changes in samples over time reflect increase or decrease in bacteria in tissues sampled. Following a time-course of bactericidal treatments, it would be expected to see a gradual increase in PCR CT values, indicating a decline in titer in infected plant parts sampled. This may occur as step-wise reduction following individual applications, as evidenced in the data summaries provided. This in itself is not a metric of improved plant health or economic benefit, but portends resumption of growth and response as bacterial levels decline.

- Improved tree growth response: Biological response to the lessening of pathogen pressure in infected trees is manifest in a series of indicators that trees are returning to more normal growth and development. As in the description of the onset of disease symptoms above, the progressive lessening of disease injury would be expected to show itself through leaf, branch, root and fruit symptoms. This has been observed in field experiments where therapies (both chemical and thermal) have been applied, and specific field results are presented in this petition for the products being field tested.

- Foliage response: Larger, greener, more robust flush appear in flushing periods following treatment, and the degree to which flushing phenology and the strength of new foliage resume a "normal pattern" is indicative of reduced disease.

- Canopy density improvement: Increased photosynthetic capacity is a by-product of new, healthy flush and drives plant health. Tree growth, including laying down of new phloem also can follow.

- Root health improvement: Photosynthate movement and lessening of root decline due directly to *C*Las follows resumption of tree flushing, and it is yet unclear to what extent this will occur following a treatment regime of bactericides.

- Increased capacity to utilize irrigation and nutritional applications, including improved foliar uptake. Restoration of root health has immediate impacts on the tree's ability to utilize nutrients and healthy roots buffer periods of dry and wet weather.

- Ability to combat other stresses (root disease, cold, drought). Resumption of balanced flush with restored roots has the added advantage of providing the defense against other stresses that exist in groves. Overcoming these stresses also contributes to resumption of tree health and productivity.

- Fruit set and productivity: Since successful fruiting is dependent on support from the canopy, the above improvements in tree health can be expected to contribute to improved fruiting, and in conjunction with lower *C*Las titer, less size and fruit quality issues. Metrics associated with fruit yield, size and quality thus are direct indicators of effect of treatment success.

It should be clear that expected response in diseased citrus trees from application of a regimen of bactericidal applications will first be improvement in bacterial titers, followed by reduced visual symptoms, then impacts on the production and quality of fruit. While

this is likely to occur across a full production season, it is also likely that accrued benefit of the suppression of *C*Las in infected plants will occur over multiple seasons.

While none of the above discussion pinpoints economic benefit of grower use of the proposed bactericides in this petition, it provides the context for that economic assessment. Based on the preceding discussion, improvement in tree health should lead to following economic drivers:

Fruit yield and quality improvement –
- Larger fruit set and retention through the production season;
- Increased capacity to hold fruit on the tree season-long; less pre-harvest fruit drop;
- Improved fruit size;
- Improved internal fruit quality;

Normal growth progression for young trees (up to 5 years old) to full productivity (multi-year impact); and,

Increases in new plantings with availability of tools to deter disease progression.

Impacts at the Processing Facility:

The economic loss resulting from HLB-induced reduction of quality can be measured by downgrading, which initially can be done while fruit are still on the tree. Quality standards are established for juice fruit and fresh fruit harvest per fruit variety, and delays in maturity, caused by HLB infection, postpone harvest, and allow an extended period for pre-harvest fruit drop to occur. Increasingly, harvesting of fruit, even for processing, is not "clean-picked", where the entire crop is removed at once, then graded and routed to fresh and processing streams. In the presence of HLB, fewer groves are harvested in this manner, and the fruit left behind due to irregular shape, small size, and other quality parameters is lost production.

Fresh-fruit harvest has traditionally used "spot-picking" to begin the season, where fruit of the desired size and maturity are harvested, allowing remaining, smaller fruit to "size up" and mature for later harvest. Under HLB conditions, some groves from which fresh fruit are harvested are spot-picked 3 times, dramatically increasing harvest and handling costs. In the past two seasons, fruit left after initial spot picking did not continue to size, another result of HLB disease. Ultimately, the remaining fruit on these trees are clean-picked for routing to processing plants.

