EPA Response to Inspector General Argues Against Reporting All Toxaphene Present

TECHNICAL ASSISTANCE REPORT

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Background

An audit of the Hercules 009 Landfill Superfund Site conducted by the EPA Inspector General (IG) found the toxaphene analytical method used by EPA Region 4 did not report all of the toxaphene present in samples. The IG made specific recommendations to correct the problem, and EPA Region 4 responded to the IG on June 20, 2006. However, instead of implementing the IGs' recommendations, Region 4 proposed a new method of toxaphene analysis and risk assessment. The new method proposed by EPA Region 4 and the Georgia Environmental Protection Division for measuring toxaphene referenced only a single published paper. ***This Technical Assistance Report excerpted from:*** **Review and Comments on the paper "Development of a Reference Dose for the Persistent Congeners of Weathered Toxaphene based on *In Vivo* and *In Vitro* Effects Related to Tumor Promotion" by Simon and Manning, 2006 published in the Journals of Regulatory Toxicology and Pharmacology.**

Overview

This article seeks to redefine environmental toxaphene monitoring using tumor promotion as the only result of exposure. However, rather than offer concrete scientific modeling for a tumor promotion effect of the chemical, the authors seek to minimize established use of toxaphene genetic mutation data, while at the same time ignoring compelling data showing toxaphene can, and does, cause cancer. Further, the authors propose an analysis using only three of the several hundred compounds that make up toxaphene. The paper provides no new experimental observations, no new survey data, and no new calculation algorithms. Instead, the authors use a subset of toxaphene publications to support their views.

Toxaphene Definition

The Simon and Manning paper defines toxaphene as all of 800 different chemicals possible for the chlorination of camphene. In the third paragraph, the authors offer definitions for technical toxaphene (TT), and weathered toxaphene (WT), with weathered defined as degraded technical toxaphene.

"Degraded" though, just means changes in congener (the individual chemicals in toxaphene) occurrence. Toxaphene manufacturing wastes dumped in streams and borrow-pits in Brunswick, Georgia, would be considered technical toxaphene with Simon and Manning's definition. Further, the "toxaphene-like" compounds found on elementary schoolyards and in neighborhoods throughout Glynn County, Georgia, are also technical toxaphene, as defined by Simon and Manning.

Essentially, with this definition, there is no need for any definition other than "TT" for toxaphene found anywhere on earth; and we concur with the authors' definition.

Model based on Tumor Promotion

Simon and Manning argue that environmental toxaphene monitoring should be based on tumor promotion. The authors provided three arguments in support of their logic: lack of human mutagenicity; lack of significant developmental defects; and, carcinogenicity.

Mutagenicity of Toxaphene

The authors' statement regarding toxaphene genotoxicity - the ability to cause genetic damage - in humans is confused and lacking in logic. Carcinogenicity, the formation of tumors, is a complex subject. Typically, the process requires damage to cellular DNA - but not always. Some chemicals that participate in the cancer process are promoters, not initiators, in the sequence of tumor formation. Since science cannot always predict a chemicals' carcinogenicity, best practices require that, if any type of study points to potential genotoxicity, then the material is presumed genotoxic until proven otherwise.

The science proving that toxaphene is genotoxic in bacterial systems is compelling. TT is mutagenic in the Ames test, a widely-accepted bacterial test for quantifying DNA damage. Simon and Manning correctly note in their article that toxaphene induces Sister Chromatid Exchange (SCE) in higher cells under laboratory conditions. Visual microscopic damage to chromosomes, the organized complex of DNA and proteins within higher cells that is visible during cellular division, is a good indicator of genotoxicity. Two chromosome studies of potentially exposed workers were cited by these authors. One study of eight accidentally sprayed field workers found damage from the high toxaphene concentrations. Another study of agriculture workers handling toxaphene didn't find injury from routine exposure. Simon and Manning point to the inconsistency between the two field studies as proof there is ambiguity over toxaphene and chromosome damage. However, field studies of accidentally exposed workers are independent studies, not laboratory controlled studies, and each type exists separate from the other. There are no correlations within the studies between toxin dosages or between cohorts (age, sex, size, diet, etc.). There are unequal sample sizes; and no control on when and how chromosomes are derived from cells. Under these conditions the parameters are all variables; thus, one study cannot be used to refute the other, as Simon and Manning have done. Scientists have rules for comparing data sets. Simon and Manning ignore those rules to reach the conclusion they prefer.

