AIR MANAGEMENT REGULATION XIV: CONTROL OF PERCHLOROETHYLENE FROM DRY CLEANING FACILITIES

COMMENT / RESPONSE DOCUMENT
For Dr. Finkel's Perc Presentation
at the 10/21/2009
Air Pollution Control Board Meeting

January 13, 2010

City of Philadelphia
Department of Public Health
Air Management Services

Background

On 6/18/09, Dr. Adam Finkel was hired by Philadelphia Air Management Services (AMS) as a consultant to evaluate the risks of Perchloroethylene (Perc) in accordance with proposed Air Management Regulation XIV – Control of Perchloroethylene From Dry Cleaning Facilities.

In the 10/21/09, Air Pollution Control Board meeting, Dr. Finkel presented his evaluation of Perc (see Appendix I, "Preliminary Evaluation of Perchloroethylene Risks and the Philadelphia Dry-Cleaning Proposal".) Based on his presentation, comments were received from Allan Wong and Jon Meijer (see Appendix II).

AMS is responding to comments via this document. The original comments were broken into a "table" structure to allow for a response from AMS and/or Dr. Finkel.

Response to Allan Wong comments (received via email on 10/29/09)

Allan Wong Comments	AMS Response
Due to the poor quality of the handout and visual image of the presentation it was difficult to follow the details of Dr. Finkel's presentation. For this reason and in the absence of the written report it is not possible to make a full evaluation of the study. Nevertheless, a few comments can be made.	**** AMS Response **** After receiving Dr. Wong's email, a more readable version of Dr. Finkel's presentation was placed on the AMS website. A download link was provided in the follow-up email.
Dr. Finkel speculated that the estimation of carcinogenic potency of Perc (slide #4) based on the study of MCL in male rats was too low. He speculated that "(14 rats out of 50 got leukemia at the lowest dose, but you could run the experiment again and you might see16 and 17 with leukemia just by chance)". Hence Dr. Finkel arbituarily increased the cancer incidence at the three exposure levels to create a curve represented by the solid line. By selectively keeping the cancer incidence at zero level unchanged, he managed to reduce the TD10 value and drew the wrong conclusion that EPA underestimated the cancer risk of Perc. The way that Dr. Finkel manipulated the data is not acceptable by any scientific standard.	**** Dr. Finkel Response **** Accounting for uncertainty due to randomness and small sample size, as I did here, is exactly the way EPA and every other reputable scientific body deals with uncertainty in cancer dose-response. Far from suggesting that EPA "underestimated" the cancer potency, I simply showed in slide #4 how they did use an upper confidence limit to estimate it. My statement that "14 rats with tumors doesn't rule out the possibility that the true risk at this dose might have been 16 or 17 out of 50" is EXACTLY how EPA develops its upper confidence limit, except that they express the bound as "the slope of the curve that might be compatible with the observed data" rather than "the slope of a curve that would be drawn if the experiment was run again"—but the concept is exactly the same. Now it's true that for every upper bound there is also a lower bound, and perhaps I could have said (and could add to my slide and report) that "there might also have been 10 or 11 rats with MCL out of 50 if you ran the study again, and in that case the risk estimate would be lower." But EPA doesn't mention this because it is a regulatory agency interested in avoiding errors of *underprotecting* the public, as am I. If Dr. Wong wants to argue that we should use estimators under uncertainty that give the benefit of the doubt to the chemical rather than to the public, that is his right, but that would be counter to the way risk assessments are done. In any event, neither EPA nor I "manipulate the data"—we simply report the uncertainty, in the same way as a pollster says "14 out of 50 people want the Phillies to win the Series, but there is a 5% margin of error in the poll." To say that this is "not acceptable by any scientific standard" is quite unusual, in my opinion.

In fact, none of the legible slides show any data that the 40 ppb exposure limit established by EPA is unsafe. In order to justify lowering this EPA standard, Dr. Finkel has to provide NEW and COMPELLING SCIENTIFIC EVIDENCE, not speculation that the 40 ppb standard is unsafe. Dr. Finkel's presentation provided none of these.	**** Dr. Finkel Response **** Dr. Wong seems to be confused about what the various federal recommendations and standards are. 40 ppb, as you know, is the ATSDR "Minimal Risk Level;" the existing EPA Reference Concentration is 2.4 ppb, which is much lower than 40. *I have never suggested "lowering the EPA standard,"* as should have been obvious from my emphasis that 40 ppb—a level 17 times *higher* than the EPA standard—is a reasonable stopping point. I did suggest that we should not think of 40 ppb as a "safe" level, for two reasons: (1) the non-cancer benchmarks (ASTDR of 40 and EPA of 2.4) are not "safe" levels, but should be thought of as levels that might pose a risk of as much as 5% to those in the population who happen to be more than ten times as susceptible as the average worker studied by Ferroni or the average resident studied by Altmann; and (2) because Perc is positive in so many different animal cancer bioassays, it is regarded as a (likely) human carcinogen with no threshold, so there is by definition some risk at 40 ppb. Now the cancer risk at 40 ppb *might* be very small, but I have shown that mainstream risk assessment methods do not lead to this conclusion. But again, I never said 40 ppb was "unsafe"—only that it would be equally overconfident to say it was "safe"—and again, 40 is the very number I end up saying is reasonable anyway. Finally, I dispute that anyone has to provide "new and compelling scientific evidence" to comment on where the action level should be. There is plenty of evidence, both toxicologic and epidemiologic, to work with: risk assessment is all about how we *interpret* that evidence. I stand by my interpretations.

Response to Jon Meijer comments (received via email on 10/25/09**

****The comments from Jon Meijer represent comments from the Dry Cleaning Industry**

Industry Comments	AMS Response
On October 21, 2009, Dr. Adam Finkel presented his review of the perc toxicology to the Air Pollution Control Board (APCB). Industry representatives were prohibited from making comments regarding the presentation and we were requested to provide any additional information in writing to the Board by November 30, 2009. While we are highlighting some key concerns with Dr. Finkel's "PowerPoint" presentation, we will make a full presentation once the full report is completed and there is adequate time to review Dr. Finkel's assessment.	**** AMS Response **** Industry was not prohibited from making comments. Initially, the APCB members asked that all questions and comments be submitted in written form. A brief period of questions and comments from the Dry Cleaning industry was allowed after Dr. Finkel's presentation. Industry has been expressly invited to make a presentation and offer comments in a presentation to the Ad-hoc Committee on January 20, 2010.
To the best of our knowledge, we have not been provided with complete data from plant/s that were tested by AMS. Nor have we seen anything even closely resembling quality assurance or quality control while conducting the fieldwork. It certainly appears that APCB is only looking to phase-out perc without considering options that would protect human health and the environment while saving drycleaners in Philadelphia that use perc.	**** AMS Response **** The monitoring data was presented to the APCB members as well as the Dry Cleaning industry at the various Air Pollution Control Board meetings in 2009. Data was available for all participants in paper format. The Air Management Services Laboratory routinely analyzes ambient air toxics by means of canister samples for 43 compounds including Perchloroethylene in accordance with the Environmental Protection Agency (EPA) Method TO-15. Likewise, Perchloroethylene samples from dry cleaning establishments were collected by means of evacuated canisters and analyzed along with routine ambient air canister samples following the Quality Assurance and Quality Control program approved by EPA. These results are comparable with the testing data done in New York City. The Dry Cleaning industry has repeatedly mentioned a "technology" approach as a possible option. Prior to a 1/21/09 Dry Cleaning Ad-hoc meeting, the APCB asked the Dry Cleaning industry to submit additional information regarding the "technology" approach. Information from Carol Memberg, Dale Kaplan, Jon Meijer, and Steve Risotto was received via email and reviewed by the APCB.

Over the past two years, we have offered any and all help to Air Management Services (AMS) to develop a regulation that protects human health and the environment while keeping drycleaners from going out of business. The changes we made to the original language would have made it one of the toughest drycleaning standards in the U.S., including those developed in New York and New Jersey, which did not phase-out perc use in drycleaning. For some inexplicable reason, our input has been utterly ignored. Thus far, the process we have had to rely on has been confusing and less than transparent.	**** AMS Response **** All comments and inputs from the Dry Cleaner Industry have been reviewed by AMS and the APCB. Input from Industry at the APCB and Ad-hoc meetings lead to multiple revisions of AMS' proposed regulation. Some of the industry's comments such as the definitions, gasket and timeline were incorporated into the draft regulation. At the 3/5/09 APCB meeting, input from industry along with the other comments received convinced the APCB to delay passage of any dry cleaning regulation at that time. Additionally, in an abundance of caution, AMS hired a consultant, Dr. Finkel, substantially in response to concerns raised by industry. The regulatory process is detailed in the Philadelphia Home Rule Charter and has been explained many times during the Board meetings. The current Philadelphia proposal does not completely phase-out Perc. AMS' regulation follows a strategy similar to that of New Jersey. New Jersey's 12/17/07 proposed Dry Cleaning Regulation bans Perc use in co-residential facilities by 7/27/09 (AMS by 12/31/2013). Full elimination of Perc from all dry cleaners would occur by 1/1/2021 (AMS proposes to allow stand-alone facilities to use Perc while co-commercial facilities would be allowed to use Perc for the 15 year life cycle of the machine).
(1) The analysis draws heavily (slides 4 through 9 and opinions) on EPA's external review draft of the "Toxicological Review of Tetrachloroethylene (Perchloroethylene)" in support of the IRIS database. Every page of this draft carries the warning "This document is a draft for review purposes only and does not constitute Agency policy. DRAFT – DO NOT CITE OR QUOTE". (2) This draft has been reviewed by a National Academies of Science (NAS) panel and release of the report is imminent. Among the issues believed to have been considered are whether mononuclear cell leukemia (MCL) is appropriate	**** Response by Dr. Finkel **** (1) The majority of EPA science documents are never "finalized," and continue to carry the "draft" designation forever. More importantly, I base my conclusions on OLD data contained in this report—the Japanese and other bioassays conducted many years ago. It is true that I accept as reasonable EPA's current methods for fitting these data to a dose-response model which yields a unit risk estimate, but there is not a great deal of uncertainty introduced by the various ways one could fit the data—the real question is whether the animal data are relevant to humans (see below). In addition, several other "final" conclusions of state risk assessment agencies (e.g., California's, Colorado's) estimate Perc's cancer potency to be within the 10-fold range EPA estimates, so even if the EPA 2008 document had never been written, my conclusions would not be substantially different.

