Message

From: Behl, Betsy [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=D17D5A871E0244869EA996A9DE657BCF-BETSY BEHL]
Sent: 3/1/2018 2:08:31 AM
To: Hines, Ronald [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=464f333922cc4aa68db2a1677122ab58-Hines, Ronald]
CC: Strong, Jamie [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=ea753aafefb74c268550fe6a2c187838-Benedict, Jamie]; Henry, Tala [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=8bfc0a617a4a43baa8856541c70622be-THENRY02]; Gillespie, Andrew [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=dce99ece87694a06b3009d7756e2a89e-Gillespie, Andrew]; Gallagher, Kathryn [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=a348a17672da45eb8deeef9f452ac235-Gallagher, Kathryn]
Subject: RE: SOT abstracts

Ron,
Many thanks for the summary.
Betsy

From: Hines, Ronald
Sent: Wednesday, February 28, 2018 2:32 PM
To: Behl, Betsy <Behl.Betsy@epa.gov>
Cc: Strong, Jamie <Strong.Jamie@epa.gov>; Henry, Tala <Henry.Tala@epa.gov>; Gillespie, Andrew <Gillespie.Andrew@epa.gov>
Subject: RE: SOT abstracts

Betsy,

Ex. 5 Deliberative Process (DP)

Ron

From: Behl, Betsy
Sent: Wednesday, February 28, 2018 12:54 PM
To: Hines, Ronald <Hines.Ronald@epa.gov>
Cc: Strong, Jamie <Strong.Jamie@epa.gov>; Henry, Tala <Henry.Tala@epa.gov>; Gillespie, Andrew <Gillespie.Andrew@epa.gov>
Subject: RE: SOT abstracts

Thanks very much

From: Hines, Ronald
Sent: Wednesday, February 28, 2018 12:26 PM

To: Behl, Betsy <Behl.Betsy@epa.gov>
Subject: Re: SOT abstracts

Ex. 5 Deliberative Process (DP)

Ron Hines, PhD, ATS
Associate Director for Health
US/EPA/ORD NHEERL

Sent from my iPhone

On Feb 28, 2018, at 12:04, Behl, Betsy <Behl.Betsy@epa.gov> wrote:

> Thanks Ron! If there are any other toxicity studies on GenX compounds going on in ORD we would appreciate hearing about all them as soon as possible.
>
> Thanks. Betsy
>
> ---
> **From:** Hines, Ronald
> **Sent:** Wednesday, February 28, 2018 12:00 PM
> **To:** Behl, Betsy <Behl.Betsy@epa.gov>; Gillespie, Andrew <Gillespie.Andrew@epa.gov>
> **Cc:** Bahadori, Tina <Bahadori.Tina@epa.gov>; Henry, Tala <Henry.Tala@epa.gov>
> **Subject:** RE: SOT abstracts
>
> Betsy,
>
> Andy has already seen this, but as a preface to a briefing, please see the summary that I provided based on a briefing I received from Earl at end of December 2017 (attached).
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> Ex. 5 Deliberative Process (DP)
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> Ex. 5 Deliberative Process (DP)
>
> Ron
>
> << File: GenX Studies Summary 171221.docx >>
>
> ---
> **From:** Behl, Betsy
> **Sent:** Wednesday, February 28, 2018 10:56 AM
> **To:** Gillespie, Andrew <Gillespie.Andrew@epa.gov>
> **Cc:** Bahadori, Tina <Bahadori.Tina@epa.gov>; Henry, Tala <Henry.Tala@epa.gov>; Hines, Ronald <Hines.Ronald@epa.gov>
> **Subject:** RE: SOT abstracts
>
> Andy, this is a great tool to see all the work underway on PFAS. How do I drill into column to see the underlying NHEERL toxicity testing. It is a green cell indicating work has been completed on GenX. We need to know more specifics.

thanks

From: Gillespie, Andrew
Sent: Wednesday, February 28, 2018 10:41 AM
To: Behl, Betsy <Behl.Betsy@epa.gov>
Cc: Bahadori, Tina <Bahadori.Tina@epa.gov>; Henry, Tala <Henry.Tala@epa.gov>; Hines, Ronald <Hines.Ronald@epa.gov>
Subject: RE: SOT abstracts

Hi Betsy, sure, fair question. Ex. 5 Deliberative Process (DP)

Ex. 5 Deliberative Process (DP)

Attached is a good working draft of a heat map I am building to try to track who is doing what and where. Not perfect yet but I think this is 98% right, should give you an idea of what is ongoing. I plan to keep this updated and make available to others in EPA for awareness. Columns H and I summarize work being done by NCCT and NHEERL respectively.