The second stage for quality downgrading comes at fruit load receipt at either packing houses (fresh) or processing plants (juice). Typically, fresh packing operations sort, grade and pack cartons of fruit to specifications. The percent of fruit arriving at the packinghouse that ends up in cartons is referred to as pack-out. Even with spot-picking to select higher quality fruit, pack-out percentages have dropped 20 to 40% in the past 3

years. The fruit not packed into cartons is redirected to processing streams, resulting in lower returns. For the 2014 fruit season, oranges averaged $16.31/box when utilized for fresh and $12.09/box average for processing (USDA, NASS Florida Agriculture Quick Statistics). The differential is even greater for grapefruit, where 2014 fresh grapefruit were valued at an average of $14.44 per box for fresh and $6.38 per box for processing utilization.

Fruit arriving at processing plants is sampled by load and the quality is assessed. The FDACS State Test House measures percent brix (sugar), percent acid and the ratio of brix/acid. This ratio is the initial basis for juice quality, and provides the quality data for payment to the grower. Additional data recovered from the load sampling includes pounds solids per weight of fruit, percent juice and overall weight of the load. The formula for payment is quality based and calculated for the pounds solids delivered from the entire load.

HLB-affected loads of fruit net a lower brix and lower ratio, and due to smaller size, have less percent juice, yielding less juice from processing. Based on the State Test House results, fruit loads are assigned a grade, and lower grades are discounted. In the case of shared pool processing situations, the grade determines your "pool share" at season's end, and this can be as much as 15-20 % discount for grade B compared to grade A fruit loads. The more serious impact is when lower grade loads of fruit are routed for juice concentrate production rather than inclusion in the not-from-concentrate juice processing stream. A significant differential occurs between these two forms of orange juice utilization, and this varies by processor and by season.

All of these parameters have declined progressively over the past 3 years, and are expected to continue in chronically infected trees. Treatment to suppress HLB in these infected trees would be expected to reverse this process and restore value for each of these variables.

Impacts at the Fresh Fruit Packing House:

In addition to the impact on the processing industry, the fresh fruit industry has paralleled the losses due to HLB.

The loss in fresh utilization is due to:

- Tree loss
- Increased fruit drop
- Lower pack outs, due to smaller size and quality issues associated with HLB.

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Table 10: Reduction in shipments of Fresh Fruit Varieties in Florida as a result of the impact of HLB

Change 2014-2015 from 2007-2008		
Variety	**Fresh Boxes (In 000)**	**% Reductions**
Oranges	(476)	-10.8%
Grapefruit	(4,645)	-46.8%
Tangelos	(74)	-46.1%
Early Tangerines	(730)	-63.3%
Honey Tangerines	(909)	-63.3%
All Fresh	(6,834)	-38.6%

Data sourced from: Duke Chadwell, Citrus Administrative Committee

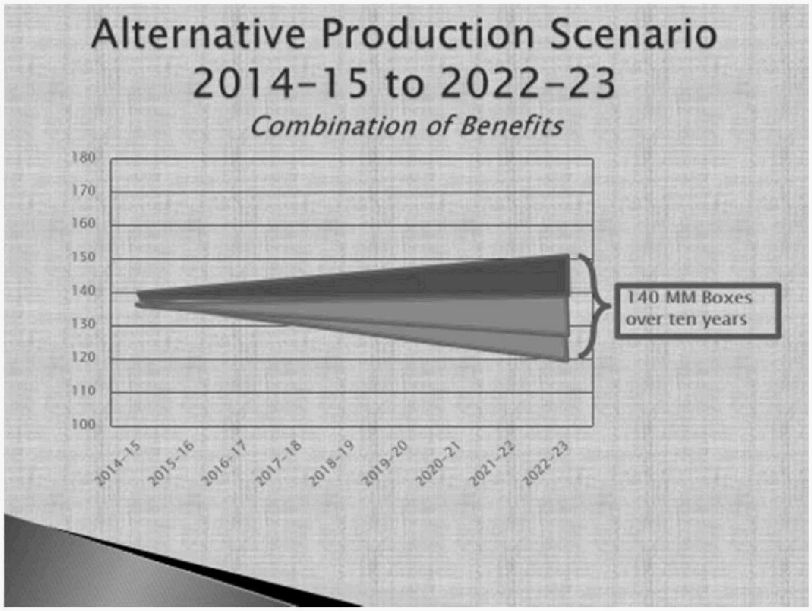
For one Florida shipper, the 3-year average pack out (fresh utilization) for the 2005, 2006, and 2007 seasons was 70.4%. The average pack out for the 2013, 2014, and 2015 seasons was 53.7%. This 16.7% pack out reduction is due to HLB impacts on the size and quality of fresh fruit produced from our groves.