for calculating human risk (EPA's worst case and the basis for Dr Finkel's predictions of risk) and whether general population studies such as Altmann et al (2005) and Schreiber et al (2002) provide a reliable basis for calculating an RfC rather than scientifically more robust occupational studies. The draft should not have been used as a basis for an assessment at this time. The findings in the report of the NAS review, when available, should be considered by Dr. Finkel and his assessment modified if necessary. (3) The tumors seen in animals are of questionable relevance to man. EPA stated very clearly that the projections of human cancer risk based on animal studies represented an "upper bound" and that the "true risk could be as low as zero". This statement certainly applies to the calculations displayed in the slides. At the very least, it should be stated that these are conservative (worst case) <u>estimates</u> of risk, not real values.	(2) Depending on when the NAS report is finally released (these are notoriously behind anticipated schedules), I will gladly summarize the Committee's findings in a revised report if requested to. For the moment, however, I need to synthesize EPA's scientific judgment (hundreds of scientists working in a public process for several decades), that of the NAS committee (a dozen or so scientists expressing their own expert judgment), and my own—no single one of these three sources of judgment should be regarded as the final word. (3) Surely the industry doesn't mean to claim that every single tumor type seen in animals is irrelevant to humans (and the comments here give no substantiation to any part of this claim). EPA's boilerplate statement that "the true risk could be as low as zero" is (in my opinion as well as that of the most recent NAS committee reviewing EPA risk assessment methods --(Science and Decisions: Advancing Risk Assessment, page 206) misleading in that it conflates two different concepts. Statistically, it is sometimes the case that the true value of the linear term in the dose-response polynomial could be as low as zero, but this is not at all the same thing as a risk of zero (if the dose-response function has no linear term, the risk at low doses is small but non-zero). The cancer risk from Perc could be zero if and only if the animal tumors are truly irrelevant to people. Furthermore, these are **not** necessarily "conservative" estimates of risk, whether EPA mistakenly says they are or not. There are elements of current risk assessment methods that tend to make them overstate expected risk, but there are also elements that err in the opposite direction (see, for example, Chapter 5 of **Science and Decisions,** which urges EPA to adjust its cancer risk estimates **upwards** by a factor of from 10 to 50 to account for individuals who are more susceptible to carcinogenesis than the average person).
Slide 4. MCL is a rat strain specific cancer with unknown relevance to man. It should not be used for quantitative risk assessment.	**** Response by Dr. Finkel **** This is an unsupported and vague assertion. The topic of site concordance is a controversial and complicated one, but in general there are too many examples of known human carcinogens where the sites differ between humans and

	rodents to accept without more information a claim that a particular tumor type should be ignored. In any event, as Slide 7 indicates, there are several other tumor types that would yield potency estimates within a factor of 10-20% of the EPA value, even if the MCL tumors were to be discarded.
Slide 5 and 6. The three models used by EPA have been superseded by more recent, more sophisticated models (shown to be more accurate). The model of Bois is distorted by use of inaccurate human data and risks based on this model should not be included.	**** Response by Dr. Finkel **** I would be interested, if time permits, to see the underlying articles that purport to show that none of the three PBPK models EPA considered are as "accurate" as some unspecified newer model. "More recent" and "more sophisticated" does not mean they are more accurate—and even "accuracy" is difficult to interpret, and should not be the only criterion (for example, a good PBPK model will fulfill most or all of the 11 criteria for reproducibility, theoretical underpinning, etc. laid out by OSHA in its 1997 methylene chloride rulemaking (see **62 Federal Register,** January 10, 1997, pp. 1533-1534). Again, the important question is *quantitatively* how an alternative method would differ from the current one(s)—does this allegedly "more accurate" model yield risk estimates that are significantly below the lower end of EPA's current range?
Slide 7. Exclude MCL, it is a type of leukemia that has no human equivalent. Do not combine male mouse hepatocellular tumors and hemangiosarcomas (completely different cell types). This leaves male rat kidney tumors as the worst case but that was a marginal response in a single study – no mention that no kidney tumors were found in several comparable studies. Plus, the flawed Bois model should be excluded.	**** Response by Dr. Finkel **** I have looked into this in detail, and have concluded (see the report text) that the EPA Figure I reproduced has a typographical error in it—EPA did *not* combine liver carcinomas and hemangiosarcomas. In addition, these arguments do not acknowledge that until fairly recently, EPA often calculated potency using "total tumor-bearing animals (TBA)" (to account for the lack of information about which site(s) would be affected in humans)—*any* of the specific sites alone will likely yield a lower risk estimate than the TBA approach.
Slide 8. Too many flaws in the Schreiber et al (2002) studies (even NY DoH has criticized the apartment studies). Similarly, Altmann et al (1995) has a very small number of subjects and their selection was probably (unintentionally) biased. Moreover, the results are not plausible when compared with much	**** Response by Dr. Finkel **** I'm not clear why there's the implication that I used the Schreiber studies—neither ATSDR nor EPA used them, and neither do I. Excluding Altmann would make a difference, though ATSDR uses Ferroni to get to 40 ppb (EPA using Altman gets to 2.4 ppb, so in a sense Altmann is a straw man). But the issue of whether the occupational studies are "more robust" is important but

more robust occupational studies.	unclear. *Why* more robust? Workers clearly are less sensitive than the population as a whole, so studying them is probably *less* robust than studying residents. More importantly, the whole aim of non-cancer epidemiology is to establish a NO-effect level (or failing that, the lowest effect level), and so by definition, a level that causes harm in one human population trumps a higher level that doesn't cause harm in another one—unless the former study is somehow invalid. I looked in detail at the 2008 HSIA comments about Altmann, and discuss them in my report.
Slide 9 and 10. See slide 8 for reasons to exclude Altmann et al 1995.	**** Response by Dr. Finkel **** See previous comment.
Slide 11 This is too simplistic! A lot depends on the shape of the dose-response curve, probability or magnitude of an effect, and how sensitive is sensitive! I agree that there no such thing as "safe" in absolute terms but in most non-cancer cases there is a practical threshold which uncertainty factors help establish	**** Response by Dr. Finkel **** The point is that we can't **know** the shape of the dose-response curve or "how sensitive is sensitive"—that's what the adjustment factors hopefully take account of. But whether each factor of 10 is enough to adjust the risk or not is an open question. The factors do NOT help establish a threshold at the individual level. My point stands: the NOAEL is not a "safe" level, but roughly a 5% risk level, for all we know. The interspecies factor of 10 (not used here anyway) only provides humans with the same risk level as rodents, unless it turns out to be the case that humans are not as much as 10 times more sensitive than rodents. The intraspecies factor of 10 only provides sensitive humans with the same risk level as average humans if it turns out to be the case that no human is as much as 10x as susceptible as the average. And even if all the statements about the adjustments are true, the sensitive human ends up at the same risk level as the rodents exposed to the "NOAEL"—that is, **only as safe as the power of the original study to detect a true zero risk.**
Slides 14 and 15. The emphases of the interpretations in the Benignus et al (2009) paper have been changed. The bottom line was that new, better, studies need to be performed before you could draw conclusions. The possible reasons for differences were purely speculative and there are reasons to reject each. The comparisons might carry more weight if the Schreiber et al (2002) and Altmann et al (1995) studies had been reasonably reliable – they are not	**** Response by Dr. Finkel **** How did an article published in July 2009 have "emphases changed" since then? Has the author issued a correction that I missed? I agree that more studies need to be done to figure out why it *appears* that chronic low-level perc exposure *may* be riskier than intermittent high-dose (occupational) exposure.

credible qualitatively or quantitatively.	
Slides 16 and 17. This is a selection from a wide range of literature, some of which (e.g. the Lynge et al, 2006 epidemiology study) supports the conclusion that drycleaning workers exposed to perc have no excess risk of cancer. The more unusual claims (schizophrenia, ALS, epilepsy) all need confirmation in independent studies – the new studies are "hypothesis setting". As for "hypersensitivity pneumonitis", if that had been a feature in dry cleaners, we are sure it would have been recognized (a single case report does not make a syndrome).	**** Response by Dr. Finkel **** I agree that the schizophrenia, ALS, and epilepsy studies need confirmation, and never said anything differently. I would add, however, that the same goes for all the "mode of action" papers about Perc that claim to have "shown" the toxic/carcinogenic mechanism—they are (at best) hypotheses that set the table for more detailed work that has yet to be done.
Slide 19 and 20. In addition to assessing the risks of substitution, it would be good to look at performance. We believe that safety of any suggested replacement solvent be examined before usage is considered.	**** Response by Dr. Finkel **** I agree that performance is also an important consideration, but it should not trump safety (if a safer substitute is marginally less effective in cleaning, it should be considered). In my opinion, the performance of a substitute such as n-propyl bromide is irrelevant, as it is too toxic to be considered even if it cleans as well as Perc (it is clearly more toxic than Perc).
Slide 21. The analysis of the evidence used by Dr. Finkel shows that 40 ppb perc is probably "safer" than he considers, and thus a "demarcation" higher than that could be considered. The 40 ppb action level is based solely on the assumption that exposure in co-located facilities are for lifetimes **of 24 hours a day, seven days a week, for 70 years**. The assumption is being made that someone is born, lives and dies adjacent to a drycleaner and never leaves their house. This is extremely over protective in residential settings, but borders on the ridiculous when co-commercial is discussed. If there are simple, cost-effective controls that reduce levels in co-located premises, these should be considered.	**** Response by Dr. Finkel **** I agree it is *possible* that both my assessment of the cancer and non-cancer hazards are "conservative," such that a higher action level might be reasonable, but I emphasize that there are many "non-conservative" elements in what I (and EPA, and ATSDR) have done as well (for example, only considering one non-cancer endpoint, not the cumulative burden of the other toxicities on top of the neurological). The second sentence is incorrect, in that the non-cancer assessments do NOT assume 24/7/70 exposure—they only assume that the residents or workers are exposed for as long as the subjects in the epi studies were. For example, the Altmann subjects lived next to dry cleaners for an average of 10.6 years (range= 1 to 30 years), and were only exposed for whatever # of hours per day they were at home (just like the residents of Philadelphia would be, we must assume, although perhaps there are Phila residents who are homebound for longer in the day than the Altmann subjects were…). The Ferroni workers

