To: Carpenter, David O[dcarpenter@albany.edu]
From: Maddaloni, Mark
Sent: Fri 7/14/2017 7:35:24 PM
Subject: RE: Clinical Research on perfluorinated compounds

Thanks for the speedy response and interest, David. I would add that in both the cross-sectional work that Alan Ducatman (U of West Virginia) did and in the limited Canadian study, cholestyramine worked better on PFOS than PFOA. I mention this because Hoosick Falls was predominantly a PFOA exposure, while Newburgh was predominantly PFOS.

From: Carpenter, David O [mailto:dcarpenter@albany.edu]
Sent: Friday, July 14, 2017 1:07 PM
To: Maddaloni, Mark <Maddaloni.Mark@epa.gov>
Subject: RE: Clinical Research on perfluorinated compounds

Hi Mark:

This is a very interesting possibility. I'm certainly very familiar with the situation at Hoosick Falls, and have followed the studies in West Virginia as well. You may know that there was some success in lowering PCB levels in people in Anniston with olestra, and I've actually supervised two people who tried to reduce their serum PCBs levels with olestra. It would not be easy or cheap to develop a full clinical trial, but is something I'd be quite interested in exploring. While the DOH is often difficult to work with, the frustrations in the exposed communities are great and they feel that all anyone wants to do is to study them, not provide any mechanisms for reducing their exposure. This is one of the few ways for which there is at least some rationale that one could reduce exposure.

It would certainly be best if a clinical trial could be done with health department buy-in. They have the PFOA levels in most of the residents at Hoosick Falls, and this might make it possible to identify the exposed population with doing another round of sampling. They also have one of the best labs for the PFOA analysis.

Let me think about this a bit more and perhaps we can talk next week. But certainly the idea is interesting. I actually have a grant from NIEHS where we are measuring the perfluorinaing compounds in Alaska Natives on a remote island in the Bering Straits. Linda visited there last year. Thanks for the thought. David

David O. Carpenter, MD

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From: Maddaloni, Mark [mailto:Maddaloni.Mark@epa.gov]
Sent: Friday, July 14, 2017 12:05 PM
To: Carpenter, David O <dcarpenter@albany.edu>
Subject: Clinical Research on perfluorinated compounds

Dear Dr. Carpenter,

I hope this e-mail finds you well. It's been awhile since we last met in 2014 at the Woods Hole PCB Workshop. Work with PCBs in NYC schools was my ticket to that delightful venue ☺ I am writing now to see if I can possibly pique your interest in a clinical research study involving another class of persistent bioaccumulative toxins: perflourinated compounds (PFCs). Briefly, these compounds have glacial biological half-lives in humans and there is evidence (see below) that an FDA approved drug (cholestyramine, indicated for treating hyperlipidemia) can significantly reduce the half-life by disrupting entero-hepatic circulation. As you can see from the e-chain below, Linda Birnbaum (NIEHS), who I'm sure you know, has expressed interest in possibly funding such a clinical trial.

I believe you occupy a unique nexus in this the scheme of things. As a physician, you have the clinical background, and as a researcher the proper bonafides, to engage in such a study. And through your position at the SUNY Albany SPH, you also have a connection to the NYSDOH which is sitting on a sizable data base of PFOA/PFOS serum sampling from communities in Hoosick Falls, NY and Newburgh, NY. I have briefly discussed this issue with Betsy Lewis-Michl (NYSDOH) but I think she needs some convincing. I have also come to learn that a physician (Alan Ducatman) involved in the large DuPont funded C8 study of residents exposed to PFOA/PFOS in Ohio and West Virginia communities also has, yet unpublished, data from a cross-sectional study of that large cohort (N= 70,000) that provides further evidence on the serum reducing effects of cholestyramine on perfluorinated compounds.

Would gladly discuss this issue in greater detail if I, in fact, have been successful in piquing your interest.

Best Regards,

Mark Maddaloni

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From: Maddaloni, Mark
Sent: Tuesday, May 23, 2017 4:55 PM
To: 'Birnbaum, Linda (NIH/NIEHS) [E]' <birnbaumls@niehs.nih.gov>
Subject: RE: Cholestyramine

Maybe I will – thanks!

From: Birnbaum, Linda (NIH/NIEHS) [E] [mailto:birnbaumls@niehs.nih.gov]
Sent: Tuesday, May 23, 2017 11:25 AM
To: Maddaloni, Mark <Maddaloni.Mark@epa.gov>
Subject: Re: Cholestyramine

We'd be happy to entertain such a clinical trial....get someone to develop it for a grant....

