1,4-Dioxane [1]

a. 2013 to 2016
b. PPG industries, Hamp and Associates, Waste Management, Toxicology Excellence for Risk Assessment (TERA), University of Cincinnati, College of Medicine, US National Toxicology Program
c. Two publications

- Dioxane occurs in foods (up to 15 ppb in dairy products).
- Dioxane causes cancer at high doses, but EPA's IRIS peer review panel thought that a nonlinear assessment might be appropriate.
- The State of Kentucky requested that the Alliance for Risk Assessment petition the government of Japan for relevant data. Four other states joined in this petition. Other collaborators included several consulting groups. Scientists from Health Canada observed.
- This TERA/RSC work was done after EPA's IRIS document and supports the IRIS peer review panel's suggestion that the cancer findings are due to a nonlinear Mode of Action (MOA).
- All of this information has been publicly available.
- Health Canada is using TERA's collaborative work in their evaluation of 1,4-dioxane.

1-Bromopropane [2]

a. 2004
b. Albemarle Corporation and Ameribrom, Inc
c. A report was generated and made publicly available.

- In 2004, occupation limits for 1-bromopropane differed by 16-fold.

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[1] Source:

- Nishimura et al., 2004. Study of 1,4-dioxane intake in the total diet using the market-basket method. Journal of Health Science 50:101-107.
- Dourson, M; Reichard, J; Nance, P; Burleigh-Flayer, H; Parker, A; Vincent, M; McConnell, EE; (2014). Mode of Action Analysis for Liver Tumors from Oral 1,4-Dioxane Exposures and Evidence-Based Dose Response Assessment. Reg. Toxicol. Pharmacol. [HYPERLINK "http://www.sciencedirect.com/science/journal/02732300/68/3"], April 2014, Pages 387–401
- Michael L. Dourson, Jeri Higginbotham, Jeff Crum, Heather Burleigh-Flayer, Patricia Nance, Norman D. Forsberg, Mark Lafranconi, John Reichard. 2017. Update: Mode of action (MOA) for liver tumors induced by oral exposure to 1,4-dioxane. Regulatory Toxicology and Pharmacology 88:45-55.
- Website is currently in transfer mode. For current version see: [HYPERLINK "http://med.uc.edu/eh/centers/rsc/risk-resources/ara"].

[2] [HYPERLINK "http://www.tera.org/Publications/TERA%20Analysis%20of%20OELs%20for%20 1-Bromopropane.pdf"].

- TERA critically evaluated the underlying information and recommended an OEL of 20 ppm based on effects in newborns.
- TERA's value was lower (i.e., safer) than EPA's.
- An NTP study was published after the TERA assessment showing cancer findings.
- New evaluations based on the cancer suggested lower limits.

PFOA-Dupont [3]

a. 2002
b. State of West Virginia
c. A report was generated and place on the website of the State of West Virginia.

- In 2002, 4 governments and one industry recommended TERA as the independent and neutral party to assist in a PFOA evaluation. A West Virginia judge agreed.
- Dr. Deanne Statts of West Virginia DEP chaired a 10-member scientific panel.
- Five panelists were government employees; 3 were from EPA.
- The panel made a unanimous determination of a safe water level of 150 ppb.
- All of this information has been publicly available.
- The science of PFOA has progressed since 2002.

Trichloroethylene (TCE) [4]

a. 2012 to 2016
b. American Chemistry Council, Toxicology Excellence for Risk Assessment (TERA) and University of Cincinnati, College of Medicine
c. The collaboration team had 6 conference calls, including scientists from Australia, 3 webinars, one of which included over 400 folks, and 1 independent peer consultation. The team gave 8 presentations, and published 1 paper.

- In 2012, the Alliance for Risk Assessment (*ARA*) was petitioned by the Alliance for Site Closures to review noncancer toxicity of TCE. The Steering Committee of the *ARA*, composed primarily of government officials, asked the collaboration to focus instead on building range in risk values.
- The team has had one training session with US states.
- All of this information has been publicly available.

Perchlorate [5]

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[3] Source: FINAL CATT REPORT WITH ATTACHMENTS, AUGUST 2002

[4] Source:

- Michael Dourson, Bernard Gadagbui, Rod Thompson, Edward Pfau, and John Lowe. 2016. Managing Risks of Noncancer Health Effects at Hazardous Waste Sites: A Case Study Using the Reference Concentration (RfC) of Trichloroethylene (TCE). Regulatory Toxicology and Pharmacology 80:125-133.
- http://med.uc.edu/eh/centers/rsc/risk-resources/ara

[5] Source: Strawson, J., Q. Zhao and M. Dourson. 2004. Reference dose for perchlorate based on thyroid hormone change in pregnant women as the critical effect. Reg. Tox. Pharm. 39: 44-65.

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a. 1995 to 2007
b. The Perchlorate Study Group (PPG)
c. TERA developed a report for peer review, monitored toxicology studies and offered comments in peer review meetings of EPA Reference Dose (RfD).