	were only exposed for several years, not 70 (although it is true that ATSDR adjusted their exposure by 5/7 and 8/24 to simulate continuous exposure, but again only over several years). It is true that the cancer potency factor is based on lifetime continuous exposure—but Slide 6 shows already the results of assuming only 8 hour/day, 10 years exposure (the cancer risk estimates here range from $3x10^{-5}$ up to $3x10^{-4}$). As I said in the public meeting, I agree with the National Academy (**Science and Judgment, 1996)** that it is generally unscientific to adjust exposure duration by a factor of 1/L to match (average) length of residence in a home or workplace, because all this would do is expose people to L times as much as they move from place to place or job to job—but nevertheless I presented the alternative (lower) cancer risk estimates in Slide 6.

Nordic Study (1) One issue that industry is greatly concerned about is the absence of information in Dr. Finkel's presentation regarding the Nordic study (Lynge et al, 2006). Dr. Finkel did not mention one of the most comprehensive, carefully planned studies ever conducted of existing drycleaner worker populations. The study of workers in four Nordic countries (Denmark, Norway, Sweden, Finland) was designed to answer specific questions that could compare cancer among exposed workers with those in similar socioeconomic groups. This study addresses those concerns that can be attributed to the 2001 NIOSH study that failed to address lifestyle issues, such as drinking and smoking and socioeconomic factors. **Nordic Study – Key Points** • (2) The Nordic is based on cradle-to-grave data gathered in those countries, all of which have government health care, which provides complete information of individual health records. • (3) **The study's findings do not show an increase incidence of esophageal cancer in drycleaning workers.** This is different from the Ruder study, which used much smaller cohorts and did not account for lifestyles or socioeconomic factors. The Nordic study takes in account life style factors, such as smoking and drinking and socioeconomic class. • (4) The Nordic study cohort contained more than 46,000 persons in comparison to the earlier NIOSH study, which contained only 1,700 persons, of whom only 625 persons used only perc. Of those, no other life style or socioeconomic factors are known, such as smoking history. • (5) According to HSIA Science Director Dr. Paul Dugard, The Nordic study "is a study with a significantly improved ability to detect the potential for increased cancer incidence resulting from exposure to perc."	**** Response by Dr. Finkel **** (1) I had read the Lynge study by the time I made my October presentation, and do not agree with most of the claims made in this comment. I will include in my written report a more comprehensive critique of this study. (2) Note that I do not refer to the 2001 NIOSH study at all in my report, so the relative merit of Lynge versus NIOSH is not relevant. (3) of the eight cancer sites analyzed, six (including esophagus) indeed show a relative risk of less than one (exposed versus unexposed). However, two sites (pancreas and bladder) show an excess in the exposed. In fact, the only statistically significant result of the eight (a confidence limit on relative risk that does not go from below 1.0 to above 1.0) is bladder, which is *positive* (all the other "negative" findings can't be made with 95% confidence). (4) I agree that this study is larger and better-controlled than the NIOSH one (which, again, I did not rely on). But power is a function of size, controls, **and exposure**, and the exposures in Lynge were much lower than in NIOSH—so even the "negative" findings are not as powerful as we would like.

APPENDIX I

Dr. Finkel Presentation at 10/21/09 APCB meeting: "Preliminary Evaluation of Perchloroethylene Risks and the Philadelphia Dry-Cleaning Proposal"

Preliminary Evaluation of Perchloroethylene Risks and the Philadelphia Dry-Cleaning Proposal

October 21, 2009

Adam M. Finkel, Sc.D., CIH

[Professor of Environmental and Occupational Health, UMDNJ School of Public Health *and* Executive Director, Penn Program on Regulation, Univ. of Pennsylvania Law School:
--Personal views only--

Topics I will Cover:

1. Cancer risk from Perc;

2. Derivation of non-cancer reference concentrations, and misunderstandings about whether such concentrations are “safe”;

3. Sampled concentrations of Perc, compared with reference levels;

4. Brief review of several very recent scientific papers;

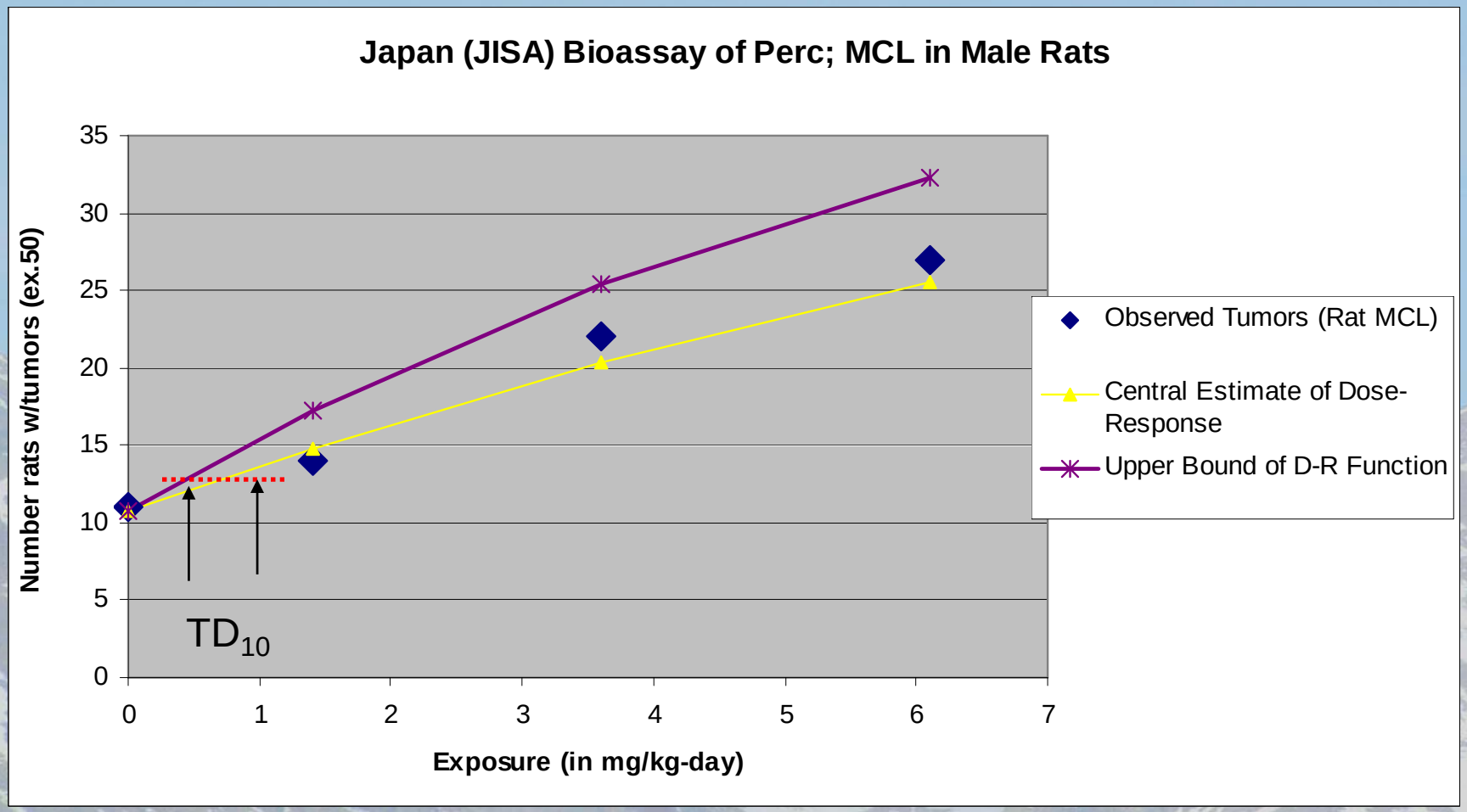
5. Invalid– and valid– concerns about “risk-risk tradeoffs” possibly resulting from dry cleaning regulation;

6. Concern about replacement of reasonable “default” risk assumptions with speculative alternatives

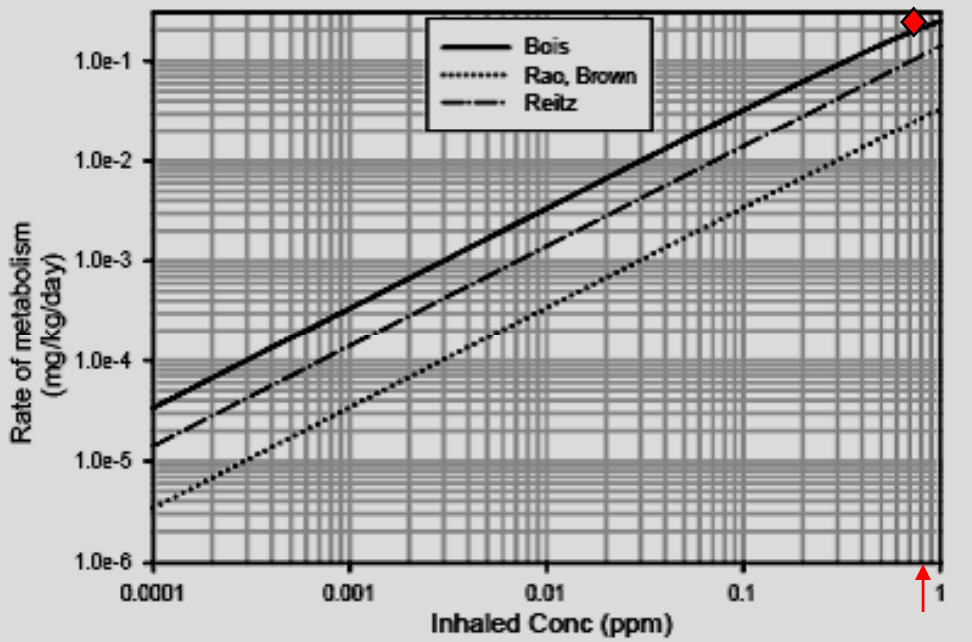
7. Summary of findings and opinions about regulatory design