Improving pack outs to pre-HLB levels would increase our company's fresh output by 126,487 boxes, or 33.0%, without considering any potential yield increases.

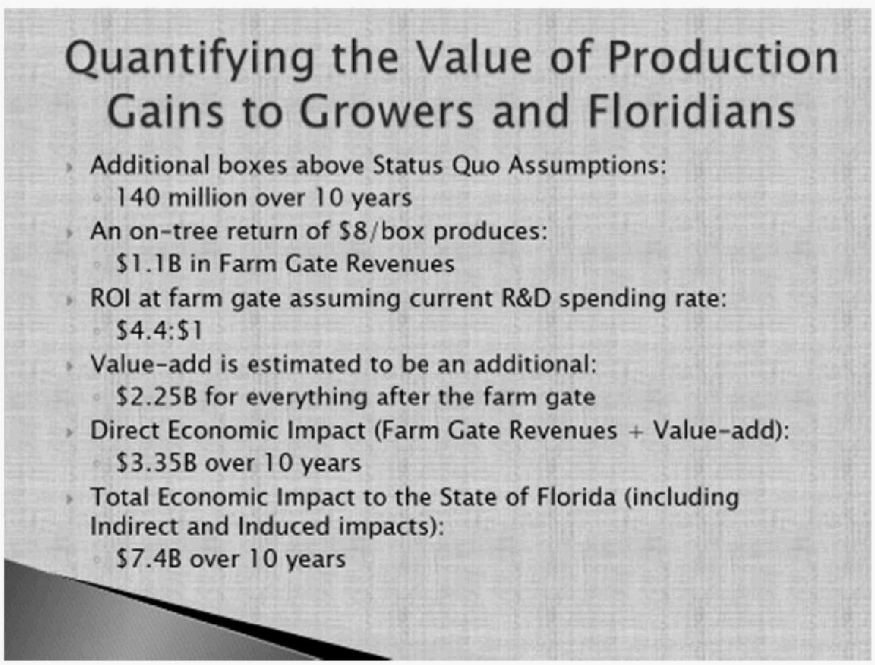
Industry Wide Impacts:

The following is a summary of previously published and presented material supplemented with data from the 2012-13 fruit season. This report was prepared by Bob Norberg, Economist, Florida Citrus Mutual, Economic and Market Research Associates, January 2014. It summarizes several previously published reports regarding the economics of the Florida Citrus Industry and the impacts of HLB on Florida Citrus economics. Data from the most recent seasons is used to generate supplemental impacts based on the logic from the previous reports.

The three factors examined in this economic evaluation were: tree mortality rates, re-planting rates, and fruit yields. Reducing the mortality, and/or increasing the replanting rate, and/or improving fruit yields all have positive economic impacts. The following chart shows the combined effects on crop size with gradual improvements to these factors over the next 10 years. Reducing the mortality rate from 4 to 3 percent in 10 years, increasing the planting rate from 2 percent to 3 percent over 10 years, and raising yields 1 percent per year would generate a total of 140 million additional boxes of fruit over the forecast horizon. Those additional boxes generate direct, indirect and induced economic impacts that would not be generated without them.



The following chart from the presentation concludes that those boxes are worth $7.4 billion dollars during those ten years. Farm gate revenues would be enhanced by $1.1 billion dollars.