Developmental Effects of Toxaphene

Both *in vitro* and *in vivo* (laboratory studies using isolated cells or whole animals, respectively) show that toxaphene causes developmental effects. There is no dispute among scientists that toxaphene changes the way organ systems develop in growing animals. Simon and Manning argue in section 2.1.2 of their paper that doses that induce developmental effects in the laboratory can be used as a not-to-exceed level for toxaphene in the environment. We could not figure out, from the information provided, how they calculated safe dosages for toxaphene using the literature cited in their article.

Toxaphene and Cancer

Toxaphene is carcinogenic. *In vivo* studies show toxaphene causes cancer in laboratory animals. It is interesting and significant that Simon and Manning do not cite studies that show toxaphene is clearly carcinogenic. We restate these findings here:

"*Two long-term carcinogenicity bioassays with toxaphene have been performed in rats and mice with both species showing a carcinogenic response."*

"*A statistically significant dose-related increased incidence of thyroid tumors (adenomas and carcinomas) was seen in both male and female rats."*

"*A statistically significantly increased incidence of liver cancer in treated animals was observed and was dose-related*."

The only question is whether or not toxaphene also causes cancer in humans. Simon and Manning offer no models or observations that disprove or prove a link between toxaphene and human cancer. As already noted, toxaphene is mutagenic and, therefore, the potential to cause the mutations that lead to cancer is a possibility. Simon and Manning correctly note that toxaphene is a tumor promoter. Numerous studies using a variety of tools show that toxaphene acts to interrupt normal cellular communication, one definition of a tumor promoter.

Simon and Manning use data on breast cancer in Inuit women to support their model. The Inuit live in the circumpolar region and have a diet high in fish stocks; toxaphene is now found in fish tissues all over the earth.

Simon and Manning incorrectly infer that levels of toxaphene congeners observed in more recent times in the Inuit have always occurred. TT concentrations may have been higher, or lower, in the past. Inuits may be more, or less, at risk than the general population based on dietary, environmental, or genetic factors. That the Inuits' experience constitutes a proof of the authors' model is an extraordinary claim that requires extraordinary proof, and Simon and Manning offer no proof at all.

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Simon and Manning chose three of the several hundred toxaphene compounds to base testing for environmental toxaphene: p-26, p-50, and p-62. More data and field surveys are needed to determine if these three compounds are indicative of dietary fish residues. For aquatic food chain and rain deposition (atmospheric reflux) these compounds may indeed prove useful for monitoring food stocks, after more data has been collected and evaluated. However, to make the leap from blood plasma levels caused by eating contaminated fish caught near the Arctic Circle, to soil cleanups in the southeastern U.S., is scientifically invalid.

We concur that the logic of the approach has merit: there may be a set of TT congeners that are especially indicative of the presence of TT in both TT standards and weathered or off-grade materials. However, the three selected by Simon and Manning are arbitrary at this junction when applied to soil cleanups; the authors offer no data, nor is there any in the literature.

Over the past dozen years, the Environmental Protection Agency's Office in Region 4, Atlanta, Georgia, has used an alternative method of testing. The so-called Toxaphene Task Force alternative methodology employed a subset of the toxaphene congeners occurring on a gas chromatograph. The EPA's Office of Inspector General has reviewed toxaphene methods used in Region 4 and found that the TTF method underreported toxaphene, and was not representative of the state-of-the-art in environmental testing. Simon and Manning's three-congener method looks curiously similar to the discredited TTF methodology. More science is needed before any conclusions can be drawn.

Summary

It is not clear why tumor promotion is offered as an endpoint driving chromatographic analysis of samples. There is no controversy between experts regarding the mutagenicity or carcinogenicity of toxaphene. Toxaphene is mutagenic. Toxaphene causes cancer. Simon and Manning offer no argument for even needing to rely on tumor promotion for a reference dose.