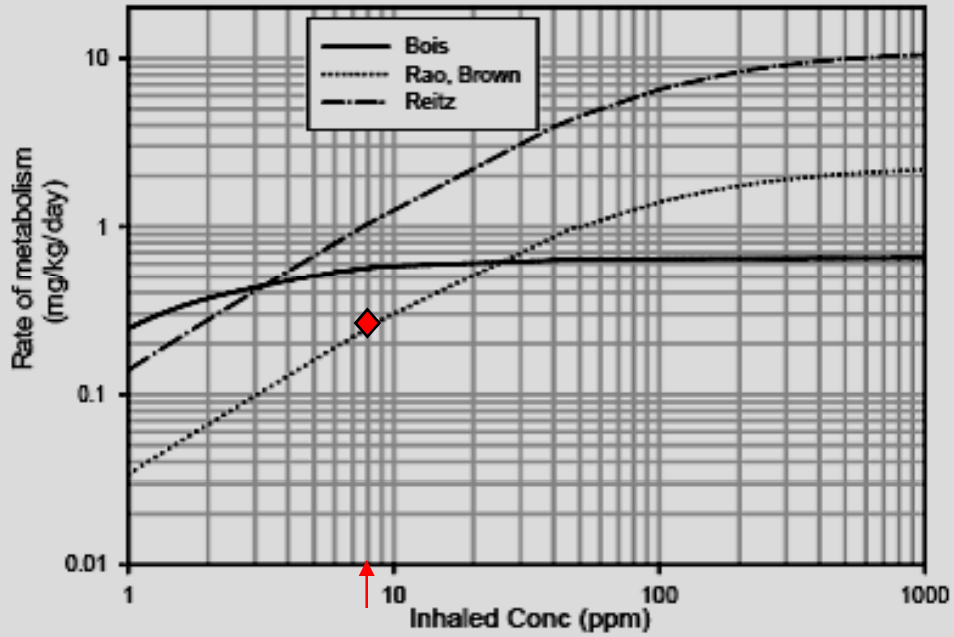
Asked by Air Management Services to:

- evaluate the carcinogenic potency of Perc;
- evaluate the science-policy choices underlying the setting of the EPA Reference Concentration (RfC) and the ATSDR Minimal Risk Level (MRL);
- comment on the 40 ppb action level in light of the cancer and non-cancer dose-response information, and in light of the pre- and post-intervention levels found in co-residential and co-commercial settings;
- comment on the draft regulations, in light of my experience drafting, enforcing, and peer-reviewing OSHA and EPA regulations

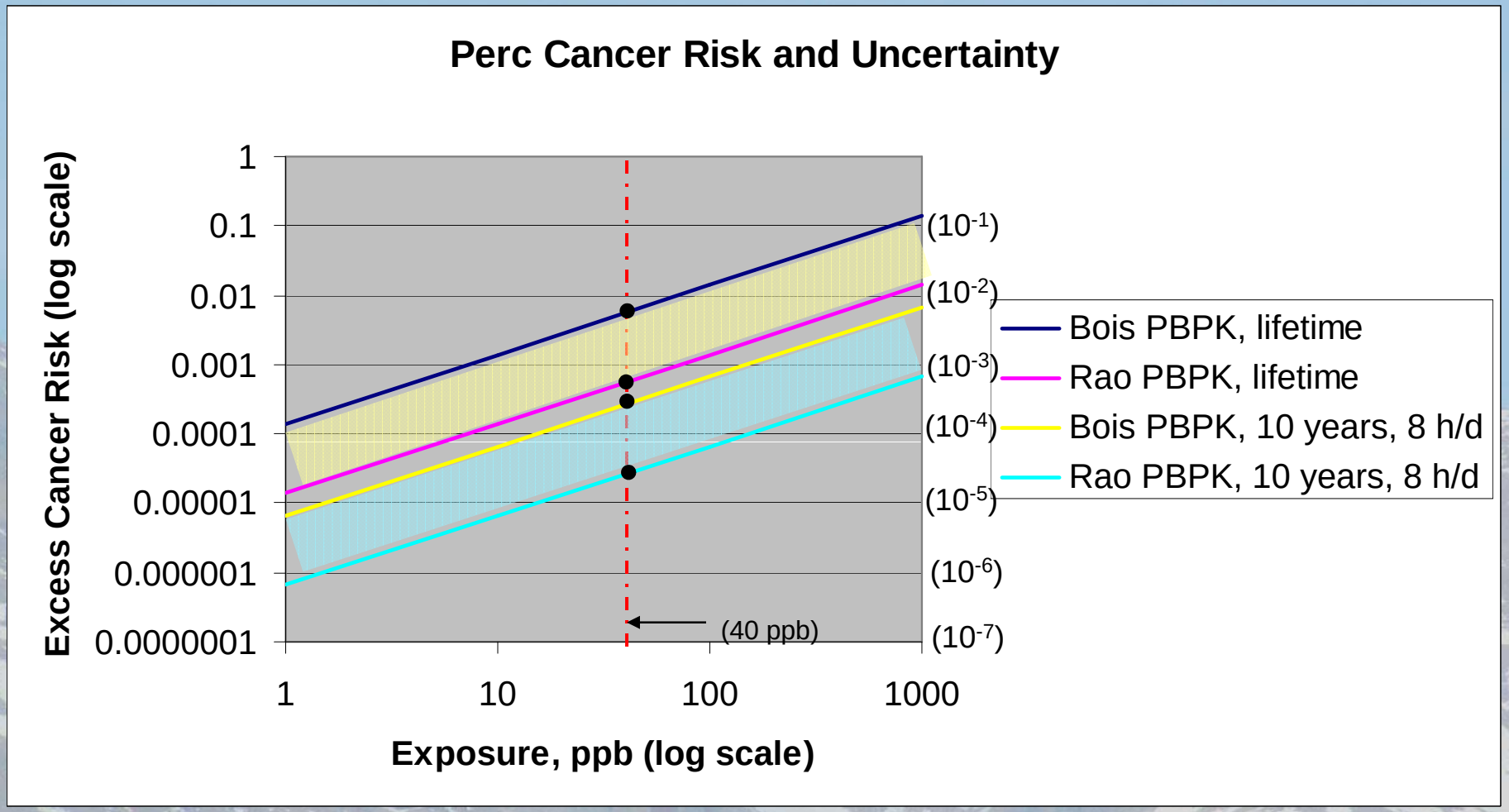


This slide shows the four groups of 50 rats given various amounts of Perc, and the number of animals who developed leukemia at each dose. The yellow function gives the best statistical fit to the observed data, but it's quite possible that the risk at low doses is as steep as that shown by the purple function (14 rats out of 50 got leukemia at the lowest dose, but you could run the experiment again and you might see 16 or 17 with leukemia just by chance]. EPA locates the point (red line) where the risk is 10 percent (above the backgroun risk at zero dose), and assumes the risk decreases in a straight line below this point.





[this slide shows three of the models EPA used to explain the relationship between the airborne concentration of Perc and the amount of Perc metabolized in humans. Depending on which model is used, the metabolized amount (0.23 mg/kg/d) that is associated with an excess lifetime cancer risk of 10^{-1} (10 percent) could arise from continuous exposure to as little as 0.8 ppm (top graph) or as much as 8 ppm– a factor of 10 uncertainty]



[At 40 ppb, the excess lifetime cancer risk lies between 6 in 10,000 and 6 in 1,000; even if you assume exposure only occurs for 8 hours/day, and for 10 years rather than 70, the excess cancer risk lies between 3 in 100,000 and 3 in 10,000]

