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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
SOLID WASTE AND EMERGENCY RESPONSE

October 2, 1996

MEMORANDUM

SUBJECT: Johnston Atoll Chemical Agent Disposal System (JACADS)
Risk Related Issues

FROM: Timothy Fields, Jr., Deputy Assistant Administrator
Office of Solid Waste and Emergency Response (5101)

TO: Julie Anderson, Director
Waste Management Division (H-1)

Thank you for your memorandum of July 25, 1996 requesting clarification of EPA's policy on risk related issues concerning the Johnston Atoll Chemical Agent Disposal System (JACADS). As you indicated in your memorandum, many of these issues are national in scope and have generated interest by members of the public at a number of combustion facilities. Specifically, we have noted that similar risk assessment issues have been raised by the public at other proposed chemical demilitarization facilities.

As you are aware, EPA's draft site-specific combustion risk assessment guidance was issued in April 1994. EPA Region VI, in concert with the Office of Solid Waste and Emergency Response (OSWER), is in the process of evaluating the 1994 guidance for the purpose of developing an update. Below please find provisional responses to the five issues raised in your memorandum. For your convenience, each request for clarification has been restated followed by the applicable response.

Issue 1:

The Agency's current method for assessing the

non-carcinogenic risks associated with dioxin exposure(s) in the context of site specific risk evaluations, especially in terms of terrestrial background dioxin levels - which have been viewed as currently posing an unacceptable carcinogenic risk (Health Assessment Document for 2,3,7,8-Tetrachlorodibenzo-p-Dioxin (TCDD) and Related Compound, EPA June 1994, EPA/600/BP-92/001).

Response:

The Agency's policy regarding risks presented from exposure to dioxin, as set forth in a September 11, 1991 memorandum from the Administrator, was to continue to evaluate risks from dioxin in accordance with the 1985 dioxin assessment until such time as the Agency's reassessment of exposures to and risks from dioxins had been completed. The 1985 assessment called for the evaluation of toxic effects of dioxin based upon their carcinogenic potential only; a reference dose for evaluating non-cancer health effects of dioxin was not established.

EPA issued the draft dioxin reassessment in 1994. The reassessment concluded that adequate evidence exists to support the inference that humans are likely to respond with a broad spectrum of effects from exposure to 2,3,7,8-tetrachloro-p-dibenzodioxin (hereafter referred to as dioxin) and related dioxin-like compounds, if exposures are sufficiently high. This conclusion was based upon results from studies in human populations, experiments with laboratory animals, and ancillary experimental studies. The effects induced may range from adaptive changes at or near background levels of exposure to adverse effects with increasing severity as exposure levels increase above background. Enzyme induction, alterations in hormone levels and indicators of altered cellular function are examples of effects of unknown clinical significance; they may or may not be early indicators of toxic response. Clearly adverse effects including, perhaps, the induction of cancer may not be detectable in experimental studies until exposures exceed background levels by one or two orders of magnitude (10 to 100 times).

The deduction that humans are likely to respond with adverse non-cancer effects to dioxin and dioxin-like compounds is based on the fact that these compounds impact cellular regulation at a

fundamental molecular level in the diverse range of animal species which have been shown to respond with adverse effects. Further, similar impacts on cellular regulation haw been demonstrated in human cells in culture. Available evidence indicates that humans most likely fall in the middle of the range of sensitivity for individual effects among animals. Thus, humans do not appear to be either extremely sensitive to or extremely insensitive to the individual effects of dioxin and dioxin-like compounds.

For the most part, the biochemical, cellular and organ-level effects have been observed in experiments in which only dioxin was studied. Specific data on the effects of dioxin-like compounds, such as the pentachlorinated and hexachlorinated dioxin and furans, generally are not available. Despite this lack of data, evidence exists that all dioxin-like compounds may exhibit similar effects to a greater or lesser degree. This derives from the concept of toxicity equivalence, specifically the fact that these compounds, like dioxin, bind to the intracellular aryl hydrocarbon (Ah) receptor and have effects on intracellular regulation. Toxic equivalency factors (TEFs) have been developed for all 17 chlorinated dioxin and furans containing chlorine substitutes in at least the 2,3,7 and 8 ring positions. The TEF for dioxin is 1.0; the TEFs for the 16 other congeners are derived from this value. Greater uncertainty exists with respect to the extent of non-cancer effects of the 16 other congeners as compared to those of dioxin due to the very limited amount of toxicology testing of these congeners. Hence, greater uncertainty is associated with the TEFs of these congeners as compared to the TEF of dioxin.

