Message

From: Smith, Robert L. [RLSmithII@Venable.com]
Sent: 8/15/2018 2:49:31 PM
To: Yamada, Richard (Yujiro) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=4c34a1e0345e4d26b361b5031430639d-Yamada, Yuj]
CC: Bolen, Derrick [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=1ffc58b0468c4deca51a8bad735b7d95-Bolen, Derr]
Subject: RE: Crumb Rubber

Richard -- are you available for a call with us? Thanks very much. --rob

From: Beck, Nancy [mailto:Beck.Nancy@epa.gov]
Sent: Tuesday, August 14, 2018 8:56 PM
To: Smith, Robert L. <RLSmithII@Venable.com>
Cc: Baptist, Erik <Baptist.Erik@epa.gov>; Yamada, Richard (Yujiro) <yamada.richard@epa.gov>; Bolen, Derrick <bolen.derrick@epa.gov>
Subject: Re: Crumb Rubber

Rob,
OCSPP is not the lead office for this product. ORD has the lead. I'm looping in Richard Yamada, the DAA in ORD, who may be a better audience for your input.

Regards,
Nancy

****
Nancy B. Beck, Ph.D., DABT
Deputy Assistant Administrator
Office of Chemical Safety and Pollution Prevention
P: 202-564-1273
M: Ex. 6
beck.nancy@epa.gov

On Aug 14, 2018, at 5:54 PM, Smith, Robert L. <RLSmithII@Venable.com> wrote:

> Nancy and Erik:
>
> On behalf of the Synthetic Turf Council, the Safe Fields Alliance and the Institute for Scrap Recycling Industries, I respectfully ask for a call with you this week to discuss the pending report to be issued by EPA regarding crumb rubber athletic turf. I understand this a busy travel time for all of us in DC, but hope you can accommodate us?
>
> Thank you for your consideration and please let me know when might work. --rob
>
> Rob Smith | Venable LLP
> t 2 Ex. 6 | f 202.344.8300 | m Ex. 6
> 600 Massachusetts Ave, NW, Washington , DC 20001
>
> rlsmith@venable.com | www.Venable.com
>
> **********

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****

Message

From: Krenik, Edward [edward.krenik@bracewell.com]
Sent: 6/13/2018 1:39:16 PM
To: Vandenberg, John [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=dcae2b98a04540fb8d099f9d4dead690-Vandenberg, John]
CC: Yamada, Richard (Yujiro) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=4c34a1e0345e4d26b361b5031430639d-Yamada, Yuj]; Orme-Zavaleta, Jennifer [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=3c5a111dc377411595e5b24b5d96146b-Orme-Zavaleta, Jennifer]; Bahadori, Tina [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7da7967dcafb4c5bbc39c666fee31ec3-Bahadori, Tina]
Subject: Re: DPE meetings
Attachments: ATT00001.txt

Thanks John. Welcome back.

Ed

EDWARD KRENIK
Senior Principal
edward.krenik@policyres.com
T: +[Ex. 6] | F: +1.800.404.3970

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-------- Original message --------
From: "Vandenberg, John" <Vandenberg.John@epa.gov>
Date: 6/13/18 9:18 AM (GMT-05:00)
To: "Krenik, Edward" <edward.krenik@bracewell.com>
Cc: "Yamada, Richard (Yujiro)" <yamada.richard@epa.gov>, "Orme-Zavaleta, Jennifer" <Orme-Zavaleta.Jennifer@epa.gov>, "Bahadori, Tina" <Bahadori.Tina@epa.gov>
Subject: RE: DPE meetings

Hi Ed,
I'm surveying the key EPA participants and it looks like dates in July will work, but not the dates suggested for June.
I'll be replying to Bob Holden's email later today (I've been on vacation until this morning).
Best regards,
John

From: Krenik, Edward [mailto:edward.krenik@bracewell.com]
Sent: Tuesday, June 12, 2018 6:32 PM
To: Vandenberg, John <Vandenberg.John@epa.gov>
Cc: Yamada, Richard (Yujiro) <yamada.richard@epa.gov>; Orme-Zavaleta, Jennifer <Orme-Zavaleta.Jennifer@epa.gov>
Subject: DPE meetings

Hi John,

I wanted to followup on the below email since the dates we proposed are coming up next week. I also have a meeting tomorrow at 10 AM with my client and I was hopeful that I could update the group on possible dates for the two meetings.

Please let me know what works best for your team as we would like to get these meetings on the calendar.

Thanks for all you do.

Ed

From: Holden, Bob
Sent: Thursday, June 7, 2018 10:21 AM
To: 'Vandenberg.John@epa.gov' <Vandenberg.John@epa.gov>
Cc: Orme-Zavaleta, Jennifer <Orme-Zavaleta.Jennifer@epa.gov>; Yamada, Richard (Yujiro) <yamada.richard@epa.gov>; Fine, Steven <fine.steven@epa.gov>; Gray, David <gray.david@epa.gov>; Holloman, Vincia <Holloman.Vincia@epa.gov>
Subject: FW: Draft Email to Dr. Vandenberg - Privileged and Confidential

Dear Dr. Vandenberg:

As you know, by letter to me dated May 30, 2018, Dr. Tina Bahadori said that I should contact you to arrange a meeting to discuss the path forward on the scientific studies being performed on behalf of Denka Performance Elastomer LLC ("DPE") concerning the development of a physiologically-based pharmacokinetic (PBPK) model to support a recalculation of the inhalation unit risk for chloroprene. Dr. Bahadori said that you would coordinate scheduling a meeting to discuss this, which meeting would include Dr. Kris Thayer and EPA's chloroprene risk assessment team.

Specifically, we would like to discuss the following:

1. The status of PBPK model work being undertaken by Dr. Harvey Clewell and the Ramboll team,
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We would be happy to meet in person at a location of your choice. The first dates on which DPE and its key consultants with Ramboll, Dr. Harvey Clewell and Dr. Ken Mundt, are available would be June 20, 21, or 22 (Wednesday, Thursday or Friday).
Although we would prefer to schedule this meeting as soon as possible, the DPE team and its consultants are also available from July 11-13, and July 16-20.
Please let us know which of these dates would work from EPA's perspective and if EPA has additional objectives for this initial meeting. We will be happy to coordinate on the schedule and attendees in advance
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We look forward to working with you and the chloroprene assessment team. Please feel free to contact me or Patrick Walsh, DPE's SHE Manager, patrick-walsh@denka-PE.com, 985-536-7573, to discuss this.

Sincerely,

Bob Holden

Robert E. Holden
Attorney
Jones Walker LLP
D: [redacted] Ex. 6 F: 504.589.8139
bholden@joneswalker.com

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The content image001.jpg of type has been blocked.

Message

From: Vandenberg, John [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=DCAE2B98A04540FB8D099F9D4DEAD690-VANDENBERG, JOHN]
Sent: 6/13/2018 1:16:59 PM
To: Krenik, Edward [edward.krenik@bracewell.com]
CC: Yamada, Richard (Yujiro) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=4c34a1e0345e4d26b361b5031430639d-Yamada, Yuj]; Orme-Zavaleta, Jennifer [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=3c5a111dc377411595e5b24b5d96146b-Orme-Zavaleta, Jennifer]; Bahadori, Tina [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7da7967dcafb4c5bbc39c666fee31ec3-Bahadori, Tina]
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Sent: Tuesday, June 12, 2018 6:32 PM
To: Vandenberg, John <Vandenberg.John@epa.gov>
Cc: Yamada, Richard (Yujiro) <yamada.richard@epa.gov>; Orme-Zavaleta, Jennifer <Orme-Zavaleta.Jennifer@epa.gov>
Subject: DPE meetings

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Thanks for all you do.

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Sent: Thursday, June 7, 2018 10:21 AM
To: 'Vandenberg.John@epa.gov' <Vandenberg.John@epa.gov>
Cc: Orme-Zavaleta, Jennifer <Orme-Zavaleta.Jennifer@epa.gov>; Yamada, Richard (Yujiro) <yamada.richard@epa.gov>; Fine, Steven <fine.steven@epa.gov>; Gray, David <gray.david@epa.gov>; Holloman, Vincia <Holloman.Vincia@epa.gov>
Subject: FW: Draft Email to Dr. Vandenberg - Privileged and Confidential

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Bob Holden

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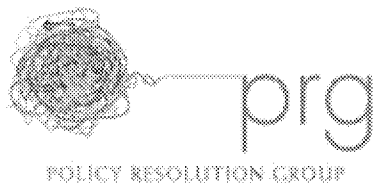

Message

From: Krenik, Edward [edward.krenik@bracewell.com]
Sent: 6/12/2018 10:31:47 PM
To: Vandenberg, John [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=dcae2b98a04540fb8d099f9d4dead690-Vandenberg, John]
CC: Yamada, Richard (Yujiro) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=4c34a1e0345e4d26b361b5031430639d-Yamada, Yuj]; Orme-Zavaleta, Jennifer [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=3c5a111dc377411595e5b24b5d96146b-Orme-Zavaleta, Jennifer]
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Cc: Orme-Zavaleta, Jennifer <Orme-Zavaleta.Jennifer@epa.gov>; Yamada, Richard (Yujiro) <yamada.richard@epa.gov>; Fine, Steven <fine.steven@epa.gov>; Gray, David <gray.david@epa.gov>; Holloman, Vincia <Holloman.Vincia@epa.gov>
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Sincerely,

Bob Holden

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Message

From: Krenik, Edward [edward.krenik@bracewell.com]
Sent: 4/19/2018 11:18:47 PM
To: Yamada, Richard (Yujiro) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=4c34a1e0345e4d26b361b5031430639d-Yamada, Yuj]
CC: Burhop, Anna [anna.burhop@bracewell.com]; Lee, John [john.lee@bracewell.com]
Subject: Request for an extension
Attachments: RFR Request for Extension of Time 4-19-2018.pdf

Richard,

I wanted to make sure you saw this. We are working on some additional data but need additional time to get it peered review and reviewed like our offer for a PBPK working group. I really feel a working group team would be beneficial and we could benefit from EPA's involvement.

Thanks for your consideration. Happy to answer any questions. We would like to know soon if it can be granted.

Ed

Sent from my Verizon, Samsung Galaxy smartphone

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Robert E. Holden
Direct Dial: 504-582-8139
Direct Fax: 504-589-8139
bholden@joneswalker.com

April 19, 2018

Via U.S. Mail and email to: quality@epa.gov
Information Quality Guidelines Processing Staff
Mail Code 2821T
USEPA
1200 Pennsylvania Ave NW
Washington, D.C. 20460

Re: Request for Extension of Time for Filing
Request of Reconsideration of Request for Correction
 # 17002 (chloroprene)
Our File: 165671-00

Dear Sir or Madam:

On January 25, 2018, the U.S. Environmental Protection Agency (EPA) denied (hereinafter referred to as "the Denial") the Request for Correction (RFC) #17002 submitted on behalf of Denka Performance Elastomer LLC (DPE) concerning the 2010 Toxicological Review of Chloroprene (CAS No. 126-99-8) (hereinafter, "the 2010 Review"). Pursuant to the EPA Information Quality Act (IQA) guidelines and the Denial itself, EPA recommends that DPE submit any appeal in the form of a Request for Reconsideration (RFR) within 90 days of the January 25 Denial. That is, by April 25, 2018.

The purpose of this letter is to request a 90-day extension of the time allowed for DPE to file its RFR. The IQA Guideline 8.6 provides:

> EPA recommends that requesters submit their RFR within 90 days of the EPA decision. If the RFR is sent after that time, EPA recommends that the requester include an explanation of why the request should be considered at this time.

DPE's RFC and the 47 page Denial involved detailed reviews of the development of the 2010 Review and the analysis of complex issues of science. DPE's RFR similarly involves a rigorous review of the record of this matter, the development process of the 2010 Review, and the underlying scientific issues. In addition, DPE has filed two Freedom of Information Act (FOIA) requests with the EPA on March 6, 2018 (EPA-HQ-2018-005179 and EPA-HQ-2018-005180), both of which concern information related to the Denial and the 2010 Review process. The agency has requested additional time to respond to these FOIA requests and has not yet responded. We have also engaged experts to assist DPE in preparing its RFR. Due to the time required to collect all relevant information and documents, and the scientific complexity of this matter, DPE requests an additional 90 days from April 25, or until July 24, 2018, to submit its RFR.

DPE's contact information for DPE is as follows:

Jorge Lavastida
Executive Officer and Plant Manager
Denka Performance Elastomer LLC
560 Highway 44
LaPlace, LA 70068
Ex. 6
jorge-lavastida@denka-pe.com

Robert E. Holden
Jones Walker LLP
201 St. Charles Avenue, Suite 5100
New Orleans, LA 70170-5100
Ex. 6
bholden@joneswalker.com
Counsel for Denka Performance Elastomer LLC

We would appreciate a response from your office as quickly as possible due to the upcoming recommended filing date. Thank you for your attention to this.

Yours very truly,

Robert E. Holden
Attorney for Denka Performance Elastomer LLC

REH/kb

{N3582529.1}

cc: Dr. Jennifer Orme-Zavaleta, Deputy Administrator for Science, ORD
Ms. Tina Bahadori, ScD ORD/NCEA Director
Dr. Stephen Fine, Ph.D., Acting Chief Information Officer
Mr. David Gray, EPA Region 6 Director of External Affairs
Ms. Vincia Holloman, Director of Enterprise Quality Management Division
Ms. Anne Idsal, JD, Region 6 Administrator
Mr. John Vandenberg, ORD/NCEA RTP Division Director
Ms. Kistina Thayer, ORD/NCEA IRIS Division Director

Message

From: Krenik, Edward [edward.krenik@bracewell.com]
Sent: 3/28/2018 7:46:43 PM
To: Yamada, Richard (Yujiro) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=4c34a1e0345e4d26b361b5031430639d-Yamada, Yuj]
Subject: PBPK Workplan
Attachments: Workplan to provide a PBPK model for chloroprene_03.23.18.pdf; Revised ltr to Jennifer Orme-Zavaleta (N3568898x7A3A0).pdf

Importance: High

Richard,

Hope you are well. I left you a voicemail but realize there is a great deal going on. The attached letter will be sent today. Attached is an unsigned copy the signed original will be coming from Bob Holden. We certainly hope EPA can participate in the work group.

All the best,

Ed

EDWARD KRENIK
Senior Principal
edward.krenik@policyres.com
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March 28, 2018

Jennifer Orme-Zavaleta, Ph.D
Principal Deputy Assistant Administrator for Science
United States Environmental Protection Agency
1200 Pennsylvania Ave NW
Washington, D.C. 20460

Re: Chloroprene Request for Correction #17002 Follow-up Request for EPA Review of PBPK Workplan
Our File: 165671-00

Dear Dr. Orme-Zavaleta:

On behalf of Denka Performance Elastomer LLC (DPE), I acknowledge receipt of EPA's denial, dated January 25, 2018, of DPE's Request for Correction (RFC) #17002 concerning the 2010 Toxicological Review of Chloroprene. DPE is very disappointed with the EPA denial, and believes the EPA should reconsider its denial. As outlined in the EPA denial, DPE plans to file a timely Request for Reconsideration.

DPE's interest, as it is EPA's, is to seek the application of the best available science to this matter. EPA recognizes that it established the inhalation unit risk (IUR) for chloroprene based on the default assumption that human beings are as sensitive to chloroprene exposure as the most sensitive species in the laboratory. Attachment 1 to the January 25 denial explained, "In accordance with the EPA Guidelines for Carcinogen Risk Assessment (2005), in the absence of data to the contrary, EPA uses the most sensitive species and sex in establishing the cancer risk to humans, which, in the case of chloroprene, is the female mouse." EPA Denial, Attachment 1, at 3.

The January 25 denial includes a cover letter and attachments 1 and 2. The attachments provide details about why EPA does not consider any currently available physiologically-based pharmacokinetic (PBPK) models to be sufficiently validated to be used to adjust the mouse-based IUR to more accurately indicate potential human response. EPA's denial states that,

among other things, it contacted Dr. Harvey Clewell in an effort to obtain computer code for some of the most recent PBPK models for chloroprene.

DPE has now retained Dr. Clewell, who recently joined Ramboll Environ, to assist in developing a PBPK model that addresses the validation issues raised in the EPA denial. Attached for your reference is a copy of the "Workplan to Provide a Physiologically-Based Pharmacokinetic (PBPK) Model to Support the Inhalation Unit Risk (IUR) for chloroprene)," dated March _, 2018. Dr. Clewell and Ramboll Environ have designed the workplan to address EPA's stated validation concerns, and to deliver to EPA the computer code that EPA can utilize for its own validation review. Dr. Clewell and Ramboll Environ believe they can complete this task in 4 to 6 months.

Although DPE has instructed Dr. Clewell and Ramboll Environ proceed with this work, we would highly value EPA's review and comment on the workplan because it is DPE's intention to provide EPA with a PBPK model that meets EPA's validation and other requirements. Towards this objective, perhaps a meeting with you and your staff to discuss this path forward would be beneficial. It might also be desirable to form a joint industry-EPA working group to help develop this PBPK model on such an accelerated schedule.

We will be contacting your office shortly to follow up on this request. Thank you for your attention to this.