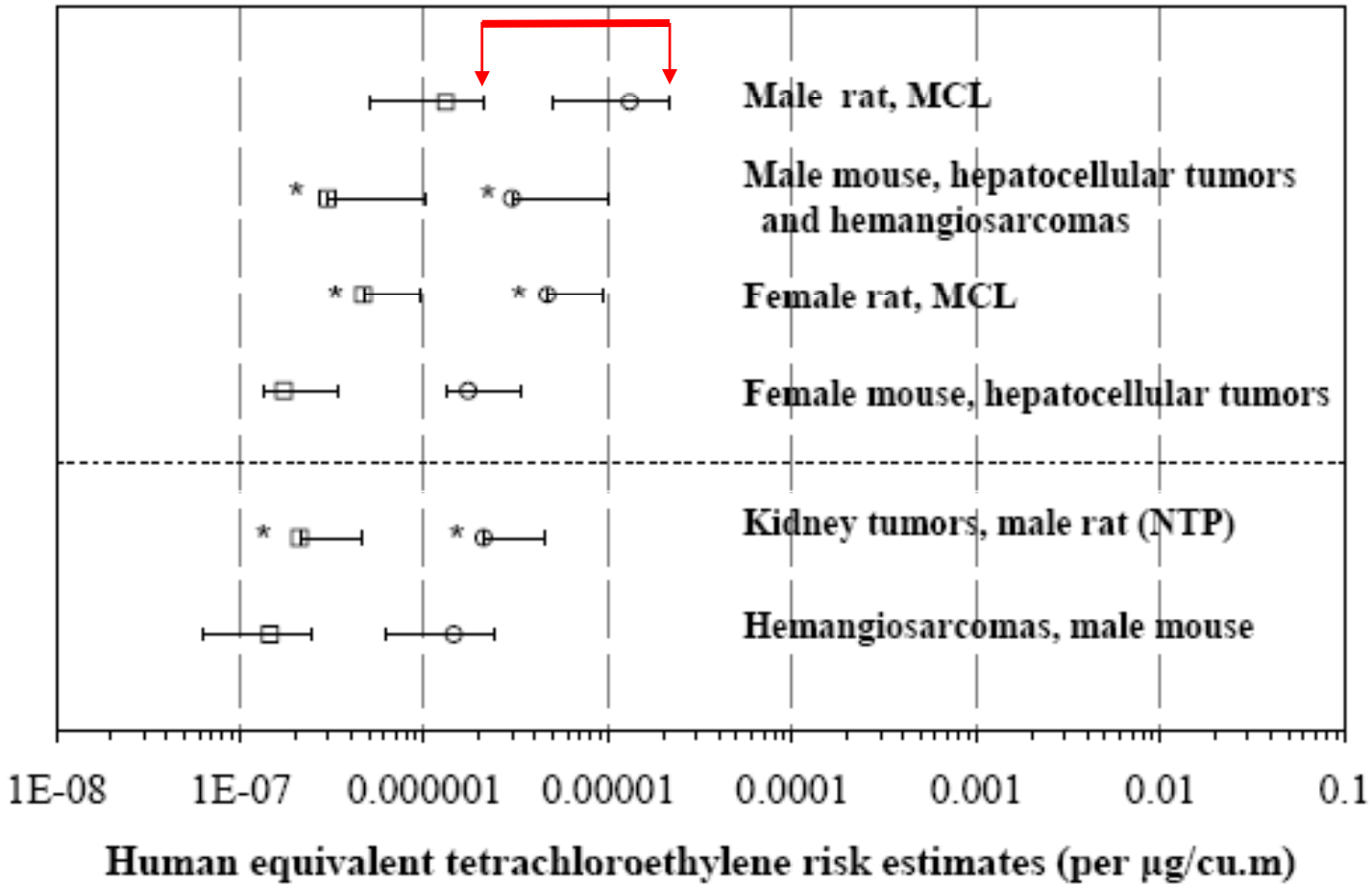


Figure 6-4. Cancer risk estimates for tumor sites associated with tetrachloroethylene exposure in rodent bioassays, using the multistage model. The four gender/species data sets are provided in the upper section of the graph while two tumor types observed in single bioassays are provided in the lower section. The symbols denote the slopes (to background risk) from the mean estimate of exposure corresponding to 10% extra risk, using the Rao and Brown (1993) PBPK model (□) and the Bois et al. (1996) model (○) to extrapolate to human equivalent exposures. The bars indicate the slopes from the lower and upper bounds on the mean estimates. * indicates lower bounds that could not be estimated.

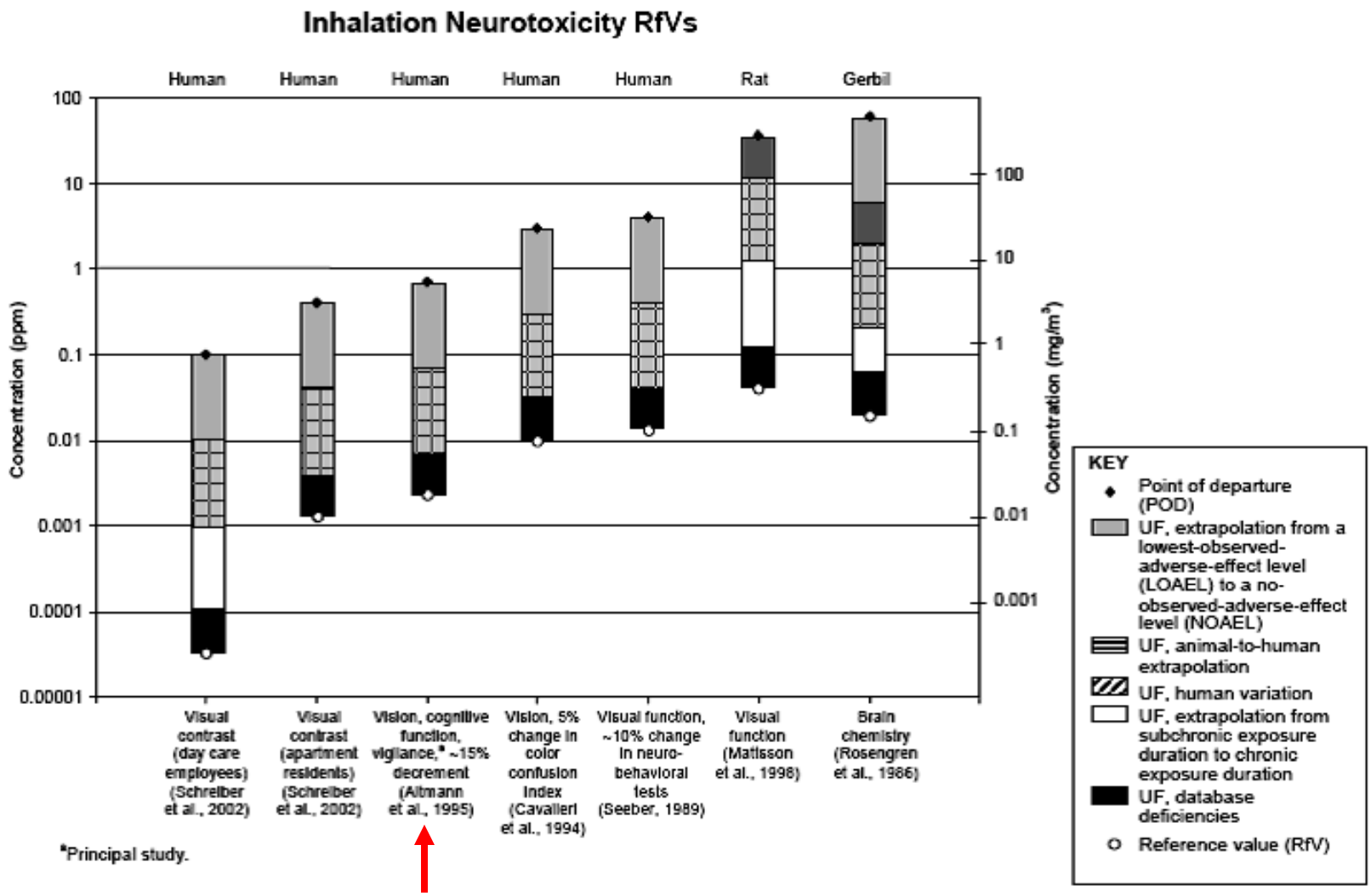


Figure 6-1. Array of PODs and reference values for a subset of neurotoxic effects in inhalation studies.

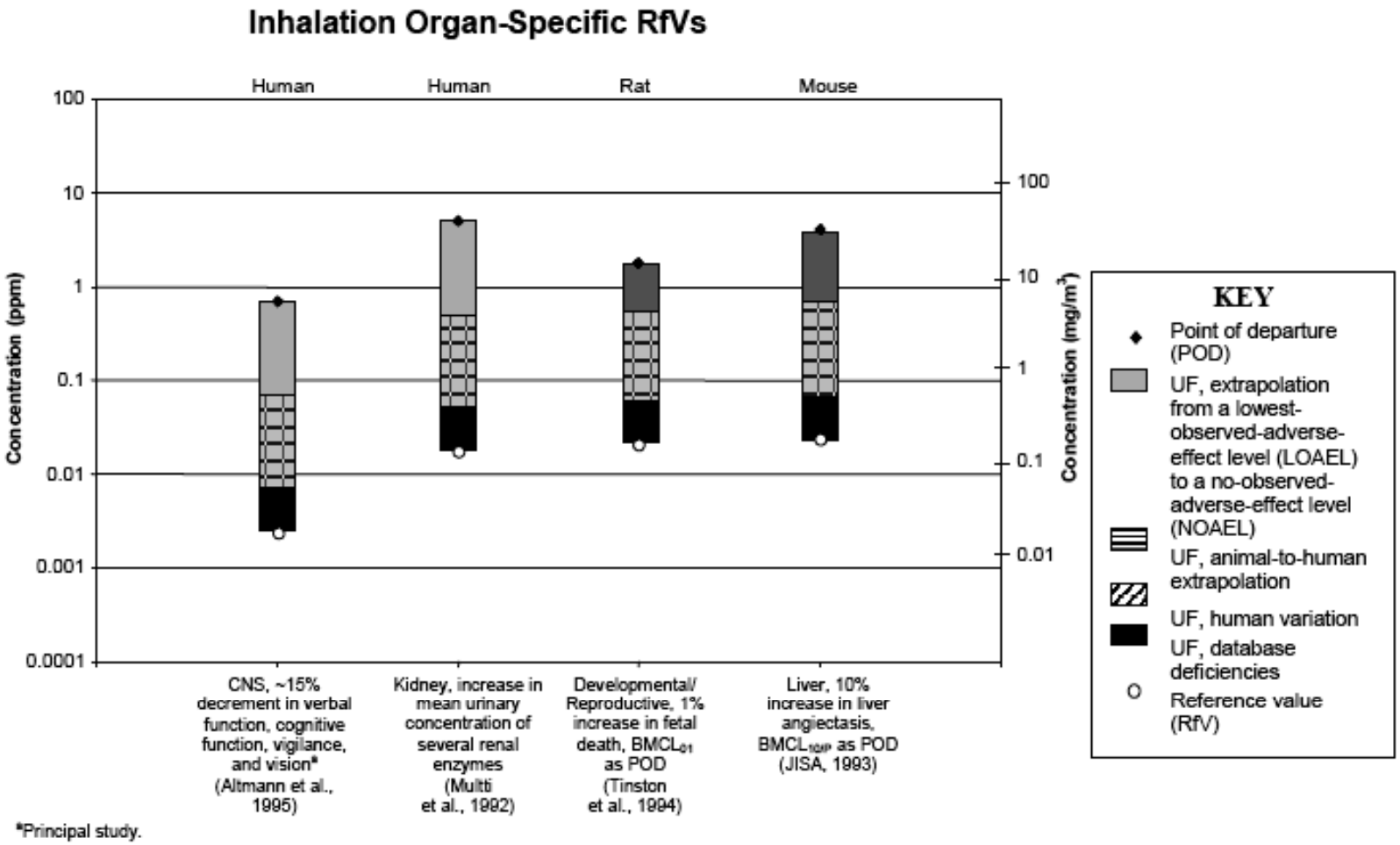


Figure 6-2. Organ-specific RfVs for inhalation exposure to tetrachloroethylene.