Linda S. Birnbaum, Ph.D., D.A.B.T., A.T.S

Director, National Institute of Environmental Health Sciences

and National Toxicology Program

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On May 23, 2017, at 11:24 AM, Maddaloni, Mark <Maddaloni.Mark@epa.gov> wrote:

Worth waiting for. Thanks for your insightful thoughts on the subject. Agree that the existing evidence for CSM in reducing PFOA/PFOS half-life is quite slender. Still…it makes mechanistic sense. Also agree that an interventional study would be the way to go. Nearly 40 years ago when I was in Pharmacy School, lots of CSM (Questran) was being dispensed to treat hypercholesterolemia. The advent of the statins changed that. These days, it's primarily prescribed for treating bile acid malabsorption syndrome associated with inflammatory bowel (e.g., Crohn's) disease. Nonetheless, there's still plenty of high cholesterol out there, so looking at a sizable cohort with elevated serum PFOA or PFOS, (Hoosick Falls or Newburgh, respectively) there should be numerous individuals on a statin regimen to manage hypercholesterolemia. Randomize the statin takers into two groups and add CSM to one. Add a third group with elevated PFOA/PFOS and not on any cholesterol-lowering meds and measure their (the three study groups) biological-half-lives prospectively. Not being absorbed, CSM has relatively few side effects – constipation, and it can interfere with the absorption of some drugs and fat soluble (A,D E & K) vitamins. Simple, right ☺

From: Birnbaum, Linda (NIH/NIEHS) [E] [mailto:birnbaumls@niehs.nih.gov]
Sent: Saturday, May 13, 2017 5:06 PM
To: Maddaloni, Mark <Maddaloni.Mark@epa.gov>
Subject: RE: Cholestyramine

I am so sorry to have taken so long to get back to you on this. But, I guess, better late than never.

It would be interesting to do a decent clinical trial. This is NOT very convincing. They did not take repeated stool samples both before and after treatments. They have no post-treatment serum. The only PFAS they may have seen a major impact on was PFHxS – kind of surprising. And they concluded only cholestyramine worked.

I think someone could do an interventional study. You would really need to do some power calculations to see how many men/women you would need and how many samples you

would want to collect. I'm not sure of how well tolerated CSM treatment is. Do you know how much it is being used? Maybe identify people already on the drug or about to start.

Anyway, happy to discuss more, but don't find this terribly convincing.

Linda S. Birnbaum, Ph.D, D.A.B.T., A.T.S.

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From: Maddaloni, Mark [mailto:Maddaloni.Mark@epa.gov]
Sent: Friday, March 17, 2017 2:36 PM
To: Birnbaum, Linda (NIH/NIEHS) [E] <birnbaumls@niehs.nih.gov>
Subject: Fw: Cholestyramine

Hi Linda,

Always a pleasure crossing paths with you at SOT. Another great meeting! Here is material, admittedly thin, on the use of cholestyramine to reduce the biological half lives of PFOS/PFOA. It makes mechanistic sense to me - using an anion exchange resin to sequester molecules that are loaded with highly anionic fluorine. I'm shopping this around to my NYSDOH colleagues who have communities with highly elevated serum PFOA (Hoosick Falls) and less highly elevated PFOS (Newburgh). Thoughts?

Regards

From: Johnson, Thomas B (HEALTH) <thomas.johnson@health.ny.gov>
Sent: Thursday, March 2, 2017 5:13 PM
To: Maddaloni, Mark
Subject: RE: Cholestyramine

Thanks so much, Mark.

Tom

Thomas B. Johnson, Ph.D.

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From: Maddaloni, Mark [mailto:Maddaloni.Mark@epa.gov]
Sent: Thursday, March 02, 2017 4:50 PM
To: Johnson, Thomas B (HEALTH) <thomas.johnson@health.ny.gov>
Subject: Cholestyramine

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This is the most persuasive, albeit limited, research study to date.

https://www.hindawi.com/journals/isrn/2013/657849/

<image001.jpg>	Gastrointestinal Elimination of Perfluorinated Compounds ... www.hindawi.com Background. While perfluorinated compounds (PFCs) are a family of commonly used synthetic compounds with many applications, some PFCs remain persistent within the ...

Here is a case study report

https://www.researchgate.net/publication/45150843_Human_detoxification_of_perfluorinated_compounds

Human detoxification of perfluorinated compounds (PDF ... www.researchgate.net There has been no proven method thus far to accelerate the clearance of potentially toxic perfluorinated compounds (PFCs) in humans. PFCs are a family of commonly ...

See Page 36 of this 3M report

https://www.fluoridealert.org/wp-content/pesticides/pfos.fr.final.docket.0007.pdf

Perfluorooctane Sulfonate: Current Summary of Human Sera ... www.fluoridealert.org Perfluorooctane Sulfonate: Current Summary of Human Sera, Health and Toxicology Data 3M January 21,1999 I 1 000014

https://en.wikipedia.org/wiki/Colestyramine

<image002.jpg>	Colestyramine - Wikipedia en.wikipedia.org Colestyramine or cholestyramine (trade names Questran, Questran Light, Cholybar, Olestyr) is a bile acid sequestrant, which binds bile in the gastrointestinal tract ...

Questran FDA package insert

http://www.iodine.com/drug/questran/fda-package-insert

Questran Package insert - Iodine.com www.iodine.com Easy to read FDA package insert, drug facts, dosage and administration, and adverse effects for Questran (Cholestyramine)

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