Yours very truly,

Robert E. Holden
Attorney for Denka Performance Elastomer LLC

REH/kb
Encls.
cc: Ms. Tina Bahadori, ScD ORD/NCEA Director
Dr. Stephen Fine, Ph.D., Acting Chief Information Officer
Mr. David Gray, EPA Region 6 Director of External Affairs
Ms. Vincia Holloman, Director of Enterprise Quality Management Division
Ms. Anne Idsal, JD, Region 6 Administrator
Mr. John Vandenberg, ORD/NCEA RTP Division Director
Ms. Kistina Thayer, ORD/NCEA IRIS Division Director

Intended for

Denka Performance Elastomer, LLC

560 Highway 44

LaPlace, LA 70068

Date

March 23, 2018

WORKPLAN TO PROVIDE A PHYSIOLOGICALLY-BASED PHARMACOKINETIC (PBPK) MODEL TO SUPPORT THE INHALATION UNIT RISK (IUR) FOR CHLOROPRENE

Prepared by:
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RAMBØLL

CONTENTS

1 INTRODUCTION

Multiple physiologically-based pharmacokinetic (PBPK) models available in the published, peer-reviewed scientific literature (Allen et al. 2014; Himmelstein et al. 2004; Thomas et al. 2013; Yang et al. 2012) have been evaluated and applied in the estimation of potential cancer risks following inhalation exposure to chloroprene (CAS No. 126-99-8). Several of these were identified by the U.S. Environmental Protection Agency's (USEPA) Integrated Risk Information System (IRIS) Toxicological Review of Chloroprene (USEPA 2010) and in a recent Request for Correction (RFC) of the Inhalation Unit Risk (IUR) submitted by Denka Performance Elastomer, LLC (DPE 2017). As noted in USEPA's Denial of the RFC (USEPA 2018), one of the key reasons for the denial was the lack of model validation, noting limitations and uncertainties that need to be addressed. Also lacking was the underlying code for these models to fully evaluate and consider them in the estimation of the IUR for chloroprene. All the published models rely upon the same underlying in vivo and in vitro data and PBPK models.

We outline below an approach for addressing the limitations and uncertainties raised by the USEPA that have prevented the use of these models in the development of the IUR for chloroprene, and provide the model code(s) needed to allow for full review of the available peer-reviewed models by USEPA and their application in the estimation of an IUR for chloroprene. This workplan primarily is intended to guide the process of scientifically evaluating and improving the PBPK model for chloroprene in support of an updated and more scientifically justifiable IUR. An ancillary objective is to provide USEPA a clear representation of the model refinement process and facilitate USEPA's possible review and input at each stage.

2 PROPOSED APPROACH

As noted in the response to the RFC dated January 25, 2018, USEPA was unable to locate and obtain the final code associated with the published PBPK models. USEPA (2018) noted that PBPK code is necessary for a quality assurance and quality control review by USEPA. Because the final code is not available, USEPA cannot evaluate the internal validity of the Yang et al. (2012) PBPK modeling methods or results, or results that are dependent on this model [i.e. Allen et al. (2014)]. Further complicating this, the software platform for these models (ACSL) is no longer available; therefore, migration to a new platform, such as R, will be necessary. The proposed approach to validating the PBPK model will be focused on addressing the comments that have been provided by USEPA in the IRIS (2010) assessment, as well as the Denial of the RFC (USEPA 2018), that were discussed as limitations and uncertainties with the PBPK model for chloroprene. The workplan further describes additional analyses to be conducted using the existing model to address these limitations and uncertainties, which will provide the USEPA with the necessary PBPK model code that would allow for a quality review and application of the model in the estimation of the IUR.

The uncertainties remaining in the application of the PBPK models that have been noted by USEPA in the IRIS Assessment (USEPA 2010) and the response to the RFC (USEPA 2018) are related to four specific areas:

- Justification for selected parameters in the in vivo/in vitro models
- Ability to reproduce in vivo pharmacokinetic data
- Estimation of uncertainty in the model using Markov Chain Monte Carlo (MCMC) analyses
- Reproduction of PBPK model code in an available operating platform

How we plan to address each of these areas of uncertainty is discussed in the following sections.

2.1 Justification for selected parameters in the *in vivo/in vitro* models

USEPA (2010) noted that the PBPK model reported in Himmelstein et al. (2004) currently predicts blood chloroprene and delivery of chloroprene to metabolizing tissues based on metabolic constants and partition coefficients based on in vitro data. Loss of chamber chloroprene is attributed to uptake and metabolism by test animals and was used to test the metabolic parameters and validate the model. However, Himmelstein et al. (2004) did not provide results of sensitivity analyses indicating whether chamber loss was sensitive to metabolism, and therefore it is uncertain whether chamber loss is useful for testing the metabolic parameters used in the model. We will conduct a sensitivity analysis using the current ASCL model in vitro and in vivo code and the results provided to USEPA for consideration.

The USEPA has further noted that the female mouse lung metabolism and internal doses in Yang et al. (2012) are not consistent with results for male mice. Vmax is approximately five times higher for male mice than for female mice, yet the tumor response is similar. This has implications for biological basis for the site-specific dose-response, and parameterization of extra-hepatic metabolism. Additional analyses will be conducted to evaluate the uncertainty in the Vmax estimates. The results of these analyses will determine if pharmacokinetic differences can explain the sex-specific differences in response in the mouse, or if there is evidence of pharmacodynamic differences or sex-specific sensitivity.

The dose metrics relied upon in all the modeling publications have focused on metabolism in the liver, lung or kidney. The USEPA has noted that lung metabolism does not account for tumor responses at other sites outside the lung, which also need to be incorporated into a risk assessment. Additional analyses will be conducted to determine if data are available to suggest significant metabolic capability

in organ systems other than the liver, lung or kidney and how critical the potential contribution of this metabolism might be to the overall composite risk.

2.2 Ability to reproduce *in vivo* pharmacokinetic data

In the IRIS Assessment (USEPA 2010), the USEPA noted that the model's ability to reproduce in-vivo PK data [i.e. from Himmelstein et al. (2004)] has not been evaluated. In the chloroprene docket is a report in which blood chloroprene was measured in mice following single (6-hour) and repeated (5- or 15-day) inhalation exposures (unpublished). Chloroprene blood levels were higher following single exposures, which was postulated to be because of higher minute volume due to stress. The authors conclude that these blood data are suitable for validation of a PBPK model, but it is unclear whether the data were used for the validation of the PBPK model in Yang et al. (2012). The report did not investigate chloroprene levels in the organs of interest (namely the lungs, liver, or kidneys). Additional simulations will be conducted to determine if the in vivo model can be validated using the datasets in the mouse provided in the chloroprene docket (DuPont 2009).

Of additional concern in the IRIS Assessment (USEPA 2010) was that Himmelstein et al. (2004) had to reduce alveolar ventilation and total blood flow values predicted from the in vitro data by 50% to match the in vivo PK data presented. Mice are well known to suppress respiration (RD) and cardiac output in response to irritant gases. However, the response would be dose dependent. Change in respiration and cardiac output is necessary to fit the available data and has been observed with and incorporated into models for other compounds. Although there are no data specific to chloroprene to characterize respiratory and cardiac output suppression, additional analyses will be conducted to increase the confidence in this adjustment and to find additional scientific data to support this adjustment.

2.3 Estimation of uncertainty in the model using Markov Chain Monte Carlo (MCMC) analyses

In the 2010 IRIS assessment, USEPA noted the need to use distributions of the PBPK model parameters to represent variability in intra-population rates of chemical absorption, distribution, metabolism, and elimination to estimate human variability. The MCMC analyses conducted as part of the Yang et al. (2012) publication was to investigate potential variability in parameters, but also understand the potential uncertainty and its impact on estimating potential cancer risks from exposure to chloroprene. So, while Yang et al. (2012) addresses part of USEPA's (2010) comments, additional relevant comments were noted in the USEPA (2018) response to the RFC. USEPA (2018) questions the form of the log-likelihood function used in the MCMC analysis and suggests that the autocorrelation among repeated measures from a single experimental unit has not been considered. USEPA (2018) also noted that the female mouse kidney metabolism approaches zero in the MCMC optimization and that parameterization of extra-hepatic metabolism may be incorrect.

For liver metabolism, this is apparent on the log-scale for predictions of chloroprene headspace concentration data provided in Figure 2b of Yang et al. (2012), and Figures 5 and 25 of Study IISRP-17520-1388 (submitted to EPA-HQ-ORD-2009-0217). The underestimation occurs for both the point estimate results and the Monte Carlo results. Also, because the molecular form of enzymes does not vary between tissues within an individual, or males and females of a species, the Km for metabolism should be likewise constant across tissues and between sexes.

The MCMC analyses conducted by Yang et al. (2012) will be revisited to address these comments.

2.4 Reproduction of PBPK model code in an available operating platform

As noted in the USEPA (2018) response to the RFC, while several model code packages were shared with the USEPA by Dr. Harvey Clewell, these are poorly documented and do not provide sufficient instructions that allow the EPA to review or apply the available models now. Once the comments

previously outlined have been addressed, the final step in the workplan will be to provide a complete model code with adequate documentation and files to reproduce critical results needed for the quality review of the model and the application in the estimation of the IUR. Both the code for the in vivo and in vitro components of the model will be provided allowing the USEPA to reproduce the PBPK results from Himmelstein et al. (2004), Yang et al. (2012), Thomas et al. (2013) and Allen et al. (2014). The code will be provided in the R platform, with the necessary scripts to reproduce the analyses conducted as part of the workplan as well as the results provided in the publications.

3 SCHEDULE

We plan to communicate closely with the USEPA to ensure that the remaining questions and uncertainties associated with the review and application of the PBPK model for chloroprene have been addressed. We anticipate that we will be able to provide the needed model code, addressing the remaining uncertainties, to the USEPA within 4 to 6 months following acceptance of the workplan.

4 REFERENCES

Allen BC, Van Landingham C, Yang Y, Youk AO, Marsh GM, Esmen N, Gentry PR, Clewell HJ III, Himmelstein MW. 2014. A constrained maximum likelihood approach to evaluate the impact of dose metric on cancer risk assessment: Application to b-chloroprene. Regulatory Toxicology and Pharmacology, 70: 203–213.

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USEPA. 2018. Letter to Robert Holden from Jennifer Orme-Zavaleta dated January 25, 2018 in response to the Request for Correction (RFC) received by the United States Environmental Protection Agency. June 26, 2017.

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Message

From: Krenik, Edward [edward.krenik@bracewell.com]
Sent: 4/24/2018 1:13:45 PM
To: Yamada, Richard (Yujiro) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=4c34a1e0345e4d26b361b5031430639d-Yamada, Yuj]
Subject: RE: Request for an extension

Hi Richard,

Any word on our extension request?

Thanks,

Ed

From: "Krenik, Edward" <edward.krenik@bracewell.com>
Sent: Apr 19, 2018 7:18 PM
To: Richard Yamada <yamada.richard@epa.gov>
Cc: "Burhop, Anna" <anna.burhop@bracewell.com>; "Lee, John" <john.lee@bracewell.com>
Subject: Request for an extension

Richard,

I wanted to make sure you saw this. We are working on some additional data but need additional time to get it peered review and reviewed like our offer for a PBPK working group. I really feel a working group team would be beneficial and we could benefit from EPA's involvement.

Thanks for your consideration. Happy to answer any questions. We would like to know soon if it can be granted.

Ed

Sent from my Verizon, Samsung Galaxy smartphone

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Message

From: Schubert, Kai-Volker [KAI-VOLKER.SCHUBERT@chemours.com]
Sent: 2/9/2018 10:29:13 AM
To: Yamada, Richard (Yujiro) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=4c34a1e0345e4d26b361b5031430639d-Yamada, Yuj]
Subject: My contact information

Dear Richard,

Thank you very much for attending the meeting with FluoroCouncil on January 31. I saw that you are connecting with me via LinkedIn but I am not very active on that network. Please contact me directly by e-mail or phone with any questions you might have.

Have a great Friday and a nice weekend.

Kind regards,

Kai

Kai-Volker Schubert
Sustainability
Ex. 6
m
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Wilmington, DE 19899 (USA)

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Message

From: Krenik, Edward [edward.krenik@bracewell.com]
Sent: 1/12/2018 7:43:03 PM
To: Yamada, Richard (Yujiro) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=4c34a1e0345e4d26b361b5031430639d-Yamada, Yuj]
Subject: Denka
Attachments: DenkaAOCcompletion.pdf

Richard,

Welcome back. I thought the attached might be of interest to you. The press release went out yesterday.

Happy to discuss further at your convenience.

Best,

Ed

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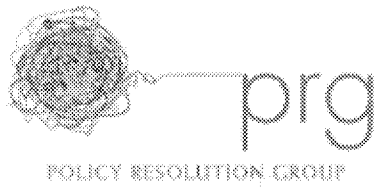

Denka Performance Elastomer LLC
560 Highway 44
LaPlace, LA 70068

FOR IMMEDIATE RELEASE
JANUARY 11, 2018

Contact:
Jim Harris
Harris Deville & Associates
jharris@hdaissues.com
Phone: Ex. 6

Denka Performance Elastomer Begins Operation of Regenerative Thermal Oxidizer (RTO) Unit at LaPlace Facility

LaPlace, LA – Denka Performance Elastomer (Denka) began operating all the equipment by the end of 2017 specified in the Administrative Order on Consent (AOC) the company signed with the Louisiana Department of Environmental Quality (LDEQ) on January 6, 2017.

Included in the new emissions control technology is Denka's Regenerative Thermal Oxidizer (RTO), the most significant voluntary emissions reducing project undertaken by the company under the AOC. The RTO is one of four main projects in the AOC designed to significantly reduce chloroprene emissions from operations of the LaPlace facility. The equipment included in the four projects was installed at a cost of nearly $30 million.

"We are pleased to have completed installation and started operation of all of our emission reduction projects," said Jorge Lavastida, Denka plant manager. "Our voluntary emissions reduction plan represents Denka's commitment to our community. We have followed through on a promise made to our neighbors, employees and the state of Louisiana. I want to congratulate our many employees and contractors who committed their time over the last year to making these four projects a reality." In addition to the RTO, these projects included installing a brine condenser on the poly kettles vent, a vacuum pump and vent condenser on the CD Refining Column and routing various emission sources to an existing combustion unit.

Denka will continue to monitor ambient air concentration alongside the U.S. Environmental Protection Agency (EPA) through the first half of 2018 to determine the impact and effectiveness of its reduction efforts and track its progress. The company expects to see significant reductions in ambient concentrations of chloroprene measured over that period.

- MORE -

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The LaPlace facility produces Neoprene, a product used in a wide variety of applications including laptop sleeves, orthopedic braces, electrical insulation and automotive parts.

Denka purchased the Neoprene business at DuPont's Pontchartrain Works Site in late 2015. The Neoprene plant employs 235 full-time workers. More than 250 additional contractors were also employed to install the emissions reduction equipment.

The emissions reduction projects were developed in response to an EPA National Air Toxics Assessment (NATA) report published in December 2015 that suggested a high risk of health impacts in the area surrounding the LaPlace was published in December 2015, one month after Denka began to operate the facility. External experts and reviewers have disputed the report's findings and Denka has submitted information to the EPA in a formal Request for Correction of the underlying information.

Since the NATA report was published, and throughout the process of reviewing and contesting the federal scientific information, Denka has voluntarily worked with EPA, LDEQ and parish officials to listen to and address the local community's concerns. Denka held community meetings with officials from regulatory agencies and St. John residents.

For additional information on the company and the voluntary emissions reduction projects, visit Denka-pe.com.

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About Denka Performance Elastomer

Denka Performance Elastomer LLC acquired DuPont's Neoprene manufacturing operations at the Pontchartrain Works site in LaPlace. Denka employs 235 individuals at the site and its new LaPlace, LA headquarters.

Denka intends to make strategic investments in the LaPlace facility while adhering to a key Denka guideline to develop and supply products that are safe and environmentally friendly. Denka considers the careful handling of materials and products and the prevention of their unauthorized release into the environment as its most important mission as a chemical manufacturer.

Message

From: Krenik, Edward [edward.krenik@bracewell.com]
Sent: 10/30/2017 5:10:34 PM
To: Kirby, Kevin [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=cbb65672f6f34545be460a66ff6fa969-Kirby, Kevin]
CC: Vandenberg, John [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=dcae2b98a04540fb8d099f9d4dead690-Vandenberg, John]; Thayer, Kris [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=3ce4ae3f107749c6815f243260df98c3-Thayer, Kri]; Davis, Allen [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=a8ecee8c29c54092b969e9547ea72596-Davis, Allen]; Yamada, Richard (Yujiro) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=4c34a1e0345e4d26b361b5031430639d-Yamada, Yuj]; Simons, Andrew [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=652da36feb75460da864ef6504ae0f42-ASIMONS]; Holloman, Vincia [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=e7e9f8511bc84976ae1eae93e17062fa-Holloma, Vincia]; Moser, Rebecca [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=43e2794f849243dfae064ab3f3bacf93-Moser, Rebecca]
Subject: RE: RE:
Attachments: Chloroprene RFC Meeting 10.30.17.pptx

Kevin,

Here is the final presentation that we will be using today. See you at 3:00.

Thank you for all your help.

Ed

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From: Kirby, Kevin [mailto:KIRBY.KEVIN@EPA.GOV]
Sent: Thursday, October 26, 2017 3:58 PM
To: Krenik, Edward
Cc: Vandenberg, John; Thayer, Kris; Davis, Allen; Yamada, Richard (Yujiro); Simons, Andrew; Holloman, Vincia; Moser,

Rebecca
Subject: RE:

Hello Ed,
I Hope that you're enjoying these beautiful entry days into fall. We are looking forward to meeting you here at EPA HQ in Federal Triangle next week, Oct. 30 at 3:00. We will be meeting specifically in the EPA West building located at 1301 Constitution Ave.