How EPA and ATDSR arrived at their non-cancer risk benchmarks:

EPA:

- mean exposure of subjects showing neurological deficits in Altmann et al. (1995) = 700 ppb;
- divide by 10 to estimate a NOAEL from this LOAEL;
- divide by 10 to account for human-to-human variability;
- divide by 3 to account for database deficiencies…

700/300 = 2.4 ppb

ATSDR:

- median exposure of subjects in Ferroni et al. (1992) showing neurological deficits = 15 ppm;
- adjust to continuous exposure by multiplying by (8hr/24hr) and (5d/7d);
- divide by 10 to estimate a NOAEL from this LOAEL;
- divide by 10 to account for human-to-human variability;

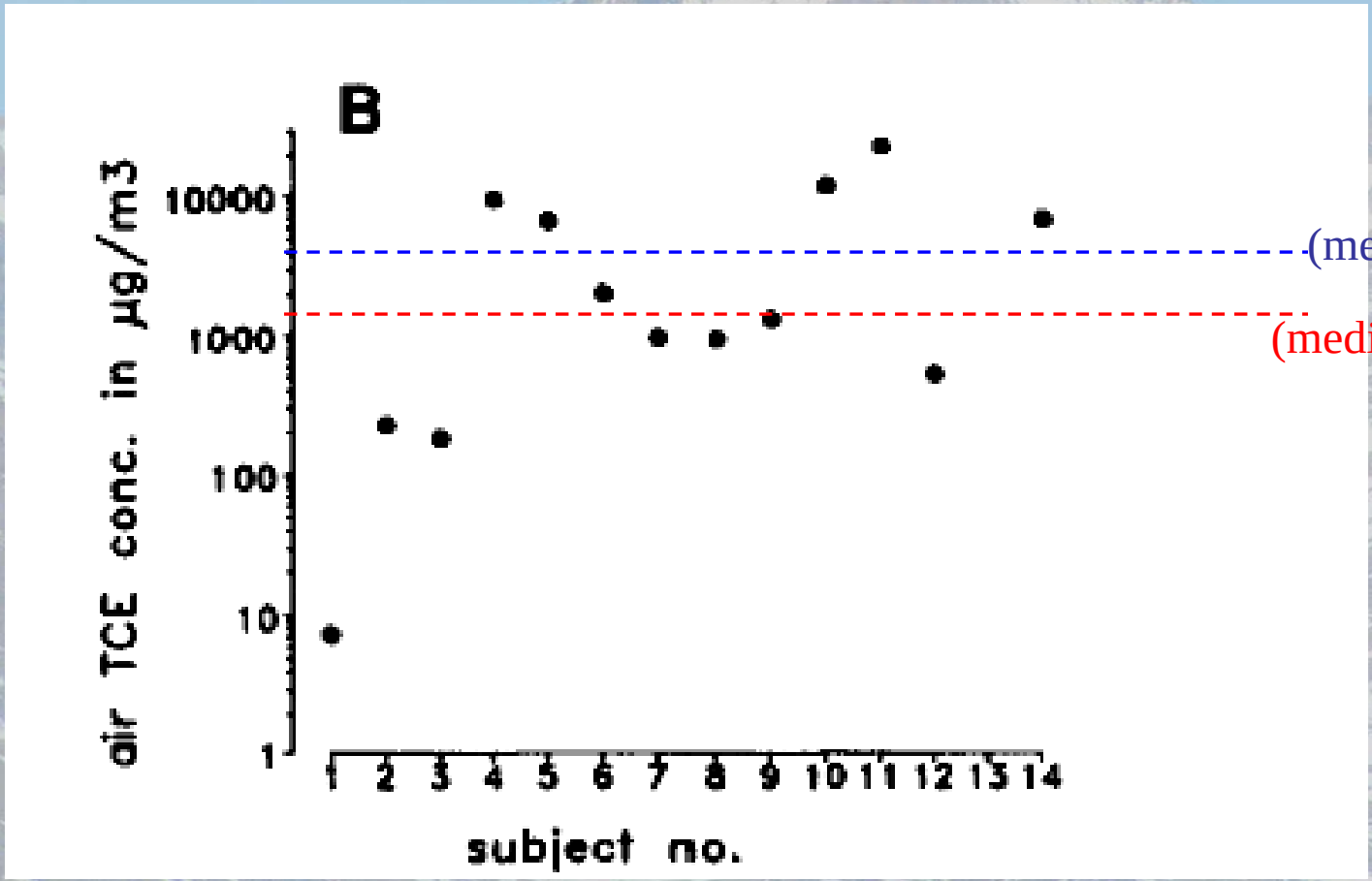
(15,000)(8/24)(5/7)/(10)(10) = 36 ppb (rounded up to 40)

The MRL (the RfC) is not necessarily a “safe” level:

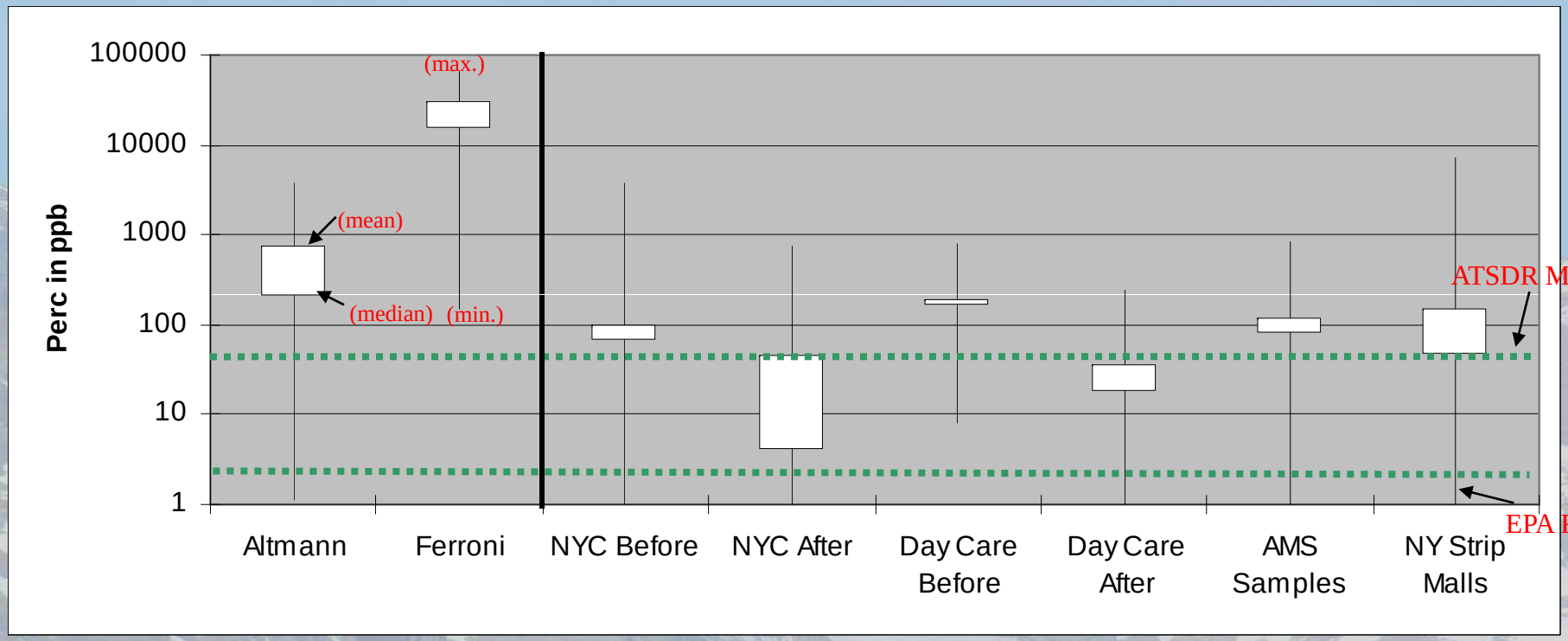
For many chemicals, exposures at 1/10th the LOAEL appear not to cause harm to populations (a NOAEL); for many substances, 1/10th the NOAEL also protects sensitive individuals. *If both these statements are true for Perc*, then 40 ppb (1/100th the LOAEL from Ferroni) would indeed be a level unlikely to cause harm in nearly all people.

In other words, 40 ppb (or 2.4 ppb using the Altmann study and EPA’s logic) <u>might</u> be right at the NOAEL for sensitive subgroups– but the NOAEL itself is not a true “no-effect” level, but a level associated with an incidence too small to detect in a bioassay or epidemiologic study [that is, roughly a 5 percent risk or lower].