Further increases in pre-season fruit drop and reductions in fruit size were forecasted in the January 2014 estimate highlighted in the table above and are expected to continue that trend in future production estimates. The reduced yields have contributed to the smallest orange crop since the freeze impacted crop of 1989/90. It is uncertain, but

likely, that these yield effects will be seen in future seasons without dramatic advances in production management practices, disease mitigation strategies, and solutions from the comprehensive research efforts.

Update on Economic Impacts, January, 2014:

Using the methodology previously established by Hodges and Spreen in their 2012 analysis, an updated estimate of the annual economic impacts of HLB (and other calamities) can be calculated. Although unit FOB values have risen recently, these increases do not compensate for the loss of volumes since the value-added portion of total economic output is a significant factor and is directly correlated to volumes of orange juice case goods produced and distributed.

The following table shows the losses to be $3.3 billion over the period from 2011/12 to 2013/14 (January forecast) and 10,089 annual jobs. Combined with the losses estimated previously, losses to date from the 2006/07 season are $7.8 billion.

The annual rate of losses in both economic output and jobs is accelerating from the previous estimate. The average annual loss was $908.2 million per year between 2006/07 and 2010/11, while the annual loss rate for the period 2011/12 to 2013/14 is $1.1 billion. Currently total economic losses versus a non-HLB forecast is estimated to be $1.8 billion for the 2013/14 season based on the January crop forecast.

Table 11: Impact of HLB to the Florida Citrus Industry the three Previous Seasons

CROP SEASONS 2011/12 – 2013/14	Non-HLB	HLB	Difference
FOB REVENUES (MM)	$7,356	$6,103	($1,253)
DIRECT ECONOMIC OUTPUT (MM)	$7,088	$5873	($855)
TOTAL ECONOMIC OUTPUT	$19,245	$16,096	($3,329)
ANNUAL EMPLOYMENT	58,865	48,776	(10,089)

This information has not been updated to include the 17 percent production loss experienced during the 2014-15 citrus season.

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ESTIMATED REVENUES FOR THE SITES TO BE TREATED (166.20(b)(4)(ii) & (iii)) (166.20(b)(4)(ii) & (iii))

Florida accounts for:
66 percent of the total U.S. value for oranges;
65 percent of the total U.S. value for grapefruit.

Florida currently ranks 1st in the U.S. in the value of both the production of oranges and grapefruit.

Table 12: Florida Production Information, Oranges

Florida Orange Production Information*					
Season	Total Bearing Acres	Total Production (1000 boxes**)	Yield per Acre (total boxes)	Price per Box	Total On-Tree Value (Millions)
2013-14	418,700	104,600	250	$7.58	$ 792.7
2012-13	429,200	133,600	311	$7.43	$ 992.5
2011-12	433,400	146,700	338	$9.92	$1,455.7
2010-11	440,000	140,500	319	$8.41	$1,181.9
2009-10	451,000	133,700	296	$6.96	$ 929.9
5-Year Average	434,460	131,820	303	$8.06	$1,070.5

* Source: Latest Available Florida Agricultural Statistics Service Citrus Summary, February 2015.
** Box = 90 pounds

Table 13: Florida Production Information, Grapefruit

Florida Grapefruit Production Information*					
Season	Total Bearing Acres	Total Production (X 1000 boxes)	Yield per Acre (total boxes)	Price per Box	Total On-Tree Value (Millions)
2013-14	43,100	15,650	363	$6.44	$100.8
2012-13	44,900	18,350	409	$6.47	$118.7
2011-12	45,500	18,850	414	$7.17	$135.3
2010-11	46,500	19,750	425	$6.72	$132.7
2009-10	48,100	20,300	422	$7.50	$152.2
5-Year Average	45,620	18,580	407	$6.86	$127.9

* Source: Latest Available Florida Agricultural Statistics Service Citrus Summary, February 2015.
** Box =85 pounds

Economics associated with HLB and potential impacts of Section 18 bactericidal treatments:

Processed Oranges Metrics (>90% of Florida citrus Crop)

Table 14: Emergency Loss When compared to Baseline Florida Orange Production Prior to HLB.