There is no belief in the general scientific community that toxaphene is extraordinarily difficult to measure. The EPA's standardized Total Area method for measuring multi-component pesticides works. Gas chromatography negative ion mass spectroscopy works quite well.

Since there is no technological need for toxaphene analysis based on only three components, and no scientific rationale for using tumor promotion to drive that analysis, Simon and Manning propose a solution to a problem that doesn't even exist.

The Simon and Manning paper raises several issues related to analysis of environmental toxaphene. Unfortunately, the authors generalize, speculate, and infer to such a degree that meaningful conclusions cannot be drawn. One of greatest dangers in research is to assume what one is trying to prove. Assuming at the outset, that a particular conclusion should result, inevitably introduces bias in the conclusions. Such bias is evident in the Simon and Manning paper. The authors clearly state that just 3 of 800 toxaphene congeners can be used to determine the safety of soil at any cleanup site anywhere in the world.

"…*continued use of the more stringent toxicity assessment for technical toxaphene will result in inaccurate risk/hazard estimates and possibly unnecessary and overly costly cleanups."* (Section 4.3, last paragraph).

"More stringent toxicity assessments" refers to practices advocated by the EPA's Ombudsman. The authors argue that these three congeners are predictive regardless of the origin of the toxaphene, regardless of the form of environmental degradation, regardless of any extraction or instrument bias. In the process of selecting studies to support their view Simon and Manning ignored facts that disagree with their model.

Studies on the Inuit Indians do not exonerate TT as a potential source of carcinogenic chemicals. At this time, the numerous studies showing increases in breast cancer and other tumors in the Inuit have not been traced to a single source. Therefore, a contribution by TT to the overall cancer rate cannot be overruled. Further, this single endpoint cannot be the sole determining factor for soil cleanup in North America. Superfund law is based on multiple criteria: meets all laws; implementability; state acceptance, community acceptance; feasibility; reduction in toxicity, mobility, or volume; and, overall health of humans and the environment. Superfund criteria clearly state that it is the overall health of humans and the environment, not just humans, that must be considered. The authors have not shown that cleanup endpoints derived from humans near the artic circle could be protective for other species in North America. Without more hard physical data there is little difference between using the Region 4 Environmental Protection Agency's discredited Toxaphene Task Force (TTF) methodology and the model described in their paper.

Finally, congener "persistence" as an endpoint is fallacy. One can pick and choose references to argue that some congeners are only present at key points in the onset of a tumor as transient species. One can argue, using a subset of references, that congeners below the limits of detection are influential in cancer onset. However, to do either would be as invalid as Simon and Manning's flimsy thesis.

Conclusions and Recommendations

At this point in time, it is very clear that lines are drawn between the Region 4 EPA and practically everyone else regarding toxaphene analysis for the purposes of cleaning sites in the southeastern USA. The EPA seems intent on using the Toxaphene Task Force methodology, or its Simon and Manning clone. On the other side are numerous environmentalists and academic scientists, with similar credentials relative to the EPA, who argue current practices underreport toxaphene. Finally, there is the EPA's own Ombudsman who has tried to find the best available science and apply it to this case; however, in the years that the Office of Inspector General has been involved little progress has been made. It appears Region 4 will continue to use some variation of the discredited TTF method unless it can be shown, without equivocation, by some third party, neither EPA nor environmentalist, that the toxaphene measurement technology Region 4 is using cannot, and will not, work.

We note that the National Research Council of the National Academy of Sciences can perform the studies needed to clarify toxaphene measurement in the environment. The NRC has undertaken chemical-specific studies on asbestos, dioxin, trichloroethylene (TCE), and on numerous other environmental issues. Progress on cleaning the environment of toxaphene will not be made until toxaphene is defined; debating that definition has become an endless process. A third-party should be consulted and there is none more accepted than the NRC. We recommend that the Glynn Environmental Coalition seek to have a thorough review of toxaphene by a committee of the National Academy of Sciences.

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