Individual Exposures in Altmann et al. (1995)



Ranges and Central Estimates of Key Perchloroethylene Concentrations Measured:



Note that: (1) regulations and site-specific intervention can lower concentrations by roughly a factor of 10; and (2) co-commercial concentrations are similar, if not slightly higher, than co-residential concentrations

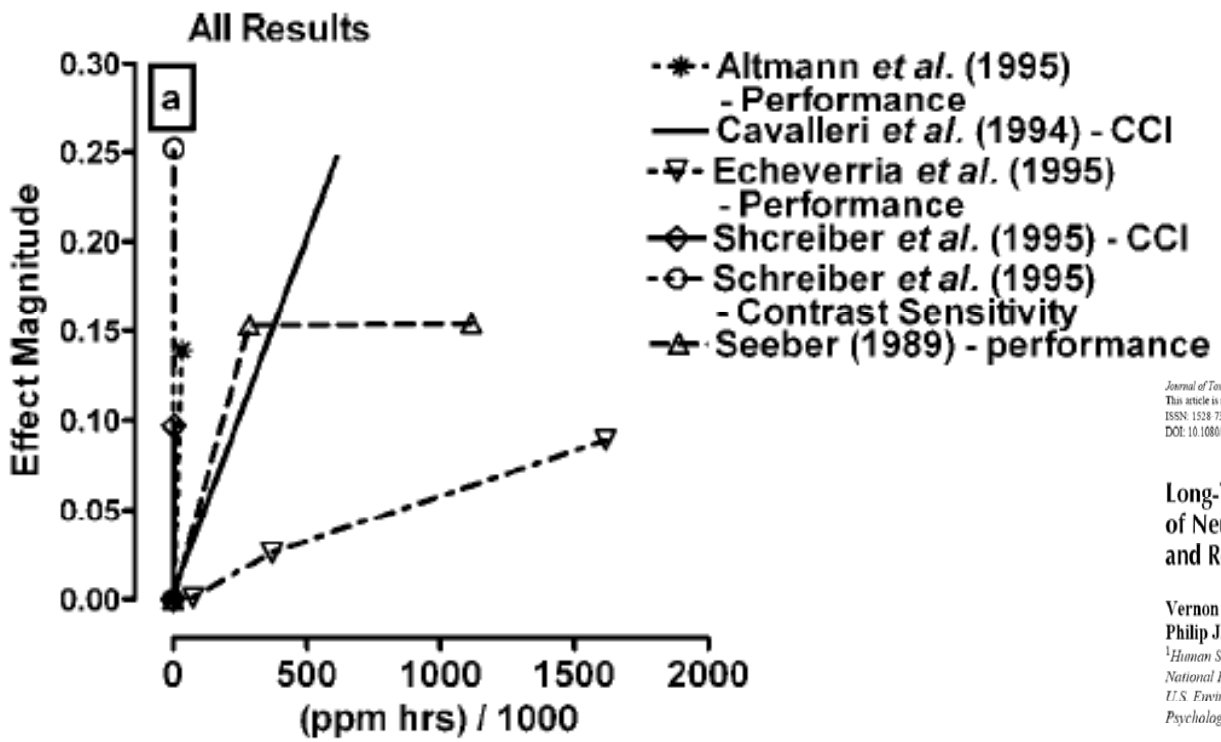
Major New Study:

Benignus et al., (U.S. EPA and UNC/Chapel Hill), July 2009 *J Tox Env Health:*

- Meta-analysis of 3 workplace, 2 residential studies
- Converted all exposures to common units of ppm-hours
- Converted all outcomes to common 0-1 effect scale

Claims slope of residential dose-response is much (40x?) higher than workplace; 3 possible reasons—

1. Workers affected by perc leave employ;
2. Workers in general are less susceptible than general population;
3. Continuous exposure is riskier than 8-hour exposure (repair and recovery)



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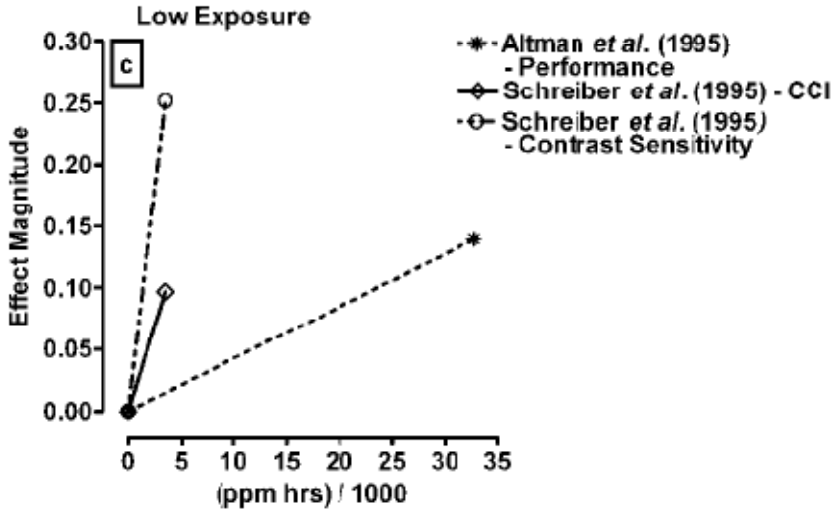
Long-Term Perchloroethylene Exposure: A Meta-Analysis of Neurobehavioral Deficits in Occupationally and Residentially Exposed Groups

Vernon A. Benignus[1,4], William K. Boyes[2], Andrew M. Geller[3], and Philip J. Bushnell[2]
[1]*Human Studies Division,* [2]*Neurotoxicology Division, and* [3]*Research Planning and Coordination Staff, National Health and Environmental Effects Research Laboratory, Office of Research and Development, U.S. Environmental Protection Agency, Research Triangle Park, North Carolina, and* [4]*Department of Psychology, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, USA*

FIG. 5. Comparison of all of the long-term exposure data: (a) all data plotted on same scale; (b) only the high-exposure, low-sensitivity data; and (c) only the low-exposure, high-sensitivity data. Note that the low-sensitivity data are all from workplace exposure and all of the high-sensitivity data are from residential exposures.



Other New Studies

- Chiappini et al., *Indoor Air*, June 2009: putting a carbon adsorber on a refrigerated machine reduced workplace concentrations from approx. 5 ppm to approx. 1 ppm, and maximal apartment levels from approx. 300 ppb to approx. 30 ppb
- Perrin et al., *Schizophrenia Research*, Feb. 2007 (RR=3.4 of schizophrenia among Israelis whose parents were dry cleaners)
- Fang et al.(NIEHS, Karolinska Inst.), *Environmental Health Perspectives*, Sept. 2009: self-reported exposures to 5 chemicals, including “dry cleaning agents,” each associated with 60 to 90% increase in relative risk of amyotrophic lateral sclerosis (“Gehrig’s disease”)

Other new studies (cont.)

- Li et al. (Karolinska Inst.), *Seizure*, Apr. 2008: increased risk of hospitalization for epilepsy among 5 occup'l groups, including dry cleaners
- Tanios et al. (Tufts-NEMC), *Respiration*, Nov-Dec 2004: case report of hypersensitivity pneumonitis in a 42-year-old dry cleaner

Features of Various Dry Cleaning Regs

	EPA	Phila. (note– assumes eff. date is 1/2011)	Calif. ARB
Freestanding	No more transfer machines	• no more transfer machines • 4th generation by 2013 •No self-serve perc machines	
Co-commercial	(No specific category)	• No perc by roughly 2024, or whenever 15 years old • 25-foot buffer	No perc by 7/2010
Co-residential	• No new perc after 7/2006 • No perc by 2021	• No perc by 2014 • 25-foot buffer	
Sensitive	(No specific category)	•No perc by 2014 • 25-foot buffer	

Concerns about “Risk-Risk Tradeoffs”

• *Many* of the purported tradeoffs reported in the media were “red herrings” that advocates knew would never come to pass (e.g., home fires after California restricted use of most toxic fire retardants), were increased risks totally offset by decreased risks elsewhere (e.g., no new trucks were built when the Superfund program was at its zenith), or should properly have been interpreted as reasons to solve two problems at once (e.g., pregnant women can obtain omega-3 acids from sources other than high-mercury fish).

• OSHA received considerable pressure from the Halogenated Solvents Industry Alliance (HSIA) in the late 1990s to consider risk-risk tradeoffs that purportedly would result from OSHA’s regulation of methylene chloride– including increased fires and explosions as customers substituted acetone and other more flammable materials for MC. With 12 years’ hindsight, it is clear that none of these “unintended consequences” has occurred.

Risk-Risk Tradeoffs (2):

HOWEVER, no one has yet mentioned that there are some substitutes for Perc that clearly *would* increase harm to workers and residents; in my opinion, at least one of these– 1-bromopropane (a.k.a. *n*-propyl bromide) should be restricted as part of a policy of promoting safer dry-cleaning:

• CDC *Morbidity and Mortality Weekly Report* (12/15/08) published a case report of a 43-year-old man in NJ who had recently begun dry cleaning with "DrySolv"– hospitalized with headaches, fatigue, visual disturbances, twitching, joint pain;

• *Journal of Envt'l and Occup'l Medicine* (9/07) reported on 4 furniture workers using 1-BP glue (18 - 254 ppm in air) who developed inability to walk, pain, numbness, vomiting– persisting for 8 years after leaving workplace;

• *European J Endocrinology* (1998) reported on 16 Korean workers using 2-BP who developed primary ovarian failure.

Summary:

- 40 ppb is not necessarily a “safe” level, but it is a reasonable place to demarcate a level of acceptable risk;
- Current methods of controlling Perc emissions can reduce concentrations in co-located facilities to < 40 ppb
- The U.S. EPA regulations improperly ignore risks in co-commercial facilities, which are likely higher than those in co-residential settings
- It may be possible to achieve 40 ppb or lower through controls different from those singled out in the draft regs; in my experience, industry often simultaneously argues against design standards without “flexible performance goals” *and* against performance standards without technological “safe harbors”
- There are safer substitutes for Perc in dry cleaning, but also riskier ones whose use should not be encouraged

APPENDIX II

Comments from Allan Wong and Jon Meijer via email

From: ALLAN WONG [allanklwong@verizon.net]
Sent: 10/29/2009 10:50 PM MST
To: Thomas Huynh
Cc: JASONKIMLG@gmail.com
Subject: Perchloroethylene Study Presentation

Mr. Huynh:

Thank you for inviting me to attend the APCB meeting on 10/21/09. The Perchloroethylene Study Presentation by Dr. Finkel was particularly interesting to me because of my background in Environmental Biochemistry, years of research in chemical carcinogens before my career in Pharmaceutical research that covers metabolism and toxicology.