Factor	Baseline (pre-HLB) 2005-06	2014-15 Harvest Season	Change (%)
Bearing Orange Acreage	529,241 acres	441,628 acres	-16.6
Annual Production (million boxes)	147,700,000	96,800,000	-34.5
Yields per acre (90 lb. box)	301 boxes/acre	250 boxes/acre	-17
Fruit Size (average number/box)	221 (2007-08)	244	10.4
Pre-harvest fruit drop (Valencia)	15 % (2007-08)	25%	10

Source: USDA, Florida Agricultural Statistics Service

Expected Benefit Due to Bactericide Treatments:

Expected impacts are calculated based on historic statistics and expected impacts of the proposed treatment on citrus productivity and fruit quality. The factors that are most likely to show improvement following season-long treatments as described in the petition are improvement in fruit size, retention of more fruit on tree, and return crop production increases.

Reduction in Fruit Drop: One of the most devastating impacts of HLB is loss of yield through fruit drop just prior to harvest. The impacts of 20 percent and 50 percent reduction in fruit drop are calculated here.

A 20 percent reduction in the current 25 percent fruit drop rate would restore five percent to harvested yield for the same crop load. This five percent retention adds 12.5 boxes per acre and at $12.09, on-tree value of $151.13 per acre. **That translates into 5,520,350 boxes of fruit saved from falling to the ground with a 25 percent reduction in the amount of fruit drop, and this is valued at $66,743,240 for orange acreage per year.**

Using the same calculations for fifty percent reduction in fruit drop would restore 12.5 percent to yield. This translates into 31.25 boxes per acre additional impact on yield and, at $12.09, is valued at $378 per acre per season. **Calculated benefit across all orange acreage provides addition of 13,800,875 boxes of fruit, or an economic benefit of $166,935,384 to Florida orange growers per season.**

Similar calculations can also be made for other citrus varieties and for the added value of fresh market, especially for grapefruit.

Improvement in Fruit Size: HLB has reduced fruit size, and tree health recovery is expected to improve fruit size. The impact is calculated for 20 percent reduction and 50 percent reduction in fruit size.

Comparison of fruit size shows 23 additional fruit were needed to fill a 90 pound box because of HLB in 2014-15.

A 20 percent treatment improvement in fruit size would lead to 4.6 fewer fruit per box (239.4 fruit/box), across 250 boxes per acre, for a total of 1,150 pieces, and at 239.4 fruit/box, this would add 4.8 boxes per acre. **The per-acre economic benefit of a 20 percent change in fruit size reduction would lead to 4.8 boxes x $12.09 (on-tree price, 2014-15) or $58.03 per acre. Across all orange acreage (441,628 acres), this benefit would be 2,119,814 additional boxes of oranges, and $25,628,556 per season for just this minor improvement to fruit size.**

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A 50 percent treatment improvement in fruit size reduction would similarly lead to 11.5 fewer fruit needed to fill a 90 pound box (232.5 fruit), across 250 boxes per acre, for a total of 2,875 pieces, and at 232.5 fruit/box, that improves yield by 12.4 boxes per acre. **The per-acre economic benefit of a 50 percent change in fruit size reduction would therefore lead to 12.4 additional boxes x $12.09, or $149.50 per acre. Across all orange acreage, this would add 5,343,699 boxes of yield worth $64,605,321 per season at 2014-15 prices.**

Similar calculations could be developed for non-orange varieties, and additional value could be calculated for considering fresh fruit value-added for the portion of the crop that is marketed fresh.

Both of the above improvements to orange yields are possible within the existing crop load of fruit, and reflect within season improvements that could occur with effective bactericidal treatment. Additional value could be obtained with expected improvements in fruit quality (brix/acid ration, pounds solids and flavor-impacting components. These benefits are not included in the size and fruit drop considerations above.

Improved annual production (successive years): In crop years following application of the emergency treatments, it is expected that restored tree health would lead to higher fruit set and increased yields above and beyond the benefits discussed above.