Attached is the Agenda that I will be circulating to individuals participating in our RFC meeting next week. If you have any additional materials, such as the presentation you referenced, please send them to me by COB Friday so that I can circulate these as well. There is no need to bring any projection equipment, but you do need to send me the materials *prior to the meeting* so that I can scan them and load them.

For logistics, please plan on entering EPA West through our main entrance at 1301 Constitution Ave. NW We will be meeting in Conference Room 6122, Yellowstone. You and your colleagues will be required to go through security and be escorted to the room once on premise. You may reach me at my desk 202 566-1656 or via cell at 703 489-2862.

See you Monday,
Kevin Kirby
US EPA

From: Krenik, Edward [mailto:edward.krenik@bracewell.com]
Sent: Tuesday, October 24, 2017 5:15 PM
To: Kirby, Kevin <KIRBY.KEVIN@EPA.GOV>
Cc: Vandenberg, John <Vandenberg.John@epa.gov>
Subject:

Hi Kevin,

I hope you are well. Attached is the agenda and attendees list for the upcoming meeting. I will be sending you our power point presentation at the end of this week so that you can get it to some of the EPA attendees who may be on by phone or video. Couple logistic questions, which door should we come to for the meeting? Where ORD is in the RR Building or another entrance? Also, since we would like to show a power point will projector equipment be available or should we bring our own?

Thanks much. See you Monday.

Ed

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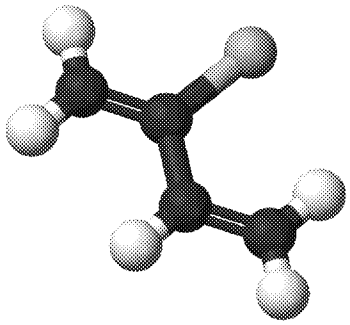
REQUEST FOR CORRECTION OF THE EPA'S 2010 IUR FOR CHLOROPRENE

Kenneth A. Mundt, PhD, FACE

P. Robinan Gentry, PhD, DABT

Sonja Sax, ScD



RAMBOLL ENVIRON

EXECUTIVE SUMMARY 1

- EPA published the IRIS Toxicological Review of Chloroprene in 2010, with an inhalation unit risk (IUR) of 5×10^{-4} per $\mu g/m^3$.
- This is the 5th highest IUR derived by IRIS for any chemical classified by IARC as carcinogenic (Group 1) or probably carcinogenic (Group 2a).
- IARC classified chloroprene as possibly carcinogenic (Group 2b).
- Ramboll Environ was requested to conduct a detailed review of the 2010 IRIS, and to derive an IUR for Chloroprene.

EXECUTIVE SUMMARY 2

- **Key Findings: All lines of evidence indicate that the IUR should be corrected:**
- The highest quality epidemiological studies demonstrated no excess lung or liver cancer risk.
- Toxicological data do not support a mutagenic mode of action.
- Multiple lines of evidence indicate large differences across species.
- Using NRC best practices recommendations, EPA methods and pharmacokinetic data, the Ramboll Environ IUR is 156 times lower than the 2010 IRIS IUR.
- Cancer risk estimates based on the Ramboll Environ IUR are consistent with the epidemiological data.

INTRODUCTION

- EPA published the IRIS Toxicological Review of Chloroprene* in 2010, with an inhalation unit risk **(IUR) of 5 x 10^{-4} per $\mu g/m^3$.**
- Denka Performance Elastomer (DPE) acquired the Neoprene production facility in LaPlace, Louisiana from DuPont on November 1, 2015.
- On December 17, 2015, EPA published the 2011 National Air Toxics Assessment (NATA), including a risk assessment based on the facility's emissions and the 2010 IRIS IUR.
- The NATA study identified DPE's facility as associated with **one of the highest offsite cancer risks** of any chemical facility in the US.
- DPE retained Ramboll Environ to evaluate the scientific validity of the 2010 IRIS IUR.
- Using EPA standard methods and publicly available data, Ramboll Environ determined that the 2010 IRIS **IUR is overestimated by a factor of 156**.

* U.S. Environmental Protection Agency, Washington, DC, EPA/635/R-09/010F, 2010.

OBJECTIVES

- Evaluate the 2010 IRIS Review of Chloroprene, especially the IUR, in light of NRC (2011, 2014) guidance on improving IRIS assessments:
  - How studies are evaluated: quality assessment and weighting
  - Better integration of data across all lines of evidence
- Critically review and integrate the published epidemiological, toxicological, and mode of action evidence on chloroprene carcinogenicity.
- Apply a standard pharmacokinetic correction to the chloroprene IUR.
- Provide a "reality check" for the IUR.

EPIDEMIOLOGICAL EVIDENCE

RAMBOLL ENVIRON

COMPARISON OF KEY CRITERIA ACROSS STUDIES

Key Criteria	US and Europe (Marsh *et al.* 2007)	Armenia (Bulbulyan *et al.* 1999)	Russia (Bulbulyan *et al.* 1998)	China (Li *et al.* 1989)
Sample Size	12,430	2,314	5,185	1,258
Follow-up	1949–2000	1979–1993	1979–1993	1969-1983
Exposure Assessment	Exposure modeling – 7 categories	Index (none, low, high)-before/after 1980	Index (none, med, high)-IH (inadequate) + job	High vs. low based on recall
Baseline rates	National, local plant area counties 1960–1994	Armenian rates 1980-1989	Moscow rates 1979–1993 or 1992–1993 (liver)	From "local area" 1973–1975 expected lung cancers: 0.4
Confounding	Used local rate comparisons; Low prevalence of other liver cancer risk factors	Alcohol use (high cirrhosis rates) and smoking prevalent	Alcohol use (high cirrhosis rates) and smoking; Co-exposure to VC	Hepatitis B and aflatoxin; Co-exposures to VC

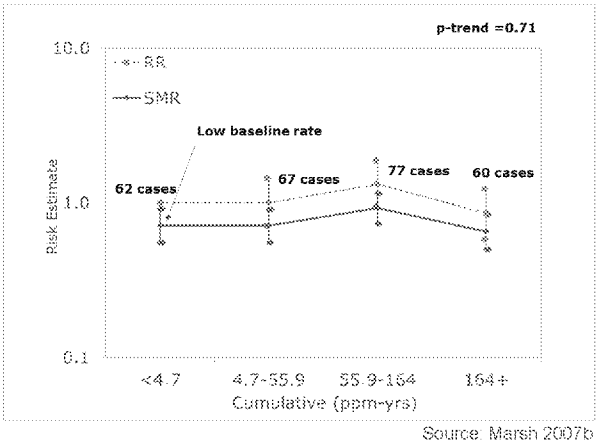
MARSH STUDY RECEIVES HIGHEST QUALITY RANK

US EPA Criteria	Marsh et al. (2007 a,b) Study				Other Studies			
	Kentucky[1]	North Ireland	Louisiana[1]	France-Mortality[1]	Armenia[2]	France-Incidence[3]	Russia[4]	China[5]
Clear objectives	H‡	H	H	H	H	H-M	H	M
Comparison groups	H	H-M	H-M	M	M	M	M-L	L
Exposure	H	H	H	H	M	M	L	L
Follow-up	H	H-M	H	H-M	M-L	M-L	M-L	M-L
Case ascertainment	H	H-M	H-M	H-M	M	M	M	H-M
Control of bias	H-M	H-M	H-M	M	M-L	M	M	M-L
Sample size	H	H	M	L	M-L	L	H-M	M-L
Data collection and evaluation	H	H	H	H	M	M	M-L	M-L
Adequate response	H	H	H	H	M	M	M	H-M
Documentation of results	H	H	H	H	M-L	M	M	L
Overall rank (1=best)	**1**	**2**	**3**	**4**	**5**	**5**	**5**	**6**

Source: Bukowski 2009 ‡ Subjective estimate of study quality for each specific criterion H=high, M=medium, L=low; 1 – Marsh et al. 2007; 2 – Bulbulyan et al. 1999; 3 – Colonna and Laydevant 2001; 4 – Bulbulyan et al. 1998; 5 – Li et al. 1989

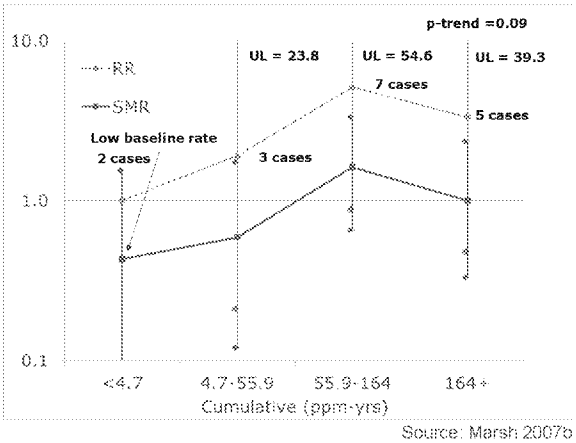
MARSH STUDY SHOWS NO INCREASED LUNG OR LIVER CANCER RISKS

Respiratory cancers RRs and SMRs by cumulative chloroprene exposure, Louisville plant



Source: Marsh 2007b

Liver cancers RRs and SMRs by cumulative chloroprene exposure, Louisville plant



Source: Marsh 2007b

LOCAL COMMUNITY-LEVEL CANCER RATES

- Cancer incidence data from the Louisiana Tumor Registry for St. John the Baptist Parish (where DPE plant is located) and for the state of Louisiana
- Five most recent years

Cancer site	Parish Rate	State Rate	Ranking (1=lowest cancer rate)
All cancers	463.2	478.7	15/64
Respiratory cancers	60.1	70.5	7/64
Liver cancers	< 3 cases (too few to report)		Unknown*

*Unknown as as there were 28 parishes with too few liver cancer cases

Source: https://statecancerprofiles.cancer.gov/incidencerates/index.php?stateFIPS=22&cancer=001&race=00&sex=0&age=001&type=incd&sortVariableName=rate&sortOrder=default#results

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RAMBOLL ENVIRON

OCCUPATIONAL CANCER RATES IN THE PONTCHARTRAIN FACILITY, LA

- Marsh et al. (2007a) results for 1,357 workers at the Pontchartrain facility in LA (US and local reference rates)

Cancer site	US-based SMR	Local-based SMR
All cancers	0.74 (0.51-1.04)	0.68 (0.47–0.95)
Respiratory cancers	0.72 (0.37-1.26)	0.62 (0.32-1.09)
Liver cancers	None reported	None reported

MARSH ET AL. (2007) CONCLUSION

Marsh et al. (2007) should be given greater weight than studies from Asia, Russia and Armenia:

"*We conclude that persons exposed to chloroprene or vinyl chloride at the levels encountered in the four study sites* ***did not have elevated risks of mortality from any of the causes of death*** *examined, including all cancers combined and* ***lung*** *and* ***liver*** *cancer, the cancer sites of a priori interest.*"

"*This* ***conclusion is corroborated by our detailed analyses of mortality*** *in relation to* ***qualitative and quantitative exposures to CD*** *and VC at each of the four study sites.*"

Source: G.M. Marsh et al. / Chemico-Biological Interactions 166 (2007) 285–300

TOXICOLOGICAL EVIDENCE

RATIONAL ENVIRON

ANIMAL STUDIES

- Studies conducted in B6C3F1 mice and Fischer rats (NTP, 1998), and in Wistar rats and Syrian hamsters (Trochimowicz et al., 1998) at chloroprene concentrations ranging from 10 to 80 ppm.
- A significant incidence of tumors seen across many organ sites, primarily in mice and at the highest exposure levels.
- The most sensitive species/tumor site is the female mouse and the lung.
- Fewer tumors in Wistar rats and Syrian hamsters; little consistency across species both in the number of tumors and in tumor location.
- Differences in tumor incidence can be explained by using PBPK modeling and the calculated internal dose of metabolized chloroprene.

SUMMARY OF ANIMAL DATA (DERIVED FROM HIMMELSTEIN ET AL. 2004)

Species	Exposure concentration (ppm)	PBPK internal dose (mg/g)	Lung tumor incidence	Number of animals
Syrian Hamster (Trochimowicz et al., 1998)	0	0	0	100
	10	0.18	0	97
	50	0.88	0	97
Wistar rat (Trochimowicz et al., 1998)	0	0	0	97
	10	0.18	0	13
	50	0.89	0	100
Fischer rat (NTP, 1998)	0	0	3	50
	12.8	0.22	3	50
	32	0.55	6	49
	80	1.37	9	50
B6C3F1 mouse (NTP, 1998)	**0**	**0**	**15**	**50**
	12.8	**3.46**	**32**	**50**
	32	**5.3**	**40**	**50**
	80	**7.18**	**46**	**50**

15

In vitro mutagenicity results are inconsistent

Study	Method	Exposure	Response
Bartsch *et al.*, 1979	Desiccator	4 hours	+
Westphal *et al.*, 1994	Pre-incubation	2 hours	-
NTP, 1998	Pre-incubation	20 min.	-
Willems, 1980	Desiccator	24-48 hours	+

In vivo results are mostly negative, and mutagenicity profile is different from 1,3-butadiene

Chemical	*In Vivo* (B6C3F1 mouse)		
	CA	SCE	MN
Chloroprene	-	-	-
1,3 - Butadiene	+	+	+

CA – chromosome aberrations; SCE - sister chromatid exchange;MN - micronucleus test; Source: Tice 1988

Weight of evidence is not consistent with a mutagenic MOA. An alternative MOA should be considered in accordance with EPA and NRC guidelines.

RAMBOLL ENVIRON

CHLOROPRENE IUR

ENVIRON

Compound (Year of Review)	IUR per ug/m^3	Basis	PBPK adjustment	Classification	Ratio
Chloroprene (2010)	**5 x 10^{-4}**	Multiple tumors in mice, mutagenic MOA	No	Possibly Carcinogenic	1
1,3 Butadiene (2002a)	3 x 10^{-5}	Human occupational studies	No	Known Carcinogen	~20
Benzene (2002b)	2 x 10^{-6} – 7.8 x 10^{-6}	Human occupational studies	No	Known Carcinogen	250
Vinyl Chloride (2000)	4.4 x 10^{-6}	Liver tumors in rats	Yes	Known Carcinogen	~100

Adjusted IUR of chloroprene is more in line with other known carcinogens; e.g., VC IUR is based on animal data, but with PBPK model adjustments.

RAMBOLL ENVIRON

UNCERTAINTIES IN THE 2010 IUR

Step	IUR per ug/m^3	Basis
Most sensitive endpoint/species (portal-of-entry DAF=1.7)	1.06 x 10^{-4}	Lung tumors in female mice as a portal-of-entry effect
Most sensitive endpoint/species (systemic lesion DAF=1)	1.81 x 10^{-4}	Lung tumors in female mice as a systemic effect
Multiple tumor adjustment	2.7 x 10^{-4}	Multiple tumors
Rounding	3 x 10^{-4}	Rounding
Application of ADAF	**5 x 10^{-4}**	Adjustment (assuming mutagenicity)

ENVIRON

PHARMACOKINETIC CORRECTION OF THE ANIMAL DATA

	IUR per ug/m^3	Basis	Resulting decrease in IUR
US EPA (2010)	**5 x 10^{-4}**	Fully adjusted composite value in female mice with ADAF correction	Referent
Allen et al. (2014)	1.86 x 10^{-6}	PBPK dosimetric adjustment of lung tumors in female mice in target organ; includes animal and human data	~250 fold decrease
Ramboll Environ (2017)	3.2 x 10^{-6}	PBPK dosimetric adjustment of lung tumors in female mice in the target organ; based on animal data only	156 fold decrease

PHARMACOKINETIC CORRECTION OF THE CHLOROPRENE IUR

- PBPK model was published by Himmelstein et al. (2004).
- Data were provided to EPA at the time of the review to check the validity of the model; however, EPA did not incorporate these data into the final IUR estimate.
- Data provided to EPA have been published (Yang et al., 2012; Thomas et al., 2013).
- Allen et al. (2014) reported that an IUR that incorporates pharmacokinetic differences 250 times lower than the 2010 IRIS IUR.
- Using the internal dose estimates from PBPK modeling from Yang et al. (2012) Ramboll Environ derived an IUR of **3.2×10^{-6}** per $\mu g/m^3$ which is **156 times lower** than the 2010 IRIS IUR.

"REALITY CHECK"

Source	Unit Risk (per ppm)	Mean Exposure* (ppm)	Excess Cancers (Risk Estimate)	Excess Cancers (Observed–Expected) Local referent
US EPA (2010) lung tumor	0.65	8.42	5.5	
multi tumor	1.08	8.42	9.1	-84 (lung)
w/ADAF	1.80	8.42	15.2	-1.9 (liver)
Allen et al. (2014) lung tumor	0.0067	8.42	0.06	
Ramboll Environ lung tumor	0.012	8.42	0.1	

*Mean exposure reported by Marsh et al. 2007a

IUR corrected for pharmacokinetic differences results in a cancer risk estimate consistent with epidemiological results (i.e., no observable excess risk).

DAMES & MOORE ENVIRON

CANCER CLASSIFICATION

CANCER CLASSIFICATION OF CHLOROPRENE

EPA classified chloroprene as "likely to be a human carcinogen" based on:

- National Toxicology Program (NTP, 1998) chronic inhalation bioassay;
- Associations between chloroprene exposure and liver cancer in four of nine epidemiological studies;
- Limited evidence of lung cancer;
- Proposed mutagenic mode of action; and
- Analogies with 1,3-butadiene and vinyl chloride

Critical review of the evidence indicated that four of these five cannot be substantiated.