- Afterwards EPA and the DOD disagreed on the safe dose.
- TERA independently made its safe dose 500-fold more protective than PPG's original RfD and published it.
- The NAS also developed a safe dose, which was 25 times higher than EPA's, 12-fold lower than DoD's, but within 3 fold of TERA's value; EPA adopts the NAS value.

Chlorpyrifos [6]

a. 2004 to 2006
b. Dow AgroSciences
c. Two publications

- The science for chlorpyrifos has progressed since the time of these publications.
- One epidemiology study shows associations of neurological effects at exposures lower than the current RfD; other studies do not show this association.
- Based on how chlorpyrifos works this association is not expected.
- The raw data from this epidemiology study are not available for review.

Alachlor and Acetochlor [7]

a. 2009-2010
b. Dow AgroSciences and Monsanto
c. A public peer review meeting and one publication

- Michael Dourson talked with senior US EPA leaders to determine their interest. EPA stated that they had developed RfDs for the parent chemicals and did not consider the degradates to be more toxic.

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[6] Source:

- Zhao, Q., B. Gadagbui and M. Dourson. 2005. [HYPERLINK "http://www.tera.org/pubs/Chlorpyrifos%20RTP%20version.pdf"]. Reg. Toxicol. Pharmacol. 42:55-63.
- Zhao, Q., M. Dourson and B. Gadagbui. 2006. [HYPERLINK "http://www.tera.org/pubs/CPF%20Manuscript%20revision.pdf"] Reg. Toxicol. Pharmacol. 44:111-124.

[7] Source:

- [HYPERLINK "http://www.tera.org/ART/Degradates/index.html"];
- Gadagbui, B; Maier, *M; Dourson*, M; Parker, A; Willis, A; Christopher, JP; Hicks, L; Ramasany, S; Roberts, SM. 2010. Derived Reference Doses (RfDs) for the Environmental Degradates of the Herbicides Alachlor and Acetochlor: Results of an Independent Expert Panel Deliberation. Regulatory Toxicology and Pharmacology 57:220-234.

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- Dow AgroSciences and Monsanto petitioned the Alliance for Risk Assessment (*ARA*) for their review. The *ARA* Steering Committee endorsed a collaborative approach.
- TERA formed a team of risk assessment scientists from 3 states and the EPA to develop these RfDs. The resulting values were based on a unanimous consensus.

Diacetyl [8]

a. 2009-2010
b. Food Producers Association
c. One report that was made available to the public

- At the time of TERA's work no standards existed for worker protection.
- TERA's standard published in 2010 (i.e., range from 70 to 200 ppb) was based on the best science at the time, through careful consideration of toxicology, epidemiology, and background exposures.
- Subsequent analyses published by various organizations, including NIOSH, developed standards of 5 to 20 ppb based on different emphasis on toxicology and epidemiology data.
- TERA is continuing its ongoing relationship with NIOSH since 2010 through an Interagency Personnel Agreement Fellowship.

Acrylamide [9]

a. 2007-1009
b. Burger King Corporation, Frito-Lay, Inc., H.J. Heinz Company, KFC Corporation, McDonald's Corporation, The Proctor & Gamble Manufacturing Company, The Proctor & Gamble Distributing Company, and Wendy's International, Inc.
c. Litigation support under proposition 65 of California, and several publications

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[8] Maier, AM; Kohrman-Vincent, M; Parker, A; Haber, LT. (2010)[HYPERLINK "http://www.ncbi.nlm.nih.gov/pubmed/20600455"]. Reg. Toxicol. and Pharmacol. 58(2): 285-296.

[9] Source:

- Dourson, M., Hertzberg, R., Allen, B., Haber, L., Parker, A., Kroner, O., Maier, A. and Kohrman, M. 2008. Evidence-Based Dose Response Assessment for Thyroid Tumorigenesis from Acrylamide. Regulatory Toxicology and Pharmacology 52 (2008) 264–289.
- Haber, LT; Maier, A; Kroner, OL; Kohrman, MJ. (2009) [HYPERLINK "http://www.tera.org/Publications/Haber%20et%20al.%202009.pdf" \t "_blank"] Regul. Toxicol. Pharmacol. 53(2): 134-149.
- Maier, A., Kohrman-Vincent, M., Hertzberg, R., *Dourson, M.*, Haber, L.T and Allen, B. 2012. Critical review of dose-response options for F344 rat mammary tumors for acrylamide – Additional insights based on mode of action. Food Chem. Toxicol. 50:5, 1763-1775.

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- TERA determined that the MOA for the most sensitive endpoint, thyroid tumors, was bimodal, with linear at the low dose and an acceleration of thyroid tumors above a threshold for hormonal action.
- TERA's first publication was supported by industry.
- TERA's next two publications were in large part self-supported.
- All of these publications include more findings than EPA's older IRIS document.

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