Calculations of the value of this for varying rates of improved yield are:

> Five percent yield response would increment yield of 250 boxes to 262.5 per acre, or an increase of $151.13 per acre. **The all-orange impact would be 5,520,350 boxes and $66,736.800 per season, the same benefit (additive) to the reduction in fruit drop.**
>
> 10 percent yield response would increment yield of 250 boxes by 25 boxes per acre, or $302.25. **Across all orange acres, this 10% improvement in current tree productivity would add 11,040,700 boxes of fruit and an economic benefit of $133,482,063 per season.**
>
> 25 percent yield response nets 62.5 boxes per acre additional fruit, or $755.63 per acre benefit. Across all orange acreage, this estimated benefit is 27,601,750 boxes, or when added to 2014-15 season yields, 124,401,750 boxes per season. **The estimated economic value of the additional production improvement of 25 percent is $333,705,158 per season.**
>
> The actual benefit can be approximated by adding the improvement in fruit drop reduction, increased fruit size, and finally the gain in production that treatment to reduce *C*Las titer in infected trees might bring. Again, these calculations represent oranges and the acreage currently dedicated to this major element of the industry. Similar composite benefits could be calculated.

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Using the minimal improvements calculated above (20% reduction in fruit drop, 20% improvement in fruit size reduction and 5% production increase in new crop) the economic benefit calculated for the orange acreage in Florida is $66,743,240 + $25,628,556 + $66,736,800 or $159,108,596 per season.

Finally, the treatment benefits would encourage new plantings, and the new benefit would then by be multiplied as new plantings come into production.

From: Harbottle, Heather </O=FDA/OU=FIRST ADMINISTRATIVE GROUP/CN=RECIPIENTS /CN=HHARBOTT>
To: Singh, Ruby
Sent: 5/16/2016 3:48:24 PM
Subject: RE: Teleconference Cancellation and EPA updates

They sent me a bunch of files, so I'm trying not to send you duplicates since they had to resend me some that never came in through email. So I'm hoping I don't send you too many dups. J

From: Singh, Ruby
Sent: Monday, May 16, 2016 11:33 AM
To: Harbottle, Heather
Subject: RE: Teleconference Cancellation and EPA updates

Thanks Heather. No rush from my end, anytime will be fine. Just trying to get a handle on some of the work we have done with EPA. I won't be sharing/forwarding any docs.

Thanks again!
Ruby

From: Harbottle, Heather
Sent: Monday, May 16, 2016 11:29 AM
To: Singh, Ruby
Subject: FW: Teleconference Cancellation and EPA updates

Hey Ruby,
This is the last email I got with some of their updates/mitigations they decided on.

I'll send the reviews (and submissions, if I have them) to you. I definitely have the reviews, looking for the submissions.

J H

From: Hill, Shaunta [mailto:Hill.Shaunta@epa.gov]
Sent: Tuesday, March 15, 2016 4:18 PM
To: Patel, Jean (CDC); Craig, Michael R (CDC); Harbottle, Heather; Gilbert, Jeffrey M; Wan, Ellen (CDC)
Cc: Jennings, Susan; Kough, John; Chandgoyal, Tara; Hicks, Karen; Blackwell, Ian
Subject: Teleconference Cancellation and EPA updates

Good Afternoon Everyone-
First I would like to apologize for the delay in communicating details on the scheduled teleconference for tomorrow.
EPA hands have been busy working with the Section 18 – FL request, which has taken a number of turns since our initial discussion in February.
Instead of proceeding with the teleconference tomorrow, we thought we send an update email.

Status as of 3/15/16:

B5

B5

B5

B5

Once the Section 18 is finalized, we can share the authorization letter. Additionally, once we outline the details of the monitoring program, details will be provided. I can say with some certainly, that assistance will be requested from both CDC and FDA with respect to identifying protocols suitable for water sampling.

Thank you for your continued assistance during this review process. We do appreciate it !
Have a great evening and I'll be in touch on the monitoring protocols soon.

Regards,
++
Shaunta Hill-Hammond, Ph. D.
Plant Pathologist
U.S. EPA: Office of Chemical Safety and Pollution Prevention

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