The classification should be revisited and a clearer narrative provided.

https://cfpub.epa.gov/ncea/iris2/chemicalLanding.cfm?substance_nmbr=1021

ENVIRON

SUMMARY AND CONCLUSIONS

PARSONS ENVIRON

BASES FOR A REQUEST FOR CORRECTION OF THE 2010 IUR

- The highest quality epidemiological studies do not demonstrate a causal relationship between occupational exposures to chloroprene and cancer.
- Many lines of evidence point to pharmacokinetic differences across species.
- PBPK modelling is the best approach for correcting the IUR because of large pharmacokinetic differences between the mouse and humans.
- Using PBPK model output and standard EPA methods, Ramboll Environ calculated an IUR that is 156 times lower than the 2010 IRIS IUR.
- The IRIS classification of chloroprene as "likely to be a human carcinogen" should be reclassified given our understanding of the MOA.

Integration of the full body of evidence indicates that the pharmacokinetic differences between the mouse and humans require that the IUR be corrected using PBPK model results.

THANK YOU

Ken Mundt
kmundt@ramboll.com
Robinan Gentry
rgentry@ramboll.com
Sonja Sax
ssax@ramboll.com

Message

From: Krenik, Edward [edward.krenik@bracewell.com]
Sent: 10/27/2017 6:37:47 PM
To: Kirby, Kevin [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=cbb65672f6f34545be460a66ff6fa969-Kirby, Kevin]
CC: Vandenberg, John [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=dcae2b98a04540fb8d099f9d4dead690-Vandenberg, John]; Thayer, Kris [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=3ce4ae3f107749c6815f243260df98c3-Thayer, Kri]; Davis, Allen [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=a8ecee8c29c54092b969e9547ea72596-Davis, Allen]; Yamada, Richard (Yujiro) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=4c34a1e0345e4d26b361b5031430639d-Yamada, Yuj]; Simons, Andrew [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=652da36feb75460da864ef6504ae0f42-ASIMONS]; Holloman, Vincia [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=e7e9f8511bc84976ae1eae93e17062fa-Holloma, Vincia]; Moser, Rebecca [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=43e2794f849243dfae064ab3f3bacf93-Moser, Rebecca]
Subject: Draft DPE presentation
Attachments: DRAFT RambollEnviron_Chloroprene_RFCmeeting102717.pdf

Hi Kevin,

Happy Friday. Attached is a draft of our power point that will be used in our meeting with you on Monday. There may be a few additional tweaks to this presentation but please feel free to circulate this copy to your team.

Thanks for all your help.

Best,

Ed

EDWARD KRENIK
Partner
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this transmission in error, please notify the sender by reply e-mail and delete the message and any attachments.

From: Kirby, Kevin [mailto:KIRBY.KEVIN@EPA.GOV]
Sent: Thursday, October 26, 2017 3:58 PM
To: Krenik, Edward
Cc: Vandenberg, John; Thayer, Kris; Davis, Allen; Yamada, Richard (Yujiro); Simons, Andrew; Holloman, Vincia; Moser, Rebecca
Subject: RE:

Hello Ed,
I Hope that you're enjoying these beautiful entry days into fall. We are looking forward to meeting you here at EPA HQ in Federal Triangle next week, Oct. 30 at 3:00. We will be meeting specifically in the EPA West building located at 1301 Constitution Ave.

Attached is the Agenda that I will be circulating to individuals participating in our RFC meeting next week. If you have any additional materials, such as the presentation you referenced, please send them to me by COB Friday so that I can circulate these as well. There is no need to bring any projection equipment, but you do need to send me the materials *prior to the meeting* so that I can scan them and load them.

For logistics, please plan on entering EPA West through our main entrance at 1301 Constitution Ave. NW We will be meeting in Conference Room 6122, Yellowstone. You and your colleagues will be required to go through security and be escorted to the room once on premise. You may reach me at my desk 202 566-1656 or via cell at 703 489-2862.

See you Monday,
Kevin Kirby
US EPA

From: Krenik, Edward [mailto:edward.krenik@bracewell.com]
Sent: Tuesday, October 24, 2017 5:15 PM
To: Kirby, Kevin <KIRBY.KEVIN@EPA.GOV>
Cc: Vandenberg, John <Vandenberg.John@epa.gov>
Subject:

Hi Kevin,

I hope you are well. Attached is the agenda and attendees list for the upcoming meeting. I will be sending you our power point presentation at the end of this week so that you can get it to some of the EPA attendees who may be on by phone or video. Couple logistic questions, which door should we come to for the meeting? Where ORD is in the RR Building or another entrance? Also, since we would like to show a power point will projector equipment be available or should we bring our own?

Thanks much. See you Monday.

Ed

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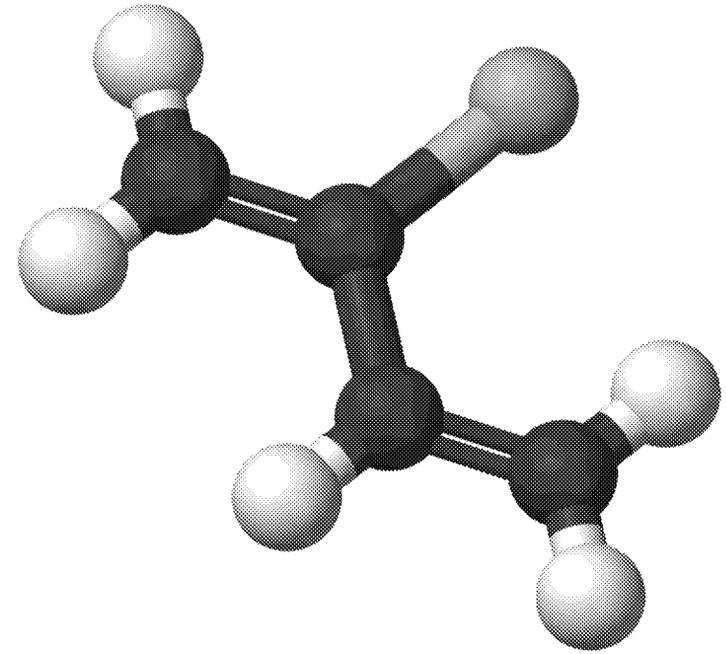
DRAFT PRESENTATION

REQUEST FOR CORRECTION OF THE EPA'S 2010 IUR FOR CHLOROPRENE

Kenneth A. Mundt, PhD, FACE

P. Robinan Gentry, PhD, DABT

Sonja Sax, ScD



RAMBOLL ENVIRON

EXECUTIVE SUMMARY 1

- EPA published the IRIS Toxicological Review of Chloroprene in 2010, with an inhalation unit risk (IUR) of 5×10^{-4} per $\mu g/m^3$.
- This is the 5th highest IUR derived by IRIS for any chemical classified by IARC as carcinogenic (Group 1) or probably carcinogenic (Group 2a).
- IARC classified chloroprene as possibly carcinogenic (Group 2b).
- Ramboll Environ was requested to conduct a detailed review of the 2010 IRIS, and to derive an IUR for Chloroprene.

EXECUTIVE SUMMARY 2

- **Key Findings: All lines of evidence indicate that the IUR should be corrected:**
- The highest quality epidemiological studies demonstrated no excess lung or liver cancer risk.
- Toxicological data do not support a mutagenic mode of action.
- Multiple lines of evidence indicate large differences between across species.
- Using NRC best practices recommendations, EPA methods and pharmacokinetic data, the Ramboll Environ IUR is 156 times lower than the 2010 IRIS IUR.
- Cancer risk estimates based on the Ramboll Environ IUR are consistent with the epidemiological data.

RAMBOLL ENVIRON

INTRODUCTION

- EPA published the IRIS Toxicological Review of Chloroprene* in 2010, with an inhalation unit risk **(IUR) of 5 x 10^{-4} per $\mu g/m^3$**.
- Denka Performance Elastomer (DPE) acquired the Neoprene production facility in LaPlace, Louisiana from DuPont on November 1, 2015.
- On December 17, 2015, EPA published the 2011 National Air Toxics Assessment (NATA), including a risk assessment based on facility's emissions and the 2010 IRIS IUR.
- The NATA study identified DPE's facility as associated with **one of the highest offsite cancer risks** of any chemical facility in the US.
- DPE retained Ramboll Environ to evaluate the scientific validity of the 2010 IRIS IUR.
- Using EPA standard methods and publicly available data, Ramboll Environ determined that the 2010 IRIS **IUR is overestimated by a factor of 156**.

* U.S. Environmental Protection Agency, Washington, DC, EPA/635/R-09/010F, 2010.

RAMBOLL ENVIRON

OBJECTIVES

- Evaluate the 2010 IRIS Review of Chloroprene, especially the IUR, in light of NRC (2011, 2014) guidance on improving IRIS assessments:
  - How studies are evaluated: quality assessment and weighting
  - Better integration of data across all lines of evidence
- Critically review and integrate the published epidemiological, toxicological, and mode of action evidence on chloroprene carcinogenicity.
- Apply a standard pharmacokinetic correction to the chloroprene IUR.
- Provide a "reality check" for the IUR.

RAMBOLL ENVIRON

EPIDEMIOLOGICAL EVIDENCE

RAMBOLL ENVIRON

COMPARISON OF KEY CRITERIA ACROSS STUDIES

Key Criteria	US and Europe (Marsh *et al.* 2007)	Armenia (Bulbulyan *et al.* 1999)	Russia (Bulbulyan *et al.* 1998)	China (Li *et al.* 1989)
Sample Size	12,430	2,314	5,185	1,258
Follow-up	1949–2000	1979–1993	1979–1993	1969-1983
Exposure Assessment	Exposure modeling – 7 categories	Index (none, low, high)- before/after 1980	Index (none, med, high)- IH (inadequate) + job	High vs. low based on recall
Baseline rates	National, local plant area counties 1960–1994	Armenian rates 1980-1989	Moscow rates 1979–1993 or 1992–1993 (liver)	From "local area" 1973–1975 expected lung cancers: 0.4
Confounding	Used local rate comparisons; Low prevalence of other liver cancer risk factors	Alcohol use (high cirrhosis rates) and smoking prevalent	Alcohol use (high cirrhosis rates) and smoking; Co-exposure to VC	Hepatitis B and aflatoxin; Co-exposures to VC

RAMBOLL ENVIRON

MARSH ET AL. (2007) STUDY FINDINGS SHOULD HAVE GREATEST WEIGHT

US EPA Criteria	Marsh et al. (2007 a,b) Study				Other Studies			
	Kentucky[1]	North Ireland	Louisiana[1]	France-Mortality[1]	Armenia[2]	France-Incidence[3]	Russia[4]	China[5]
Clear objectives	H‡	H	H	H	H	H-M	H	M
Comparison groups	H	H-M	H-M	M	M	M	M-L	L
Exposure	H	H	H	H	M	M	L	L
Follow-up	H	H-M	H	H-M	M-L	M-L	M-L	M-L
Case ascertainment	H	H-M	H-M	H-M	M	M	M	H-M
Control of bias	H-M	H-M	H-M	M	M-L	M	M	M-L
Sample size	H	H	M	L	M-L	L	H-M	M-L
Data collection and evaluation	H	H	H	H	M	M	M-L	M-L
Adequate response	H	H	H	H	M	M	M	H-M
Documentation of results	H	H	H	H	M-L	M	M	L
Overall rank (1=best)	**1**	**2**	**3**	**4**	**5**	**5**	**5**	**6**

Source: Bukowski 2009 ‡ Subjective estimate of study quality for each specific criterion H=high, M=medium, L=low; 1 – Marsh et al. 2007; 2 – Bulbulyan et al. 1999; 3 – Colonna and Laydevant 2001; 4 – Bulbulyan et al. 1998; 5 – Li et al. 1989

RAMBOLL ENVIRON

MARSH STUDY SHOWS NO INCREASED LUNG OR LIVER CANCER RISKS

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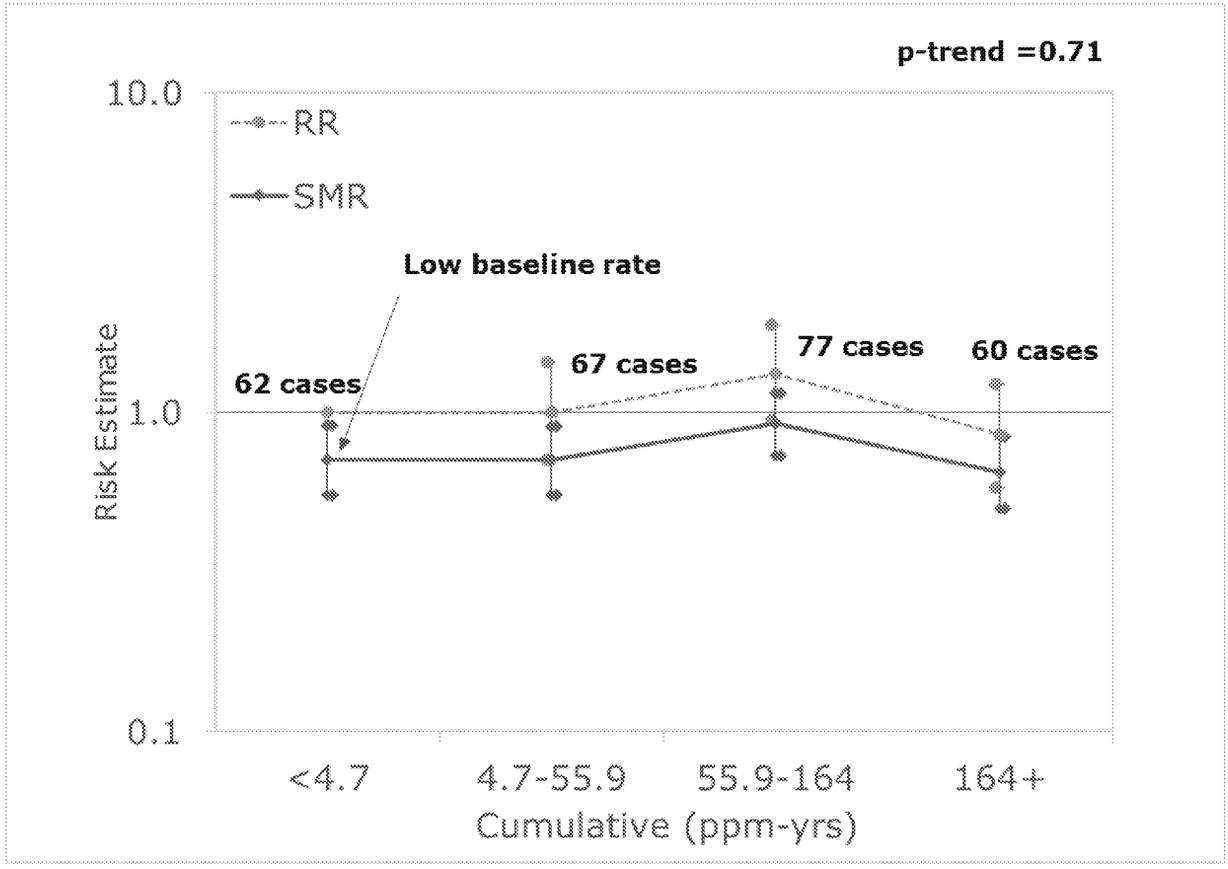

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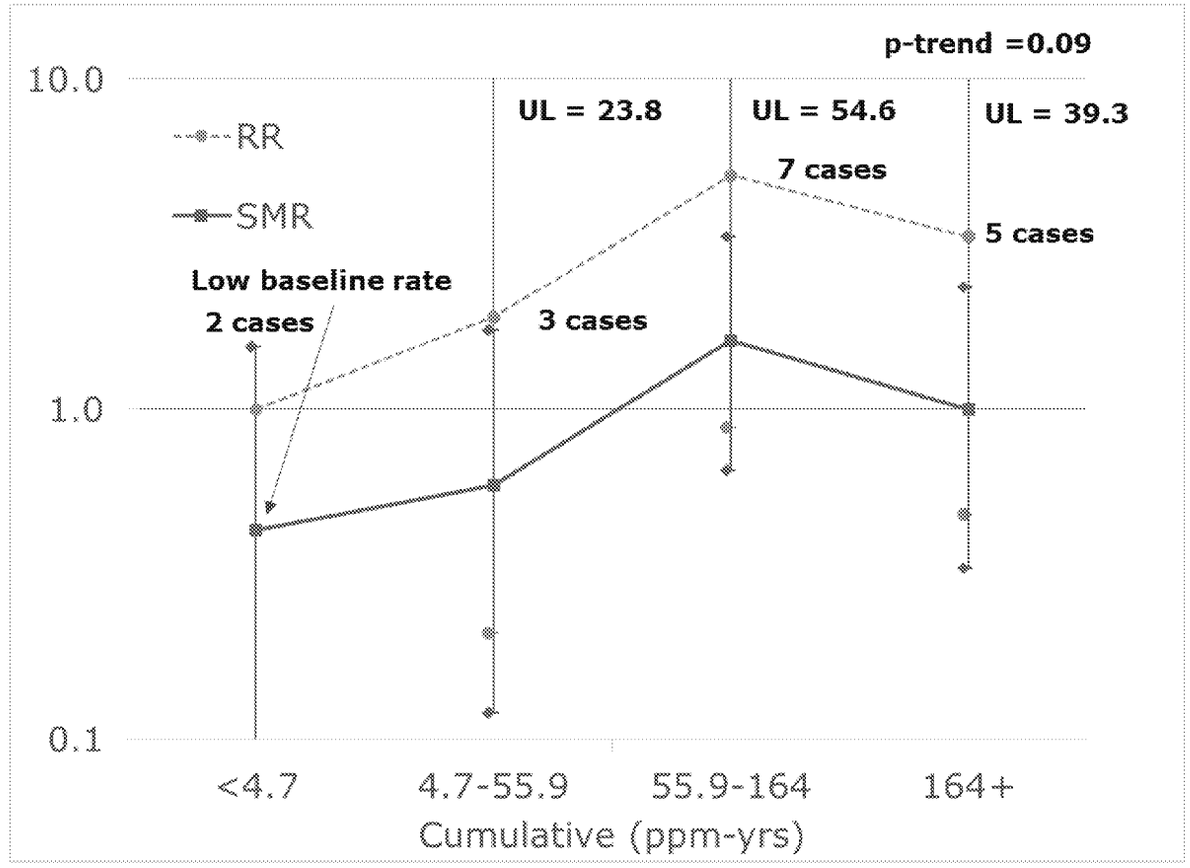

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RAMBOLL ENVIRON

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RAMBOLL ENVIRON

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RAMBOLL ENVIRON

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RAMBOLL ENVIRON

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RAMBOLL ENVIRON

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EVIDENCE OF GENOTOXICITY

In vitro mutagenicity results are inconsistent

Study	Method	Exposure	Response
Bartsch *et al.*, 1979	Desiccator	4 hours	+
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In vivo results are mostly negative, and mutagenicity profile is different from 1,3-butadiene

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Chloroprene	-	-	-
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CA – chromosome aberrations; SCE - sister chromatid exchange; MN - micronucleus test; Source: Tice 1988

Weight of evidence is not consistent with a mutagenic MOA. An alternative MOA should be considered in accordance with EPA and NRC guidelines.