<< File: ORD ACTIVE PFAS 2018 02 26_rnh.xlsx >>

Ron is the best person to brief you on NHEERL effects work. Please include me also in that briefing, I would be interested in getting up to speed.

Thanks, Andy

Andrew J. R. Gillespie, Ph. D.
Associate Director, US EPA/ORD/NERL
ORD Executive Lead for PFAS R&D

From: Behl, Betsy
Sent: Wednesday, February 28, 2018 9:33 AM
To: Gillespie, Andrew <Gillespie.Andrew@epa.gov>
Cc: Bahadori, Tina <Bahadori.Tina@epa.gov>
Subject: FW: SOT abstracts

Andy, we found out recently that ORD has GenX testing underway. It was a presentation from Reeder Sams to the ORD ECOS group that mentioned several studies, including a developmental toxicity study being conducted by Earl Grey. If there is any research in ORD underway now for GenX could you please tell us what it is, if results are available what they are, and if it is being released publically (e.g. at SOT) when and where that is expected.

We really don't want any surprises and would like to mention such ongoing work in the toxicity document, if relevant. For example, we would not like to have ORD publish on GenX toxicity just before or after we release the EPA assessment with results we are not aware of.

Ron Hines is arranging for a briefing for us of Earl's (and others) work. We will also make sure OPPT is aware.

Thanks Andy

From: Strong, Jamie
Sent: Tuesday, February 27, 2018 8:53 AM
To: Jacobs, Brittany <jacobs.brittany@epa.gov>; Behl, Betsy <Behl.Betsy@epa.gov>
Cc: Henry, Tala <Henry.Tala@epa.gov>
Subject: FW: SOT abstracts

This is the only SOT abstract I found online by Earl on GenX...

1783 Biological Relevance of Key Events (KE) *In Utero* in the Androgen Adverse Outcome Pathway Network (AOPn) to Adverse Effects in F1 Male Rats

L. E. Gray1, J. Conley1, C. Lambright1, N. Evans1, V. Wilson1, and P. Foster2. 1*US EPA, Durham, NC; and* 2*NIEHS, Durham, NC.*

We are conducting studies to evaluate the biological relevance of changes in KEs and molecular initiating events (MIE) in AOPs to determine if these can accurately predict of the dose levels of chemicals that disrupt the androgen signaling pathway *in utero*. Herein, we focus on chemicals that disrupt fetal testis endocrine function or act as androgen receptor (AR) antagonists. Our objective is to determine if KE ED50s or MIE EC50s can be used to predict the doses that produce adverse effects after exposure during sexual differentiation. While several MIEs for the phthalate AOP have been proposed, the data indicate that PPAR alpha agonists (pirinixic acid, clofibirate and FRD-903, GenX), and a COX inhibitor (Paracetamol) do not reduce fetal testis testosterone production (TPROD) or gene expression profiles, in contrast with the phthalate esters (PE). Because the MIE is unknown, we have developed a statistical model of the relationships between the KEs and the adverse effects of PEs. This model uses data from several different PE studies and compares reductions in fetal TPROD and testis gene expression with the doses that produce reproductive malformations. For AR antagonists, statistical analyses of data for >50 chemicals indicate that the *in vitro* EC50 values for AR antagonism are poorly correlated the ED50 values for effects on male rat reproductive development (R2<10%). For example, potency rankings of the *in vitro* EC50s are negatively correlated with the *in vivo* ED50s for BPC, BPA, vinclozolin and pyrifluquinazon. In contrast, the ED50 values for the inhibition of androgen-dependent tissue growth in short-term *in vivo* assays are highly correlated (R2>85%) with the ability of the chemical to disrupt androgen-dependent reproductive tract development *in utero*. At present, we are unable to entirely replace animals to interrogate the *in utero* effects of chemicals using the MIEs for PEs or AR antagonists, these models do enable us to significantly reduce animal use by using two short term assays to identify points of departure for hazard identification. However, these KEs would not predict the adverse effects of chemicals that disrupt this AOPn via different AOPs. Research is needed to identify as yet unquantified AOPs in the AOPn to improve the predictive ability across all MIEs and to integrate these into a predictive statistical model. *This abstract does not reflect Agency Policy.*