Due to the poor quality of the handout and visual image of the presentation it was difficult to follow the details of Dr. Finkel's presentation. For this reason and in the absence of the written report it is not possible to make a full evaluation of the study. Nevertheless, a few comments can be made.

Dr. Finkel speculated that the estimation of carcinogenic potency of Perc (slide #4) based on the study of MCL in male rats was too low. He speculated that "(14 rats out of 50 got leukemia at the lowest dose, but you could run the experiment again and you might see16 and 17 with leukemia just by chance)". Hence Dr. Finkel arbituarily increased the cancer incidence at the three exposure levels to create a curve represented by the solid line. By selectively keeping the cancer incidence at zero level unchanged, he managed to reduce the TD10 value and drew the wrong conclusion that EPA underestimated the cancer risk of Perc. The way that Dr. Finkel manipulated the data is not acceptable by any scientific standard.

In fact, none of the legible slides show any data that the 40 ppb exposure limit established by EPA is unsafe. In order to justify lowering this EPA standard, Dr. Finkel has to provide NEW and COMPELLING SCIENTIFIC EVIDENCE, not speculation that the 40 ppb standard is unsafe. Dr. Finkel's presentation provided none of these.

I look forward to receiving a copy of the Perchloroethylene Study Report that is 100% legible so that it can be evaluated fully. I also recommend the APCB to send a copy of this report to EPA for their comment.

Allan Wong, Ph.D.
Commissioner, Mayor's Commission on Asian American Affairs
Executive Vice-President, Organization of Chinese Americans-Greater Philadelphia
Liaison, Chinese Freemasons of Philadelphia
Liaison, Hoy Sun Ning Yung Benevolent Association of Philadelphia

November 25, 2009

Mr. Thomas Huynh, AMS Director
Department of Public Health: Air Management Services
321 University Ave., 2nd. Floor
Philadelphia, PA 19104

Re: Additional Information Regarding Perchloroethylene Use by Drycleaners in Philadelphia

Mr. Huynh:

The drycleaning industry appreciates the opportunity to provide written information to the Department of Public Health: Air Pollution Control Board, Ad-hoc Working Group regarding perc and perc use by drycleaners in the City of Philadelphia. The following notations were developed in partnership with the Drycleaning & Laundry Institute (DLI), Neighborhood Cleaners Association (NCA), Pennsylvania and Delaware Cleaners Association (PDCA), Korean Drycleaners Association of Philadelphia (KDAP) and the Halogenated Solvents Industry Alliance Inc. (HSIA).

On October 21, 2009, Dr. Adam Finkel presented his review of the perc toxicology to the Air Pollution Control Board (APCB). Industry representatives were prohibited from making comments regarding the presentation and we were requested to provide any additional information in writing to the Board by November 30, 2009. While we are highlighting some key concerns with Dr. Finkel's "PowerPoint" presentation, we will make a full presentation once the full report is completed and there is adequate time to review Dr. Finkel's assessment.

Over the past two years, we have offered any and all help to Air Management Services (AMS) to develop a regulation that protects human health and the environment while keeping drycleaners from going out of business. The changes we made to the original language would have made it one of the toughest drycleaning standards in the U.S., including those developed in New York and New Jersey, which did not phase-out perc use in drycleaning. For some inexplicable reason, our input has been utterly ignored. Thus far, the process we have had to rely on has been confusing and less than transparent.

At the August 8, and the March 8, 2009 meetings of the APCB, testimony provided by Nora Nealis of NCA offered both her time and expertise to AMS regarding the issues related to engineering controls that will help plants reduce indoor air levels to acceptable limits. So far, not one person from AMS has called her, even though at both meetings AMS staff said they were willing to take Nora up on her offer.

To the best of our knowledge, we have not been provided with complete data from plant/s that were tested by AMS. Nor have we seen anything even closely resembling quality assurance or quality control while conducting the fieldwork. It certainly appears that APCB is only looking to phase-out perc without considering options that would protect human health and the environment while saving drycleaners in Philadelphia that use perc.

The following are some key points regarding Dr. Finkel's testimony and other related issues.

Perchloroethylene: Perspectives on Dr. Adam Finkel's Analysis for the City of Philadelphia

General:

The analysis draws heavily (slides 4 through 9 and opinions) on EPA's external review draft of the "Toxicological Review of Tetrachloroethylene (Perchloroethylene)" in support of the IRIS database. Every page of this draft carries the warning "This document is a draft for review purposes only and does not constitute Agency policy. DRAFT – DO NOT CITE OR QUOTE".

This draft has been reviewed by a National Academies of Science (NAS) panel and release of the report is imminent. Among the issues believed to have been considered are whether mononuclear cell leukemia (MCL) is appropriate for calculating human risk (EPA's worst case and the basis for Dr Finkel's predictions of risk) and whether general population studies such as Altmann et al (2005) and Schreiber et al (2002) provide a reliable basis for calculating an RfC rather than scientifically more robust occupational studies. The draft should not have been used as a basis for an assessment at this time.
The findings in the report of the NAS review, when available, should be considered by Dr. Finkel and his assessment modified if necessary.

The tumors seen in animals are of questionable relevance to man. EPA stated very clearly that the projections of human cancer risk based on animal studies represented an "upper bound" and that the "true risk could be as low as zero". This statement certainly applies to the calculations displayed in the slides. At the very least, it should be stated that these are conservative (worst case) estimates of risk, not real values.

Specific Notations

Slide 4.
MCL is a rat strain specific cancer with unknown relevance to man. It should not be used for quantitative risk assessment.

Slide 5 and 6.
The three models used by EPA have been superseded by more recent, more sophisticated models (shown to be more accurate). The model of Bois is distorted by use of inaccurate human data and risks based on this model should not be included.

Slide 7.
Exclude MCL, it is a type of leukemia that has no human equivalent. Do not combine male mouse hepatocellular tumors and hemangiosarcomas (completely different cell types). This leaves male rat kidney tumors as the worst case but that was a marginal response in a single study – no mention that no kidney tumors were found in several comparable studies. Plus, the flawed Bois model should be excluded.

Slide 8.
Too many flaws in the Schreiber et al (2002) studies (even NY DoH has criticized the apartment studies). Similarly, Altmann et al (1995) has a very small number of subjects and their selection was probably (unintentionally) biased. Moreover, the results are not plausible when compared with much more robust occupational studies.

Slide 9 and 10.
See slide 8 for reasons to exclude Altmann et al 1995.

Slide 11
This is too simplistic! A lot depends on the shape of the dose-response curve, probability or magnitude of an effect, and how sensitive is sensitive! I agree that there no such thing as "safe" in absolute terms but in most non-cancer cases there is a practical threshold which uncertainty factors help establish.

Slides 14 and 15.
The emphases of the interpretations in the Benignus et al (2009) paper have been changed. The bottom line was that new, better, studies need to be performed before you could draw conclusions. The possible reasons for differences were purely speculative and there are reasons to reject each. The comparisons might carry more weight if the Schreiber et al (2002) and Altmann et al (1995) studies had been reasonably reliable – they are not credible qualitatively or quantitatively.

Slides 16 and 17.
This is a selection from a wide range of literature, some of which (e.g. the Lynge et al, 2006 epidemiology study) supports the conclusion that drycleaning workers exposed to perc have no excess risk of cancer. The more unusual claims (schizophrenia, ALS, epilepsy) all need confirmation in independent studies – the new studies are "hypothesis setting". As for "hypersensitivity pneumonitis", if that had been a feature in dry cleaners, we are sure it would have been recognized (a single case report does not make a syndrome).

Slide 19 and 20.
In addition to assessing the risks of substitution, it would be good to look at performance. We believe that safety of any suggested replacement solvent be examined before usage is considered.

Slide 21.
The analysis of the evidence used by Dr. Finkel shows that 40 ppb perc is probably "safer" than he considers, and thus a "demarcation" higher than that could be considered. The 40 ppb action level is based solely on the assumption that exposure in co-located facilities are for lifetimes **of 24 hours a day, seven days a week, for 70 years**. The assumption is being made that someone is born, lives and dies adjacent to a drycleaner and never leaves their house. This is extremely over protective in residential settings, but borders on the ridiculous when co-commercial is discussed. If there are simple, cost-effective controls that reduce levels in co-located premises, these should be considered.

Nordic Study
One issue that industry is greatly concerned about is the absence of information in Dr. Finkel's presentation regarding the Nordic study (Lynge et al, 2006). Dr. Finkel did not mention one of the most comprehensive, carefully planned studies ever conducted of existing drycleaner worker populations. The study of workers in four Nordic countries (Denmark, Norway, Sweden, Finland) was designed to answer specific questions that could compare cancer among exposed workers with those in similar socioeconomic groups. This study addresses those concerns that can be attributed to the 2001 NIOSH study that failed to address lifestyle issues, such as drinking and smoking and socioeconomic factors.

Nordic Study – Key Points

- The Nordic is based on cradle-to-grave data gathered in those countries, all of which have government health care, which provides complete information of individual health records.
- **The study's findings do not show an increase incidence of esophageal cancer in drycleaning workers.** This is different from the Ruder study, which used much smaller cohorts and did not account for lifestyles or socioeconomic factors. The Nordic study takes in account life style factors, such as smoking and drinking and socioeconomic class.
- The Nordic study cohort contained more than 46,000 persons in comparison to the earlier NIOSH study, which contained only 1,700 persons, of whom only 625 persons used only perc. Of those, no other life style or socioeconomic factors are known, such as smoking history.
- According to HSIA Science Director Dr. Paul Dugard, The Nordic study "is a study with a significantly improved ability to detect the potential for increased cancer incidence resulting from exposure to perc."

We appreciate the opportunity to provide additional information to the Ad-hoc committee regarding Dr. Finkel's review of the perc toxicology and other related issues. If you have any questions or need additional information, please do not hesitate to call.

Respectfully Submitted,

DLI, NCA, PDCA, KDAP, HSIA