RAMBOLL ENVIRON

CHLOROPRENE IUR

RAMBOLL ENVIRON

IUR INCONSISTENCIES

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Vinyl Chloride (2000)	4.4×10^{-6}	Liver tumors in rats	Yes	Known Carcinogen	~100

Adjusted IUR of chloroprene is more in line with other known carcinogens; e.g., VC IUR is based on animal data, but with PBPK model adjustments.

UNCERTAINTIES IN THE 2010 IUR

Step	IUR per ug/m³	Basis
Most sensitive endpoint/species (portal-of-entry DAF=1.7)	1.06×10^{-4}	Lung tumors in female mice as a portal-of-entry effect
Most sensitive endpoint/species (systemic lesion DAF=1)	1.81×10^{-4}	Lung tumors in female mice as a systemic effect
Multiple tumor adjustment	2.7×10^{-4}	Multiple tumors
Rounding	3×10^{-4}	Rounding
Application of ADAF	**5×10^{-4}**	Adjustment

RAMBOLL ENVIRON

PHARMACOKINETIC CORRECTION OF THE ANIMAL DATA

	IUR per ug/m^3	Basis	Resulting decrease in IUR
US EPA (2010)	**5 x 10^{-4}**	Fully adjusted composite value in female mice with ADAF correction	Referent
Allen et al. (2014)	1.86 x 10^{-6}	PBPK dosimetric adjustment of lung tumors in female mice in target organ; includes animal and human data	~250 fold decrease
Ramboll Environ (2017)	3.2 x 10^{-6}	PBPK dosimetric adjustment of lung tumors in female mice in the target organ; based on animal data only	156 fold decrease

RAMBOLL ENVIRON

PHARMACOKINETIC CORRECTION OF THE CHLOROPRENE IUR

- PBPK model was published by Himmelstein et al. (2004).
- Data were provided to EPA at the time of the review to check the validity of the model; however, EPA did not incorporate these data into the final IUR estimate.
- Data provided to EPA have been published (Yang et al., 2012; Thomas et al., 2013).
- Allen et al. (2014) reported that an IUR that incorporates pharmacokinetic differences 250 times lower than the 2010 IRIS IUR.
- Using the internal dose estimates from PBPK modeling from Yang et al. (2012) Ramboll Environ derived an IUR of **3.2×10^{-6}** per $\mu g/m^3$ which is **156 times lower** than the 2010 IRIS IUR.

"REALITY CHECK"

Source	Unit Risk (per ppm)	Mean Exposure* (ppm)	Excess Cancers (Risk Estimate)	Excess Cancers (Observed–Expected) Local referent
US EPA (2010) lung tumor	0.65	8.42	5.5	-84 (lung) -1.9 (liver)
multi tumor	1.08	8.42	9.1	
w/ADAF	1.80	8.42	15.2	
Allen et al. (2014) lung tumor	0.0067	8.42	0.06	
Ramboll Environ lung tumor	0.012	8.42	0.1	

*Mean exposure reported by Marsh et al. 2007a

IUR corrected for pharmacokinetic differences results in a cancer risk estimate consistent with epidemiological results (i.e., no observable excess risk).

RAMBOLL ENVIRON

CANCER CLASSIFICATION

RAMBOLL ENVIRON

CANCER CLASSIFICATION OF CHLOROPRENE

EPA classified chloroprene as "likely to be a human carcinogen" based on:

- National Toxicology Program (NTP, 1998) chronic inhalation bioassay;
- Associations between chloroprene exposure and liver cancer in four of nine epidemiological studies;
- Limited evidence of lung cancer;
- Proposed mutagenic mode of action; and
- Analogies with 1,3-butadiene and vinyl chloride

Critical review of the evidence indicated that four of these five cannot be substantiated.

The classification should be revisited and a clearer narrative provided.

https://cfpub.epa.gov/ncea/iris2/chemicalLanding.cfm?substance_nmbr=1021

RAMBOLL ENVIRON

SUMMARY AND CONCLUSIONS

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BASES FOR A REQUEST FOR CORRECTION OF THE 2010 IUR

- The highest quality epidemiological studies do not demonstrate a causal relationship between occupational exposures to chloroprene and cancer.
- Many lines of evidence point to pharmacokinetic differences across species.
- PBPK modeling is the best approach for correcting the IUR because of large pharmacokinetic differences between the mouse and humans.
- Using PBPK model output and standard EPA methods, Ramboll Environ calculated an IUR that is 156 times lower than the 2010 IRIS IUR.

Integration of the full body of evidence indicates that the pharmacokinetic differences between the mouse and humans require that the IUR be corrected using PBPK model results.

THANK YOU

Ken Mundt

kmundt@ramboll.com

Robinan Gentry

rgentry@ramboll.com

Sonja Sax

ssax@ramboll.com

RAMBOLL ENVIRON

Message

From: Kirby, Kevin [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=CBB65672F6F34545BE460A66FF6FA969-KIRBY, KEVIN]
Sent: 10/26/2017 7:58:04 PM
To: Krenik, Edward [edward.krenik@bracewell.com]
CC: Vandenberg, John [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=dcae2b98a04540fb8d099f9d4dead690-Vandenberg, John]; Thayer, Kris [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=3ce4ae3f107749c6815f243260df98c3-Thayer, Kri]; Davis, Allen [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=a8ecee8c29c54092b969e9547ea72596-Davis, Allen]; Yamada, Richard (Yujiro) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=4c34a1e0345e4d26b361b5031430639d-Yamada, Yuj]; Simons, Andrew [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=652da36feb75460da864ef6504ae0f42-ASIMONS]; Holloman, Vincia [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=e7e9f8511bc84976ae1eae93e17062fa-Holloma, Vincia]; Moser, Rebecca [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=43e2794f849243dfae064ab3f3bacf93-Moser, Rebecca]
Subject: RE:
Attachments: 17002 Technical Meeting Agenda 20171030.doc

Hello Ed,
I Hope that you're enjoying these beautiful entry days into fall. We are looking forward to meeting you here at EPA HQ in Federal Triangle next week, Oct. 30 at 3:00. We will be meeting specifically in the EPA West building located at 1301 Constitution Ave.

Attached is the Agenda that I will be circulating to individuals participating in our RFC meeting next week. If you have any additional materials, such as the presentation you referenced, please send them to me by COB Friday so that I can circulate these as well. There is no need to bring any projection equipment, but you do need to send me the materials *prior to the meeting* so that I can scan them and load them.

For logistics, please plan on entering EPA West through our main entrance at 1301 Constitution Ave. NW We will be meeting in Conference Room 6122, Yellowstone. You and your colleagues will be required to go through security and be escorted to the room once on premise. You may reach me at my desk 202 566-1656 or via cell at 703 489-2862.

See you Monday,
Kevin Kirby
US EPA

From: Krenik, Edward [mailto:edward.krenik@bracewell.com]
Sent: Tuesday, October 24, 2017 5:15 PM
To: Kirby, Kevin <KIRBY.KEVIN@EPA.GOV>
Cc: Vandenberg, John <Vandenberg.John@epa.gov>
Subject:

Hi Kevin,

I hope you are well. Attached is the agenda and attendees list for the upcoming meeting. I will be sending you our power point presentation at the end of this week so that you can get it to some of the EPA attendees who may be on by phone or video. Couple logistic questions, which door should we come to for the meeting? Where ORD is in the RR Building or another entrance? Also, since we would like to show a power point will projector equipment be available or should we bring our own?

Thanks much. See you Monday.

Ed

EDWARD KRENIK
Partner
edward.krenik@policyres.com
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Request for Correction (RFC) #17002:
IRIS -Toxicological Review of Chloroprene

Technical Meeting Agenda

When: **Monday, October 30, 2017, 3:00 – 4:00pm**
Where: EPA HQ, EPA West, 1301 Constitution Ave.
- Conference Room #6122
Call-In #: Ex. 6

1. Introductions

2. Information Quality Guidelines (IQG) Request for Correction (RFC) Process – Kirby

3. Technical presentation by IQG requesters – Dr. Ken Mundt, Ramboll Environ

4. Discussion: Questions / answers on RFC presentation materials - All

5. Discussion – Process and next steps - Kirby
    a. Information Owners develop draft response
    b. Circulate draft response with Scoping Team members
    c. Information Owners' AA concurrence on draft to send to OMB
    d. OMB clears response for release

Participants representing submitted RFC:

- Jorge Lavastida, Plant Manager,
- Patrick Walsh, Director of Safety, Health and Environment
- Dr. Kenneth Mundt, Ramboll Environ;
- Dr. Robinan Gentry, Ramboll Environ (by telephone);
- Ed Krenik, Bracewell;
- Jonathan Leibowitz, Karv Communications, and
- Robert Holden, Jones Walker LLP

Participants representing EPA:

- Dr. Richard Yamada, Deputy Assistant Administrator. ORD
- Dr. John Vandenberg, Division Director, ORD, NCEA, RTP
- Dr. Kris Thayer, Division Director, ORD, NCEA, IRIS
- Allen Davis, ORD, NCEA, IRIS Chemical Manager
- Andrew Simons, OGC
- Rebecca Moser, Office Director, OEI, OEIP
- Vincia Holloman, Division Director, OEI, OEIP, EQMD
- Kevin Kirby, IQG Case Manager, OEI, OEIP, EQMD

Message

From: Segal, Scott [scott.segal@bracewell.com]
Sent: 8/16/2017 6:16:17 PM
To: Yamada, Richard (Yujiro) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=4c34a1e0345e4d26b361b5031430639d-Yamada, Yuj]
CC: Krenik, Edward [edward.krenik@bracewell.com]; Lee, John [john.lee@bracewell.com]
Subject: FW: RFC technical meeting

Richard – do you have a moment to discuss this? We are trying to get that staff meeting that we have discussed on the books as soon as possible. Thanks, ss/

SCOTT SEGAL
Partner
scott.segal@policyres.com
T: [Ex. 6] | F: +1.800.404.3970

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From: Krenik, Edward
Sent: Wednesday, August 16, 2017 11:01 AM
To: Kirby, Kevin <KIRBY.KEVIN@EPA.GOV>
Cc: Holloman, Vincia <Holloman.Vincia@epa.gov>; Vandenberg, John <Vandenberg.John@epa.gov>; yamada.richard@epa.gov; Segal, Scott <scott.segal@bracewell.com>; Lee, John <john.lee@bracewell.com>
Subject: Re: RFC technical meeting

Hi Kevin,

This will respond to your email of July 24 below, advising us that the EPA does not believe an in-person meeting concerning this matter would be helpful. We would request you to reconsider and provide us with an opportunity to meet and discuss this matter as soon as possible.

As you know, on June 26, Denka Performance Elastomer ("DPE") submitted its Request for Correction ("RfC") concerning the EPA 2010 Toxicity Review of Chloroprene ("the 2010 Review"). The RfC presents an urgent petition to EPA for the correction of scientific conclusions on a very complex matter. DPE seeks the agency's urgent attention to this matter.

As we described in the RfC, based in part on the erroneous findings in the 2010 Review, EPA, the Louisiana Department of Environmental Quality ("LDEQ"), and the public are devoting extraordinary resources to scrutinizing DPE's chloroprene emissions from its Neoprene plant located in La Place, Louisiana. In addition, subsequent to the filing of the RfC on June 26, on June 28, 2017, a class action petition was filed against DPE concerning the same matter in a case styled, "Robert Taylor, Jr., et al. v. Denka Performance Elastomer LLC and DuPont de Nemours and Company," no. 70907, 40th Judicial District Court for the State of Louisiana. EPA's attention to this matter is urgent.

While DPE wishes to be respectful of the EPA Information Quality process, the toxicological and epidemiological information presented in the RfC is very complex. DPE believes that one or more in-person meetings could short-cut what might otherwise be a time consuming written exchange of questions and answers. Moreover, DPE has the only Neoprene production facility in the United States, and has devoted very substantial efforts into the preparation of the RfC and the review of underlying scientific efforts, as set out in the supporting report by Ramboll Environ. DPE believes that its resources could be extremely helpful to the EPA in understanding the scientific issues supporting the RfC.

Two sentences from your email below stand out and highlight the need for face-to-face meetings. You state, "Your submitted Request for Correction, although extensive and detailed, is well understood by EPA subject matter experts with whom you have already spoken. This information is not new. "

With respect to your statement that this information is well understood by EPA subject matter experts, we believe to the contrary. We would note that EPA's subject matter experts have praised the 2010 Review, notwithstanding its preparation prior to and deviations from the IRIS reform initiatives recommended by the National Research Council (NRC) of the National Academies of Sciences in 2011 and 2014, and which Congress and EPA have embraced. The 2010 IRIS Review needs to be corrected in accordance with these reforms.

With respect to your statement that "the information is not new," again we believe to the contrary. The RfC cites important post-2010 scientific information about chloroprene toxicity. The 2010 Review expressly states that its results would be improved with the use of physiologically based pharmacokinetic (PBPK) models to apply laboratory results from the most sensitive laboratory species to estimate potential applicability of the results to humans. The RfC provides the data and information needed to make PBPK adjustments to the 2010 laboratory animal findings. The new information cited and relied on in the RfC includes the following important new published chloroprene studies:

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In addition, the principal exhibit to the Request for Correction is the Ramboll Environ report entitled, "Basis for Requesting Correction of the US EPA Toxicological Review of Chloroprene," dated June 2017. Among other new information presented therein, the Ramboll Environ report provides a recalculated IUR of 3.2×10^{-6} $\mu g/m^3$, a value 156 times higher than the 2010 Review estimated, and the Ramboll Environ report performs a "reality

check" to show that the epidemiological data are inconsistent with the 2010 IUR but could be consistent with the Ramboll Environ recalculated IUR.

Moreover, the Ramboll Environ report identifies fundamental errors in the 2010 Review, including for example, the statistical flaws in the 2010 Review's analysis of subgroups of the epidemiological cohorts studied by Marsh, et al., and in the 2010 Review's unsupported determination that chloroprene might have a mutagenic mode of action.

DPE believes that in-person meetings concerning this matter are extremely important and may help EPA to understand these issues better. Please let us know if the agency will reconsider and meet with us.

Thank you. We look forward to meeting.

Ed

Sent from my Verizon, Samsung Galaxy smartphone

EDWARD KRENIK
Partner
Ext. 5877
Policy Resolution Group

-------- Original message --------
From: "Kirby, Kevin" <KIRBY.KEVIN@EPA.GOV>
Date: 7/24/17 4:11 PM (GMT-06:00)
To: "Krenik, Edward" <edward.krenik@bracewell.com>
Cc: "Holloman, Vincia" <Holloman.Vincia@epa.gov>, "Vandenberg, John" <Vandenberg.John@epa.gov>
Subject: Re: RFC technical meeting

Hi Ed,

Thanks for your kind offer to present your report with a technical team, supporting your submitted Request for Correction (RFC #17002). This won't be necessary nor expected as part of the Agency's Information Quality Guidelines.

Your submitted Request for Correction, although extensive and detailed, is well understood by EPA subject matter experts with whom you have already spoken. This information is not new. As you know, these EPA individuals are quite familiar with this and other information supporting the toxicological review of chloroprene as framed in the Integrated Risk Information System (IRIS).

As part of our IGG process, we are currently bringing these and other internal subject matter experts together to consider how best to assess the information presented in the RFC, review the IRIS information and respond to your data quality concerns. Should addition clarification material for this submitted RFR be needed, we'll certainly follow-up with the you via the requester's specific point of contact.

Should you have any additional materials to share with EPA relevant to this Request, please don't hesitate to send them to me at Quality@EPA.gov with reference to RFC #17002.

Thank you for your attention in helping us ensure quality information at EPA!

Kevin

Kevin Kirby, IQG Program Manager
Enterprise Quality Management Division
Office of Enterprise Information Programs
Office of Environmental Information
US Environmental Protection Agency

From: Krenik, Edward <edward.krenik@bracewell.com>
Sent: Monday, July 24, 2017 2:16 PM
To: Kirby, Kevin
Subject: RE: RFC technical meeting

Hi Kevin,

Checking back with you on some possible dates to have our technical people present our report and RFC. Let me know some possible dates and I will coordinate with our team.

Thanks,

Ed

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From: Vandenberg, John [mailto:Vandenberg.John@epa.gov]
Sent: Friday, July 14, 2017 12:39 PM
To: Krenik, Edward
Cc: Kirby, Kevin
Subject: RE: RFC technical meeting

Hi Ed,
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The lead there is Kevin Kirby, copied here.
John

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From: Krenik, Edward [edward.krenik@bracewell.com]
Sent: 8/16/2017 3:00:38 PM
To: Kirby, Kevin [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=cbb65672f6f34545be460a66ff6fa969-Kirby, Kevin]
CC: Holloman, Vincia [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=e7e9f8511bc84976ae1eae93e17062fa-Holloma, Vincia]; Vandenberg, John [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=dcae2b98a04540fb8d099f9d4dead690-Vandenberg, John]; Yamada, Richard (Yujiro) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=4c34a1e0345e4d26b361b5031430639d-Yamada, Yuj]; Segal, Scott [scott.segal@bracewell.com]; Lee, John [john.lee@bracewell.com]
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DPE believes that in-person meetings concerning this matter are extremely important and may help EPA to understand these issues better. Please let us know if the agency will reconsider and meet with us.

Thank you. We look forward to meeting.

Ed

Sent from my Verizon, Samsung Galaxy smartphone

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-------- Original message --------
From: "Kirby, Kevin" <KIRBY.KEVIN@EPA.GOV>
Date: 7/24/17 4:11 PM (GMT-06:00)
To: "Krenik, Edward" <edward.krenik@bracewell.com>
Cc: "Holloman, Vincia" <Holloman.Vincia@epa.gov>, "Vandenberg, John" <Vandenberg.John@epa.gov>
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Should you have any additional materials to share with EPA relevant to this Request, please don't hesitate to send them to me at Quality@EPA.gov with reference to RFC #17002.

Thank you for your attention in helping us ensure quality information at EPA!

Kevin

Kevin Kirby, IQG Program Manager
Enterprise Quality Management Division
Office of Enterprise Information Programs
Office of Environmental Information
US Environmental Protection Agency

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Subject: RE: RFC technical meeting

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Sent: Friday, July 14, 2017 12:39 PM
To: Krenik, Edward
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Subject: RE: RFC technical meeting

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The lead there is Kevin Kirby, copied here.
John

Message

From: Krenik, Edward [edward.krenik@bracewell.com]
Sent: 7/14/2017 8:34:59 PM
To: Yamada, Richard (Yujiro) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=4c34a1e0345e4d26b361b5031430639d-Yamada, Yuj]
Subject: Denka RFC PPT
Attachments: Request for Correction Meeting Presentation Meeting.pdf

Hi Richard,

I hope you are well. I wanted to pass along the power point we used in our meeting with you. Please let me know if you have any further questions. I will be in the office all week and if you need my cell it is Ex. 6

Thanks again for taking the time to meet with us.

Ed

EDWARD KRENIK
Partner
edward.krenik@policyres.com
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Request to Correct IRIS' 2010 Toxicological Review of Chloroprene

June 28, 2017

DPE Presentation Agenda

- Introductions – Nao Kawamura, Vice President of Administration
- Overview of Denka Performance Elastomer – President and CEO Koki Tabuchi
- Summary of basis for requesting correction – Plant Safety, Health, and Environmental Manager Patrick Walsh, CIH

Overview of Denka Performance Elastomer

Denka Performance Elastomer LLC

- Formed to purchase Neoprene business from DuPont
- American entity with two parent companies from Japan
  - Denka Company Limited - 70% Ownership
    - Leading Chemical Co in Japan
    - 100 year history
    - Elastomers, Performance Plastics, Inorganic Materials, Electronics, Life Science
    - 6 Domestic Plants, 9 Overseas including Pontchartrain
  - Mitsui & Co. – 30% Ownership

- Always strive for excellence in safety and environmental stewardship
- Will work to maintain place as integral member of the community and a good neighbor

SITE DEMOGRAPHICS & STATISTICS

	NEOPRENE
TOTAL EMPLOYEES	*249*
RIVER PARISH RESIDENTS	*77%*
AVERAGE SERVICE YEARS	*19*
ANNUAL PAYROLL	*$33MM*
RES. CONTRACTORS	*125*
APPROXIMATE PAYROLL	*$8.1MM*
TAXES (STATE & LOCAL)	*$1.9MM*
VALUE OF PURCHASES	*$76.5MM*

Third largest private employer in St. John Parish

DPE to URE

- 11/1/15: DPE takes ownership of the only Neoprene plant in North America after purchase from DuPont
- 12/17/15: EPA released National Air Toxics Assessment – study states that emissions from plant cause highest off-site cancer risk for any source in the country
- The NATA risk calculations are based on facility emissions and on an erroneous and ultrahigh Unit Risk Estimate from IRIS' 2010 Review
- The 2010 IRIS Toxicological Review of Chloroprene established an overly stringent inhalation Unit Risk Estimate (URE) or Inhalation Unit Risk (IUR) of 5×10^{-4} /µg/m^3 for a 70-year, lifetime exposure.
- URE has been applied to calculate a 100-in-a-million cancer risk with annual average chloroprene concentrations of 0.2 µg/m^3

Summary of DPE's Request for Correction

Request for Correction – Summary of Bases

- Brings study in line with recommendations from NAS/NRC
- Toxicological evidence
- Epidemiological evidence
- IUR derivation corrections
- PBPK modeling results

NAS/NRC Recommendations

- NRC has issued guidance on IRIS process in 2011 and 2014
  - Better transparency and rigor—some portions of 2010 Review cannot be reconstructed
  - Better evaluation of weight-of-evidence—certain weaker studies in 2010 Review given higher priority
- Congress directed, and EPA agreed, to adopt the NRC recommendations
- 2010 Review published before these guidelines issued—updating the Review would bring the study in line with those recommendations

Toxicological Evidence – 1

- Too much weight was given to the most sensitive species with inconsistent results across species
  - Study identified unique sensitivity in female mice – this became a cornerstone of the IRIS Review
  - Did not attempt to account for important pharmacokinetic differences between mice and humans

Toxicological Evidence – 2

- Mode-of-action (MOA) in 2010 Review needs to be updated
  - 2010 Review hypothesizes a mutagenic MOA due to structural similarities with vinyl chloride and 1,3-butadiene
  - Published data does not support this—even NTP study states that chloroprene was not mutagenic in any of their tests

Epidemiological Evidence – 1

- Too much weight applied to poor quality epidemiological studies, and not enough to the most high quality study
  - Most robust study (Marsh, et al. 2007) treated the same as less rigorous Russian, Armenian, and Chinese studies
  - Marsh study concluded that there is no link between occupational exposure to chloroprene and cancer mortality of any type
  - 2010 Review disregarded Marsh study conclusion and focused on statistically insignificant increase in liver cancers observed in three subgroups because comparison group exhibited fewer cancers than expected

Epidemiological Evidence – 2

Rank	County	Annual Incidence Rate(†) over rate period - cases per 100,000	Average Annual Count over rate period	Rate Period	Recent Trend	Recent 5-Year Trend (‡) in Incidence Rates
53	St. John the Baptist Parish(7,9)	460.8	209	2008-2012	stable	-2.2

IARC(*), 1999: "There is inadequate evidence in humans for the carcinogenicity of chloroprene."

*International Agency for Research on Cancer

http://statecancerprofiles.cancer.gov/incidencerates/index.php?stateFIPS=22&cancer=001&race=00&sex=0&age=001&type=incd&sortVariableName=rate&sortOrder=default#results

https://monographs.iarc.fr/ENG/Monographs/vol71/mono71-9.pdf

Overly Conservative Derivation of IUR

- 2010 Review interpreted the animal studies incorrectly
  - Treated each tumor as unique event, causing animals with multiple tumors to be counted twice in the risk analysis
  - Treated lung tumors as systemic rather than portal-of-entry effects
- 2010 Review assumed that IUR for female mice applies to human exposure
- Applied age-dependent adjustment factor without sufficient evidence to support the incorrect mutagenic MOA
- Rounding intermediate results multiple times in the same calculation skews final result

EPA's Chloroprene URE Should Be Consistent with Similar Compounds

Chemical	IARC Group	EPA Carcinogenicity Assessment	URE
Benzene	1	"A"	2.2E-06
Vinyl chloride	1	"A"	8.8E-06
Tetrachloroethylene (TCE)	2A	"Likely"	2.6E-07
Acetaldehyde	2B	"Probable"	2.2E-06
Hexachlorobutadiene	3	"Possible"	2.2E-05

IARC Classifications:

1	Known Carcinogen	2B	Possible Carcinogen
2A	Probable Carcinogen	3	Not Carcinogenic

2010 Review Did Not Use PBPK Model

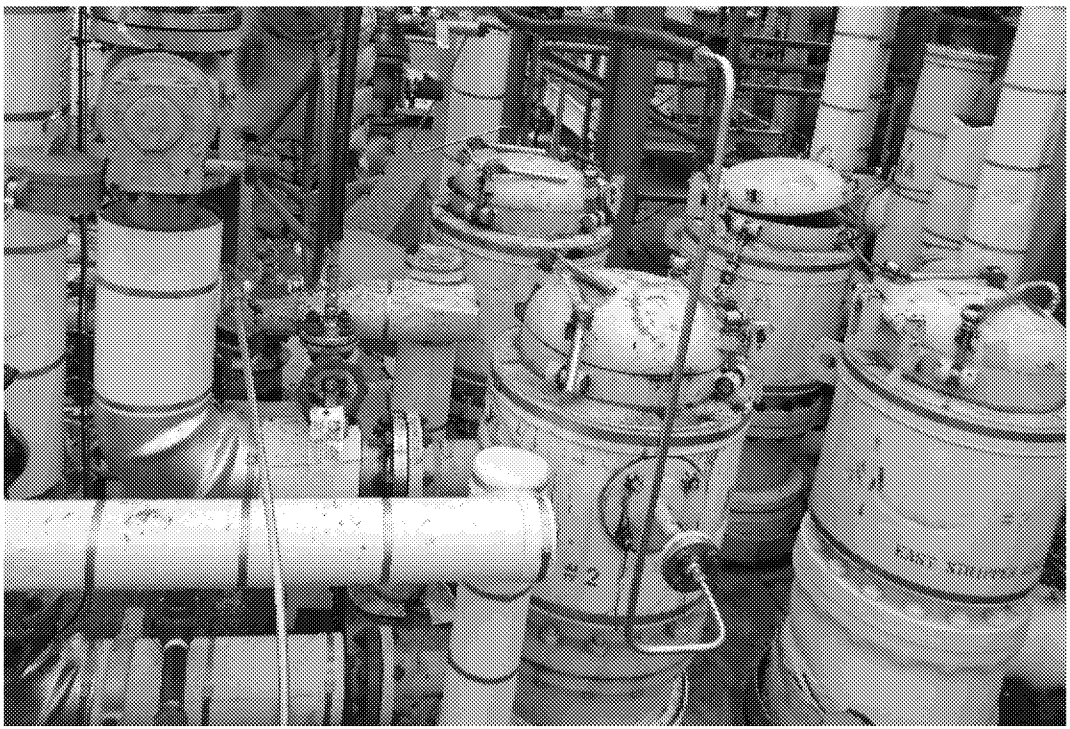
- Presented with the evidence, EPA should have used a physiologically-based pharmacokinetic (PBPK) model to extrapolate mouse toxicology data to humans
- Although a validated PBPK model (Himmelstein, 2004) was available at the time of the 2010 Review, EPA declined to use it
- Since 2010, 3 separate studies have validated the Himmelstein model
- 2010 Review even states: "Ideally, a PBPK model…would decrease some of the quantitative uncertainty in interspecies extrapolation…" (p. 141)
- Failure to use PBPK resulted in overly conservative IUR

Chloroprene is not "likely...carcinogenic"

- 2010 Review states that IRIS determined chloroprene's carcinogenicity based on the following criteria:
  1. NTP study finding early appearance of tumors
  2. Elevated liver cancer risk from occupational exposure
  3. Suggestive evidence of increased lung cancer risk from occupational exposure
  4. Proposed mutagenic mode of action
  5. Structural similarities to known carcinogens 1,3-butadiene and vinyl chloride
- RE's report shows that only 2 of these remain true
- Chloroprene carcinogenicity should be downgraded to "suggestive to be carcinogenic in humans"

Ramboll Environ's Updated IUR

- Ramboll Environ (RE) used NTP data with a PBPK model to derive a more scientifically grounded IUR
  - Applied standard EPA methodology
  - Used conservative assumptions where appropriate
- Results are consistent with other structurally similar chemicals



Ramboll Environ's Updated IUR: 3.2 x 10^{-6} /µg/m^3
(156-fold difference)

Appropriate Risk-based Ambient Target: 31.2 µg/m^3

10 month off-site average of 5.76 µg/m^3

AOC requires an 85% reduction

Conclusions

- IRIS' 2010 Toxicological Review of Chloroprene contains numerous deviations from accepted scientific practice
- The RFC shows that current emissions of chloroprene are well within acceptable cancer risk calculations. Installation of the RTO and other AOC-required emission reduction projects must achieve 85% emissions reduction

The 2010 Review needs to be updated

Thank you

Message

From: Gentry, Nathan [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=A8F7A2857A234D06B785CC36C73FDDDD-GENTRY, NATHAN]
Sent: 6/23/2017 6:25:55 PM
To: 'Krenik, Edward' [edward.krenik@bracewell.com]; Yamada, Richard (Yujiro) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=4c34a1e0345e4d26b361b5031430639d-Yamada, Yuj]
Subject: RE: Meeting Request: EPA Technical Correction of IRIS Quantitative Exposure Risk Value for Chloroprene -- June 27 or 28

There may be additional, but these are the ones I'm aware of:

Office of Research and Development
Richard Yamada
Bruce Rodan
John Vandenberg

Office of Chemical Safety and Pollution Prevention
Nancy Beck

Nathan Gentry
Scheduler for Bob Kavlock, Richard Yamada, Chris Robbins and Bruce Rodan
Assistant Deputy Ethics Official
EPA Office of Research and Development
Phone: Ex. 6
Fax: 202-565-2430

From: Krenik, Edward [mailto:edward.krenik@bracewell.com]
Sent: Friday, June 23, 2017 2:16 PM
To: Gentry, Nathan <Gentry.Nathan@epa.gov>; Yamada, Richard (Yujiro) <yamada.richard@epa.gov>
Subject: RE: Meeting Request: EPA Technical Correction of IRIS Quantitative Exposure Risk Value for Chloroprene -- June 27 or 28

Thanks much. If you get a chance can you send me the list of attendees from EPA.

Have a great weekend.

Ed

EDWARD KRENIK
Partner
edward.krenik@policyres.com
T: +Ex. 6 | F: +1.800.404.3970

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From: Gentry, Nathan [mailto:Gentry.Nathan@epa.gov]
Sent: Friday, June 23, 2017 2:13 PM
To: Krenik, Edward; Yamada, Richard (Yujiro)
Subject: RE: Meeting Request: EPA Technical Correction of IRIS Quantitative Exposure Risk Value for Chloroprene -- June 27 or 28

Attached are logistics for getting into our building and reaching our offices. You should call 202-564-6620 when you reach the EPA security desk, and I or someone else will come down to escort you.

Nathan Gentry
Scheduler for Bob Kavlock, Richard Yamada, Chris Robbins and Bruce Rodan
Assistant Deputy Ethics Official
EPA Office of Research and Development
Phone: 202-564-9084
Fax: 202-565-2430

From: Krenik, Edward [mailto:edward.krenik@bracewell.com]
Sent: Friday, June 23, 2017 2:04 PM
To: Yamada, Richard (Yujiro) <yamada.richard@epa.gov>
Cc: Gentry, Nathan <Gentry.Nathan@epa.gov>
Subject: RE: Meeting Request: EPA Technical Correction of IRIS Quantitative Exposure Risk Value for Chloroprene -- June 27 or 28

Nathan,

Below is the list of people who with be attending. Also we will come to the main entrance of the Ronald Reagan Building off the courtyard, correct? We will be there around 4:30 to get through security. Should I call you when I arrive or can you be waiting for us? Thanks so much for helping coordinate this meeting.

Ed

DPE attendees:
Koki Tabuchi
Patrick Walsh
Nao Kawamura
Jonathan Leibowitz
Yoshikuni Yamamoto

Bracewell:
Scott Segal
Ed Krenik
John Lee

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Partner
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From: Yamada, Richard (Yujiro) [mailto:yamada.richard@epa.gov]
Sent: Friday, June 23, 2017 12:14 PM
To: Krenik, Edward
Cc: Gentry, Nathan
Subject: RE: Meeting Request: EPA Technical Correction of IRIS Quantitative Exposure Risk Value for Chloroprene -- June 27 or 28

Hi Ed,

Could you please send Nathan a list of all the individuals who will be coming for the meeting at 5 PM on Weds. They will need to get through security, etc. Thanks much, and thanks Nathan for taking care of this,

Richard

From: Krenik, Edward [mailto:edward.krenik@bracewell.com]
Sent: Tuesday, June 20, 2017 9:32 AM
To: Beck, Nancy <Beck.Nancy@epa.gov>; Yamada, Richard (Yujiro) <yamada.richard@epa.gov>
Cc: Brown, Byron <brown.byron@epa.gov>; Segal, Scott <scott.segal@bracewell.com>; Lee, John <john.lee@bracewell.com>
Subject: Re: Meeting Request: EPA Technical Correction of IRIS Quantitative Exposure Risk Value for Chloroprene -- June 27 or 28

No problem. Let's book it for 5:00 on the 28th. Which building are you in?

Sent from my Verizon, Samsung Galaxy smartphone

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-------- Original message --------
From: "Beck, Nancy" <Beck.Nancy@epa.gov>
Date: 6/20/17 9:09 AM (GMT-05:00)
To: "Yamada, Richard (Yujiro)" <yamada.richard@epa.gov>, "Krenik, Edward" <edward.krenik@bracewell.com>
Cc: "Brown, Byron" <brown.byron@epa.gov>, "Segal, Scott" <scott.segal@bracewell.com>, "Lee, John" <john.lee@bracewell.com>
Subject: RE: Meeting Request: EPA Technical Correction of IRIS Quantitative Exposure Risk Value for Chloroprene -- June 27 or 28

5pm would work well for me.
Thanks.

Nancy B. Beck, Ph.D., DABT
Deputy Assistant Administrator, OCSPP
P: 202-564-1273
M: [redacted] Ex. 6
beck.nancy@epa.gov

From: Yamada, Richard (Yujiro)
Sent: Tuesday, June 20, 2017 8:52 AM
To: Krenik, Edward <edward.krenik@bracewell.com>
Cc: Brown, Byron <brown.byron@epa.gov>; Segal, Scott <scott.segal@bracewell.com>; Beck, Nancy <Beck.Nancy@epa.gov>; Lee, John <john.lee@bracewell.com>
Subject: RE: Meeting Request: EPA Technical Correction of IRIS Quantitative Exposure Risk Value for Chloroprene -- June 27 or 28

Hi Ed,

Let's go for the 28th – I'm looking at my schedule – hate to do this, but could we try the end of the day, say around 5 PM or so? Just let me know – I have an all day meeting which I believe is off-site but I'm checking into it. (hence the end of the day suugestion!)

Thanks much,

Richard

From: Krenik, Edward [mailto:edward.krenik@bracewell.com]
Sent: Monday, June 19, 2017 7:59 PM
To: Yamada, Richard (Yujiro) <yamada.richard@epa.gov>
Cc: Brown, Byron <brown.byron@epa.gov>; Segal, Scott <scott.segal@bracewell.com>; Beck, Nancy <Beck.Nancy@epa.gov>; Lee, John <john.lee@bracewell.com>

Subject: Re: Meeting Request: EPA Technical Correction of IRIS Quantitative Exposure Risk Value for Chloroprene -- June 27 or 28

Thanks Richard. Would 2:00 on June 27th work? Otherwise we are free on the 28th too. Just name the time on either day and we will make it work.

Thanks much,

Ed

Sent from my Verizon, Samsung Galaxy smartphone

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Subject: Re: Meeting Request: EPA Technical Correction of IRIS Quantitative Exposure Risk Value for Chloroprene -- June 27 or 28

Hi Ed,

Thanks for the note and good to hear from you.

Let me check with my schedule and get back to you - what date times work best for you???

Thanks and best,

Richard

Sent from my iPhone

On Jun 19, 2017, at 4:37 PM, Krenik, Edward <edward.krenik@bracewell.com> wrote:

Thanks Byron.

Richard great you are there. Scott and I worked with you when you were on the hill. Let me know which day/time works best for you. Nancy, we would love to have you sit in as well since you worked on this previously.

Look forward to seeing you again.

Ed

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From: Brown, Byron [mailto:brown.byron@epa.gov]
Sent: Monday, June 19, 2017 4:27 PM
To: Krenik, Edward; Segal, Scott; Beck, Nancy; Yamada, Richard (Yujiro)
Cc: Lee, John
Subject: RE: Meeting Request: EPA Technical Correction of IRIS Quantitative Exposure Risk Value for Chloroprene -- June 27 or 28

Hi Ed – Richard Yamada has joined EPA as the political deputy in ORD overseeing the IRIS program. I have copied him on this message.

From: Krenik, Edward [mailto:edward.krenik@bracewell.com]
Sent: Monday, June 19, 2017 2:53 PM
To: Segal, Scott <scott.segal@bracewell.com>; Brown, Byron <brown.byron@epa.gov>; Beck, Nancy <Beck.Nancy@epa.gov>
Cc: Lee, John <john.lee@bracewell.com>
Subject: RE: Meeting Request: EPA Technical Correction of IRIS Quantitative Exposure Risk Value for Chloroprene -- June 27 or 28

Hope your Monday is going great.

Checking back to see if we can get on your calendar for next week. Let me know what works best for you so I can finalize their travel arrangements. The CEO is flying from Japan specifically for this meeting and is asking when he can book his return flight.

Thanks to both of you.

Ed

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From: Krenik, Edward
Sent: Tuesday, June 13, 2017 3:54 PM
To: Segal, Scott; brown.byron@epa.gov; beck.nancy@epa.gov
Cc: Lee, John
Subject: Meeting Request: EPA Technical Correction of IRIS Quantitative Exposure Risk Value for Chloroprene

Hey Byron and Nancy,

I hope you are both well. I am following up on Segal's email attached below to see if we can schedule a meeting with both of you either June 27 or 28th. The CEO of Denka is flying in from Japan for this meeting and the folks from Louisiana will be here during that time as well. We are wide open either of those days to meet. In effort to get the discussion rolling, let me suggest June 27th at 1:00 or 2:00.

The Denka team wanted to meet with both of you as we are about to file the Request for Correction (RFC) for this issue. We want to ensure that as EPA looks in to this issue senior management is fully briefed and afforded the opportunity to ask any questions of or experts.

Please let me know if these times work and if not please suggest a new time and I am certain we can accommodate.

Thanks for all you do and we look forward to seeing you both.

Ed

From: Segal, Scott
Sent: Tuesday, May 23, 2017 4:59 PM
To: brown.byron@epa.gov
Cc: beck.nancy@epa.gov; Krenik, Edward
Subject: Meeting Request: EPA Technical Correction of IRIS Quantitative Exposure Risk Value for Chloroprene

Byron – attached for your review is memo prepared initially for transition regarding a mistaken IRS value that is being used inappropriately as a default value for regulation/enforcement. If uncorrected, it could endanger the last neoprene production facility in the US (LaPlace, LA)! The owner is Denka Performance Elastomer, LLC, or DPE, who purchased the plant from DuPont.

Ryan initially directed us to Nancy – who certainly knows IRIS well – and she thoughtfully reminded us that this is an ORD issue. But what is called for here is Request for Correction (RFC) to the IRIS listing, now out of date and inaccurate. Our current plan is to file the RFC the week of June 11.

Request: can you (and Nancy perhaps) sit down with the CEO of DPE, the plant manager from LaPlace, Ed Krenik, and me? The date would be June 9. Would that work? Thanks, ss/

SCOTT SEGAL
Partner
Ext. 5845
Policy Resolution Group

Message

From: Gentry, Nathan [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=A8F7A2857A234D06B785CC36C73FDDDD-GENTRY, NATHAN]
Sent: 6/23/2017 6:13:02 PM
To: 'Krenik, Edward' [edward.krenik@bracewell.com]; Yamada, Richard (Yujiro) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=4c34a1e0345e4d26b361b5031430639d-Yamada, Yuj]
Subject: RE: Meeting Request: EPA Technical Correction of IRIS Quantitative Exposure Risk Value for Chloroprene -- June 27 or 28
Attachments: Logistics for visitors.docx

Attached are logistics for getting into our building and reaching our offices. You should call 202-564-6620 when you reach the EPA security desk, and I or someone else will come down to escort you.

Nathan Gentry
Scheduler for Bob Kavlock, Richard Yamada, Chris Robbins and Bruce Rodan
Assistant Deputy Ethics Official
EPA Office of Research and Development
Phone: 202-564-9084
Fax: 202-565-2430

From: Krenik, Edward [mailto:edward.krenik@bracewell.com]
Sent: Friday, June 23, 2017 2:04 PM
To: Yamada, Richard (Yujiro) <yamada.richard@epa.gov>
Cc: Gentry, Nathan <Gentry.Nathan@epa.gov>
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Ed

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Patrick Walsh
Nao Kawamura
Jonathan Leibowitz
Yoshikuni Yamamoto

Bracewell:
Scott Segal
Ed Krenik
John Lee

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Subject: Re: Meeting Request: EPA Technical Correction of IRIS Quantitative Exposure Risk Value for Chloroprene -- June 27 or 28

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-------- Original message --------
From: "Beck, Nancy" <Beck.Nancy@epa.gov>
Date: 6/20/17 9:09 AM (GMT-05:00)
To: "Yamada, Richard (Yujiro)" <yamada.richard@epa.gov>, "Krenik, Edward" <edward.krenik@bracewell.com>
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Subject: RE: Meeting Request: EPA Technical Correction of IRIS Quantitative Exposure Risk Value for Chloroprene -- June 27 or 28

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Nancy B. Beck, Ph.D., DABT
Deputy Assistant Administrator, OCSPP
P: 202-564-1273
M: 2[Ex. 6]
beck.nancy@epa.gov

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Sent from my iPhone

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Look forward to seeing you again.

Ed

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To: Krenik, Edward; Segal, Scott; Beck, Nancy; Yamada, Richard (Yujiro)
Cc: Lee, John
Subject: RE: Meeting Request: EPA Technical Correction of IRIS Quantitative Exposure Risk Value for Chloroprene -- June 27 or 28

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Thanks to both of you.

Ed

EDWARD KRENIK
Partner
edward.krenik@policyres.com
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BRACEWELL LLP
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From: Krenik, Edward
Sent: Tuesday, June 13, 2017 3:54 PM
To: Segal, Scott; brown.byron@epa.gov; beck.nancy@epa.gov
Cc: Lee, John
Subject: Meeting Request: EPA Technical Correction of IRIS Quantitative Exposure Risk Value for Chloroprene

Hey Byron and Nancy,

I hope you are both well. I am following up on Segal's email attached below to see if we can schedule a meeting with both of you either June 27 or 28th. The CEO of Denka is flying in from Japan for this meeting and the folks from Louisiana will be here during that time as well. We are wide open either of those days to meet. In effort to get the discussion rolling, let me suggest June 27th at 1:00 or 2:00.

The Denka team wanted to meet with both of you as we are about to file the Request for Correction (RFC) for this issue. We want to ensure that as EPA looks in to this issue senior management is fully briefed and afforded the opportunity to ask any questions of or experts.

Please let me know if these times work and if not please suggest a new time and I am certain we can accommodate.

Thanks for all you do and we look forward to seeing you both.

Ed

From: Segal, Scott
Sent: Tuesday, May 23, 2017 4:59 PM
To: brown.byron@epa.gov
Cc: beck.nancy@epa.gov; Krenik, Edward
Subject: Meeting Request: EPA Technical Correction of IRIS Quantitative Exposure Risk Value for Chloroprene

Byron – attached for your review is memo prepared initially for transition regarding a mistaken IRS value that is being used inappropriately as a default value for regulation/enforcement. If uncorrected, it could endanger the last neoprene production facility in the US (LaPlace, LA)! The owner is Denka Performance Elastomer, LLC, or DPE, who purchased the plant from DuPont.

Ryan initially directed us to Nancy – who certainly knows IRIS well – and she thoughtfully reminded us that this is an ORD issue. But what is called for here is Request for Correction (RFC) to the IRIS listing, now out of date and inaccurate. Our current plan is to file the RFC the week of June 11.

Request: can you (and Nancy perhaps) sit down with the CEO of DPE, the plant manager from LaPlace, Ed Krenik, and me? The date would be June 9. Would that work? Thanks, ss/

SCOTT SEGAL
Partner
Ext. 5845
Policy Resolution Group

ORD Visitor Logistics

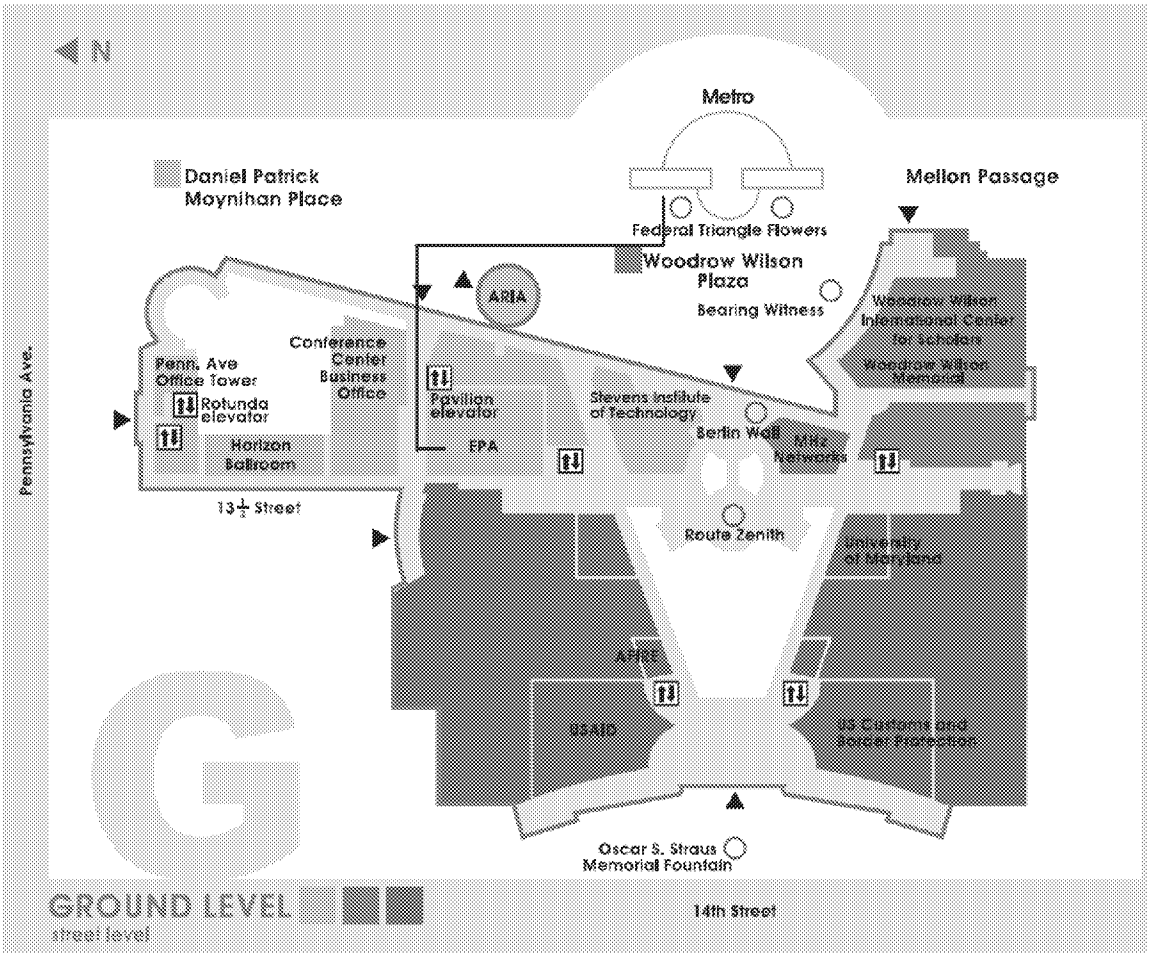
U.S. Environmental Protection Agency
Ronald Reagan Building, Fourth Floor
1300 Pennsylvania Avenue, NW
Washington, DC 20004

Point of Contact: Nathan Gentry, by email at gentry.nathan@epa.gov or by phone at 202.564.6620.

Meeting Site

Ronald Reagan Building, Fourth Floor
1300 Pennsylvania Avenue, NW
Washington, DC 20004

The meeting will be held on the fourth floor of EPA's Office of Research and Development within the Ronald Reagan Building. Everyone must pass through security at the entrance of the building, where you must present a government issued photo identification (i.e. driver's license, passport, federal employee id) and go through a metal detector. You will be asked to show photo identification and go through a metal detector again at the entrance to EPA. Once you have been cleared by security at EPA, you will be escorted to the fourth floor. Please have security call your point of contact above once you are through security.



Transportation

By Metro

EPA is located by the **Federal Triangle** Metro stop on the **Orange/Blue Line** on the Washington Metro system.

Once you get off the Metro at Federal Triangle, go up the escalators to street level. Across the courtyard in front of you is the Ronald Reagan Building. Enter the Ronald Reagan Building through the entrance to the right of Aria. You will need to go through security to enter the Ronald Reagan Building, so have a government issued identification ready. Once you are in the building, go straight and the EPA entrance will be on your left.

You can also get to EPA from the Metro Center Metro stop on the **Red/Orange/Blue/Silver** lines on the Washington Metro system. Once you get off the Metro at Metro Center take the 13th and G Street exit and walk on G Street for two blocks, then turn left and walk south along 13th street towards Pennsylvania Ave. Once you've crossed Pennsylvania Ave, the building will be off to the right of the Daniel Patrick Moynihan Place, with the EPA entrance immediately before the curve in the building (formerly Aria).

Information on the Washington Metro System can be found here: http://wmata.com/

By Car

From The North (via I-95)

1. Follow I-95 South toward Washington to I-495 and exit East.
2. Follow I-495 East to Route 50 and exit West.
3. Follow Route 50, which becomes New York Avenue, to L Street and bear right onto L Street.
4. Follow L Street to 7th Street, NW and turn left.
5. Follow 7th Street to Constitution Avenue and turn right.
6. Follow Constitution Avenue to 14th Street and turn right.
7. The Ronald Reagan Building and International Trade Center is the second building on the right, approximately mid-block.
8. Turn right into the parking garage.

From The North (via I-270)

1. Follow I-270 South toward Washington.
2. At the I-270 split bear right and follow signs for I-495, Northern Virginia.
3. Follow I-495 to the George Washington Memorial Parkway (GW Parkway).
4. Follow the GW parkway to the Theodore Roosevelt Bridge.
5. Cross the Theodore Roosevelt Bridge, staying to the right, and exit onto Constitution Avenue.
6. Follow Constitution Avenue to 15th Street and turn left.
7. Follow 15th Street to Pennsylvania Avenue and turn right.
8. Follow Pennsylvania Avenue to 13½ Street and turn right to enter the parking garage.

From The South (via I-95/I-395)

1. Follow I-95 North toward Washington.
2. I-95 becomes I-395 when you cross I-495. Continue North on I-395.

3. Follow I-395 across the bridge using either of the two left lanes.
4. After crossing the bridge, exit US-1 North/14th Street.
5. Follow US-1/14th Street to Constitution Avenue.
6. Cross Constitution Avenue and the Ronald Reagan Building and International Trade Center is the second building on the right, approximately mid-block.
7. Turn right into the parking garage.

From The East (via Route 50 and New York Avenue)

1. Follow Route 50, which becomes New York Avenue, to L Street and bear right onto L Street.
2. Follow L Street to 7th Street NW and turn left.
3. Follow 7th Street to Constitution Avenue and turn right.
4. Follow Constitution Avenue to 14th Street and turn right.
5. The Ronald Reagan Building and International Trade Center is the second building on the right, approximately mid-block.
6. Turn right into the parking garage.

From The West (via I-66)

1. Follow I-66 across the Theodore Roosevelt Bridge, staying to the right, and exit onto Constitution Avenue.
2. Follow Constitution Avenue to 15th Street and turn left.
3. Follow 15th Street to Pennsylvania Avenue and turn right.
4. Follow Pennsylvania Avenue to 13½ Street and turn right to enter the parking garage.

Public Parking

The Ronald Reagan Building and International Trade Center features on-site, public parking.

Daily Parking

Daily parking is available in the Ronald Reagan Building underground parking garage. Access is available via 13½ Street (off Pennsylvania Avenue) and via two entrances on 14th Street. The garage is open from 5:00 am until 2:00 am daily.

Guests and attendees should allow extra time for parking, as all guests will need to have a photo ID and vehicles will be screened upon entry. There is no overnight parking for guests. The maximum overhead clearance in the garage is 7 feet.

The current parking rates are as follows:

1 hour or less	$10.00
2 hours or less	$15.00
3 hours or less	$19.00
Over 3 hours to 10 hours	$22.00
Over 10 hours to close	$23.00
Evenings weekday rate	$13.00 (enter after 5:00 pm to closing)

Weekend/Holiday Rate	$13.00 (enter after 5:00 am to closing)

Airport

The Washington, DC area is served by Dulles (IAD), Baltimore (BWI) and Reagan National (DCA) airports. Reagan National is the most convenient to the meeting venue.

Message

From: Krenik, Edward [edward.krenik@bracewell.com]
Sent: 9/14/2017 8:28:33 PM
To: Kirby, Kevin [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=cbb65672f6f34545be460a66ff6fa969-Kirby, Kevin]
CC: Holloman, Vincia [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=e7e9f8511bc84976ae1eae93e17062fa-Holloma, Vincia]; Vandenberg, John [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=dcae2b98a04540fb8d099f9d4dead690-Vandenberg, John]; Yamada, Richard (Yujiro) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=4c34a1e0345e4d26b361b5031430639d-Yamada, Yuj]; Segal, Scott [scott.segal@bracewell.com]; Lee, John [john.lee@bracewell.com]
Subject: RE: RFC technical meeting

Oops I meant IRIS.

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From: Krenik, Edward
Sent: Thursday, September 14, 2017 3:54 PM
To: 'Kirby, Kevin'
Cc: Holloman, Vincia; Vandenberg, John; Yamada, Richard (Yujiro); Segal, Scott; Lee, John
Subject: RE: RFC technical meeting

Thank you Kevin.

We look forward to seeing you. I have spoken with the group who will be attending and they would like to come on October 30th. I have a few questions about the meeting since we will be bringing Dr. Mundt our technical advisor. Who will be attending from EPA? Will there be ORD/ISIS folks in attendance as well? Finally, where should we come to attend the meeting, which entrance and room number?

I will be sending an agenda over as we get closer to October 30th. If you need anything more from me, please reach out.

Again thank you for this opportunity.

Ed

From: Kirby, Kevin [mailto:KIRBY.KEVIN@EPA.GOV]
Sent: Wednesday, September 13, 2017 11:09 AM
To: Krenik, Edward
Cc: Holloman, Vincia; Vandenberg, John; Yamada, Richard (Yujiro); Segal, Scott; Lee, John
Subject: RE: RFC technical meeting

Hello Ed,

I have checked with my EPA counterparts and would like to extend an invitation for you to come in or dial-into a technical meeting to present materials concerning your request for correction RFC #17002, dealing with the IRIS toxicological assessment of chloroprene.

Please let me know which of these dates work for you and your team:

- Thursday, Oct. 19, 4:00 – 5:00pm
- Mon. Oct. 30, 3:00 – 4:00pm
- Tue. Oct. 31, 3:00 – 4:00pm
- Mon. Nov. 6, 4:00 - 5:00pm

Respectfully,
Kevin

Kevin J. Kirby,
Enterprise Data Architect

Enterprise Quality Management Division
Office of Enterprise Information Programs
Office of Environmental Information
US Environmental Protection Agency

Ex. 6 desk
cell

From: Krenik, Edward [mailto:edward.krenik@bracewell.com]
Sent: Wednesday, September 13, 2017 10:25 AM
To: Kirby, Kevin <KIRBY.KEVIN@EPA.GOV>
Cc: Holloman, Vincia <Holloman.Vincia@epa.gov>; Vandenberg, John <Vandenberg.John@epa.gov>; Yamada, Richard (Yujiro) <yamada.richard@epa.gov>; Segal, Scott <scott.segal@bracewell.com>; Lee, John <john.lee@bracewell.com>
Subject: RE: RFC technical meeting

Hi Kevin,

I hope you are well.

I am checking back with you on our request. We would like to sit down with the team to discuss the review as I think all would benefit from a face to face discussion. Let me know what works best for the group.

Happy to jump on a call if you want to discuss further.

Thanks much,

Ed

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From: Krenik, Edward
Sent: Wednesday, August 16, 2017 11:01 AM
To: Kirby, Kevin
Cc: Holloman, Vincia; Vandenberg, John; yamada.richard@epa.gov; Segal, Scott; Lee, John
Subject: Re: RFC technical meeting

Hi Kevin,

This will respond to your email of July 24 below, advising us that the EPA does not believe an in-person meeting concerning this matter would be helpful. We would request you to reconsider and provide us with an opportunity to meet and discuss this matter as soon as possible.

As you know, on June 26, Denka Performance Elastomer ("DPE") submitted its Request for Correction ("RfC") concerning the EPA 2010 Toxicity Review of Chloroprene ("the 2010 Review"). The RfC presents an urgent petition to EPA for the correction of scientific conclusions on a very complex matter. DPE seeks the agency's urgent attention to this matter.

As we described in the RfC, based in part on the erroneous findings in the 2010 Review, EPA, the Louisiana Department of Environmental Quality ("LDEQ"), and the public are devoting extraordinary resources to scrutinizing DPE's chloroprene emissions from its Neoprene plant located in La Place, Louisiana. In addition, subsequent to the filing of the RfC on June 26, on June 28, 2017, a class action petition was filed against DPE concerning the same matter in a case styled, "Robert Taylor, Jr., et al. v. Denka Performance Elastomer LLC and DuPont de Nemours and Company," no. 70907, 40th Judicial District Court for the State of Louisiana. EPA's attention to this matter is urgent.

While DPE wishes to be respectful of the EPA Information Quality process, the toxicological and epidemiological information presented in the RfC is very complex. DPE believes that one or more in-person meetings could short-cut what might otherwise be a time consuming written exchange of questions and answers. Moreover, DPE has the only Neoprene production facility in the United States, and has devoted very substantial efforts into the preparation of the RfC and the review of underlying scientific efforts, as set out in the supporting report by Ramboll Environ. DPE believes that its resources could be extremely helpful to the EPA in understanding the scientific issues supporting the RfC.

Two sentences from your email below stand out and highlight the need for face-to-face meetings. You state, "Your submitted Request for Correction, although extensive and detailed, is well understood by EPA subject matter experts with whom you have already spoken. This information is not new. "

With respect to your statement that this information is well understood by EPA subject matter experts, we believe to the contrary. We would note that EPA's subject matter experts have praised the 2010 Review, notwithstanding its preparation prior to and deviations from the IRIS reform initiatives recommended by the National Research Council (NRC) of the National Academies of Sciences in 2011 and 2014, and which Congress and EPA have embraced. The 2010 IRIS Review needs to be corrected in accordance with these reforms.

With respect to your statement that "the information is not new," again we believe to the contrary. The RfC cites important post-2010 scientific information about chloroprene toxicity. The 2010 Review expressly states that its results would be improved with the use of physiologically based pharmacokinetic (PBPK) models to apply laboratory results from the most sensitive laboratory species to estimate potential applicability of the results to humans. The RfC provides the data and information needed to make PBPK adjustments to the 2010 laboratory animal findings. The new information cited and relied on in the RfC includes the following important new published chloroprene studies:

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- Allen BC, Van Landingham C, Yang Y, Youk AO, Marsh GM, Esmen N, Gentry PR, Clewell III HJ, and Himmelstein MW. (2014). A constrained maximum likelihood approach to evaluate the impact of dose metric on cancer risk assessment: Application to b-chloroprene. *Regulatory Toxicology and Pharmacology* 70: 203–213.

In addition, the principal exhibit to the Request for Correction is the Ramboll Environ report entitled, "Basis for Requesting Correction of the US EPA Toxicological Review of Chloroprene," dated June 2017. Among other new information presented therein, the Ramboll Environ report provides a recalculated IUR of 3.2×10^{-6} $\mu g/m^3$, a value 156 times higher than the 2010 Review estimated, and the Ramboll Environ report performs a "reality check" to show that the epidemiological data are inconsistent with the 2010 IUR but could be consistent with the Ramboll Environ recalculated IUR.

Moreover, the Ramboll Environ report identifies fundamental errors in the 2010 Review, including for example, the statistical flaws in the 2010 Review's analysis of subgroups of the epidemiological cohorts studied by Marsh, et al., and in the 2010 Review's unsupported determination that chloroprene might have a mutagenic mode of action.

DPE believes that in-person meetings concerning this matter are extremely important and may help EPA to understand these issues better. Please let us know if the agency will reconsider and meet with us.

Thank you. We look forward to meeting.

Ed

Sent from my Verizon, Samsung Galaxy smartphone

-------- Original message --------
From: "Kirby, Kevin" <KIRBY.KEVIN@EPA.GOV>
Date: 7/24/17 4:11 PM (GMT-06:00)
To: "Krenik, Edward" <edward.krenik@bracewell.com>
Cc: "Holloman, Vincia" <Holloman.Vincia@epa.gov>, "Vandenberg, John" <Vandenberg.John@epa.gov>
Subject: Re: RFC technical meeting

Hi Ed,

Thanks for your kind offer to present your report with a technical team, supporting your submitted Request for Correction (RFC #17002). This won't be necessary nor expected as part of the Agency's Information Quality Guidelines.

Your submitted Request for Correction, although extensive and detailed, is well understood by EPA subject matter experts with whom you have already spoken. This information is not new. As you know, these EPA individuals are quite familiar with this and other information supporting the toxicological review of chloroprene as framed in the Integrated Risk Information System (IRIS).

As part of our IGG process, we are currently bringing these and other internal subject matter experts together to consider how best to assess the information presented in the RFC, review the IRIS information and respond to your data quality concerns. Should addition clarification material for this submitted RFR be needed, we'll certainly follow-up with the you via the requester's specific point of contact.

Should you have any additional materials to share with EPA relevant to this Request, please don't hesitate to send them to me at Quality@EPA.gov with reference to RFC #17002.

Thank you for your attention in helping us ensure quality information at EPA!

Kevin

Kevin Kirby, IQG Program Manager
Enterprise Quality Management Division
Office of Enterprise Information Programs
Office of Environmental Information
US Environmental Protection Agency

From: Krenik, Edward <edward.krenik@bracewell.com>
Sent: Monday, July 24, 2017 2:16 PM
To: Kirby, Kevin
Subject: RE: RFC technical meeting

Hi Kevin,

Checking back with you on some possible dates to have our technical people present our report and RFC. Let me know some possible dates and I will coordinate with our team.

Thanks,

Ed

EDWARD KRENIK
Partner
edward.krenik@policyres.com
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From: Vandenberg, John [mailto:Vandenberg.John@epa.gov]
Sent: Friday, July 14, 2017 12:39 PM
To: Krenik, Edward
Cc: Kirby, Kevin
Subject: RE: RFC technical meeting

Hi Ed,
I saw Bob Holder and the other Denka reps at a meeting yesterday in LaPlace, and I told Bob that the request for correction process has a lot of steps, and interactions with the requestor are handled by the Office of Environmental Information (OEI).
The lead there is Kevin Kirby, copied here.
John

Message

From: Krenik, Edward [edward.krenik@bracewell.com]
Sent: 9/14/2017 7:53:32 PM
To: Kirby, Kevin [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=cbb65672f6f34545be460a66ff6fa969-Kirby, Kevin]
CC: Holloman, Vincia [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=e7e9f8511bc84976ae1eae93e17062fa-Holloma, Vincia]; Vandenberg, John [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=dcae2b98a04540fb8d099f9d4dead690-Vandenberg, John]; Yamada, Richard (Yujiro) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=4c34a1e0345e4d26b361b5031430639d-Yamada, Yuj]; Segal, Scott [scott.segal@bracewell.com]; Lee, John [john.lee@bracewell.com]
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Kevin

Kevin J. Kirby,
Enterprise Data Architect

Enterprise Quality Management Division
Office of Enterprise Information Programs
Office of Environmental Information
US Environmental Protection Agency

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To: Kirby, Kevin <KIRBY.KEVIN@EPA.GOV>
Cc: Holloman, Vincia <Holloman.Vincia@epa.gov>; Vandenberg, John <Vandenberg.John@epa.gov>; Yamada, Richard (Yujiro) <yamada.richard@epa.gov>; Segal, Scott <scott.segal@bracewell.com>; Lee, John <john.lee@bracewell.com>
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Date: 7/24/17 4:11 PM (GMT-06:00)

To: "Krenik, Edward" <edward.krenik@bracewell.com>
Cc: "Holloman, Vincia" <Holloman.Vincia@epa.gov>, "Vandenberg, John" <Vandenberg.John@epa.gov>
Subject: Re: RFC technical meeting

Hi Ed,

Thanks for your kind offer to present your report with a technical team, supporting your submitted Request for Correction (RFC #17002). This won't be necessary nor expected as part of the Agency's Information Quality Guidelines.

Your submitted Request for Correction, although extensive and detailed, is well understood by EPA subject matter experts with whom you have already spoken. This information is not new. As you know, these EPA individuals are quite familiar with this and other information supporting the toxicological review of chloroprene as framed in the Integrated Risk Information System (IRIS).

As part of our IGG process, we are currently bringing these and other internal subject matter experts together to consider how best to assess the information presented in the RFC, review the IRIS information and respond to your data quality concerns. Should addition clarification material for this submitted RFR be needed, we'll certainly follow-up with the you via the requester's specific point of contact.

Should you have any additional materials to share with EPA relevant to this Request, please don't hesitate to send them to me at Quality@EPA.gov with reference to RFC #17002.

Thank you for your attention in helping us ensure quality information at EPA!

Kevin

Kevin Kirby, IQG Program Manager
Enterprise Quality Management Division
Office of Enterprise Information Programs
Office of Environmental Information
US Environmental Protection Agency

From: Krenik, Edward <edward.krenik@bracewell.com>
Sent: Monday, July 24, 2017 2:16 PM
To: Kirby, Kevin
Subject: RE: RFC technical meeting

Hi Kevin,

Checking back with you on some possible dates to have our technical people present our report and RFC. Let me know some possible dates and I will coordinate with our team.

Thanks,

Ed

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From: Vandenberg, John [mailto:Vandenberg.John@epa.gov]
Sent: Friday, July 14, 2017 12:39 PM
To: Krenik, Edward
Cc: Kirby, Kevin
Subject: RE: RFC technical meeting

Hi Ed,
I saw Bob Holder and the other Denka reps at a meeting yesterday in LaPlace, and I told Bob that the request for correction process has a lot of steps, and interactions with the requestor are handled by the Office of Environmental Information (OEI).
The lead there is Kevin Kirby, copied here.
John