Given the above, EPA's conclusion in the 1994 draft dioxin reassessment regarding non-cancer effects was that it is inappropriate to develop a reference dose for dioxin because these compounds are persistent in the environment and because background exposures to dioxin are not low compared to incremental environmental exposures. Most compounds to which reference doses are applied are not persistent and background exposures generally are low and not taken into account. Since existing background levels of dioxin are higher than a reference dose that could be developed, the draft dioxin reassessment concluded that it is not appropriate to use the reference dose approach in evaluating incremental exposures to dioxin. This conclusion does not mean that any incremental exposure to dioxin would cause an increase in

potential non-cancer health effects.

Based upon the findings of the 1994 draft dioxin reassessment and due to the recent increased concern regarding non-cancer effects of dioxin, the Office of Research and Development has recommended using, and OSWER agrees, on a provisional and site-specific basis, the "margin of exposure" approach for estimating potential non-cancer health effects arising from incremental exposures to dioxin. Under this approach, one determines the ratio of the estimated daily adult dose of dioxin from a particular source (e.g., the JACADS trial burn) to the average daily intake of dioxin in the general population. If the ratio of such exposures is very small (the facility specific exposures comprise a small fraction of background exposures), the non-cancer effects from the incremental exposure are judged to be negligible.

Issue 2:

The most appropriate data subset for the determination of dioxin carcinogenic potency factors. Conflicting carcinogenic potency factors derived from human epidemiologic studies versus laboratory animal findings should be reconciled.

Response:

The cancer potency factor for dioxin was verified in 1985 for use in EPA risk assessments. It was derived using results from carcinogenicity studies in experimental animals which demonstrate that dioxin is a carcinogen in multiple species of animals.

Since 1985, results from additional human mortality studies have become available which support an association between exposure to dioxin and related compounds and increased cancer mortality in humans. However, uncertainties exist in interpreting these studies because not all confounding exposures (e.g., smoking) has been ruled out and coincident exposures to other carcinogens were likely. It is the conclusion of the 1994 draft dioxin reassessment that dioxin and related compounds are probable human carcinogens. The EPA Science Advisory Board, an independent group of experts, peer reviewed the draft dioxin reassessment in 1995 and also concluded that dioxin is a probable human carcinogen

based upon sufficient evidence of carcinogenicity in animals and limited evidence in humans.

In the draft dioxin reassessment EPA presented a potential cancer potency factor based upon the results of one human study, but concluded that the existing data from human studies alone do not provide the best estimate of the cancer potency of dioxin. The Agency concluded that a weight-of-the-evidence approach should be used that considers all relevant data from studies in humans and experimental animals, as well as data on mechanisms of action. In that document the Agency proposed a new cancer potency factor for dioxin which is slightly lower than the slope factor adopted in 1985. The Science Advisory Board also concluded that a cancer potency factor based upon the one human study utilized in the dioxin reassessment was not appropriate for use.

Until such time as the dioxin reassessment is finalized and a new cancer slope factor is adopted by EPA, the Agency will continue to use the cancer slope factor (156,000 per mg/kg/day) developed in 1985. This represents a plausible upper bound on risk based on the evaluation of animal and human data. "True" risks are not likely to exceed this value, may be less, and may even be zero for some members of the population.

Issue 3:

The Agency's method for assessing the risks associated with exposure to either the sulfur or brominated analogs of dioxin - given precursor presence in waste feed stocks.

Response:

At this point in time, the Agency does not evaluate risks associated with exposure to sulfur analogs of dioxin. Although there have been some reports of the formation of chlorinated dibenzothiophenes (sulfur analog of dibenzofuran), EPA is not aware of similar reports on the formation of chlorinated dioxin thioethers (sulfur analogs of chlorinated dibenzo-p-dioxins). The furan compound, which is part of the dibenzofuran structure, is more stable than thiophene, part of the dibenzothiophene structure. Chlorinated dioxin thioethers may not have been observed to date because of the potential instability of these

compounds. The carbon-oxygen bond is stronger than the carbon-sulfur bond; chlorinated dioxin thioethers contain two carbon-sulfur bonds in the central ring of the structure whereas chlorinated dibenzodioxins contain two carbon-oxygen bonds.

With respect to brominated and chlorobrominated analogs of dioxin, studies (Zacharewski et al, 1988; Mason et al, 1987) have shown selected brominated and chlorobrominated dioxins to be comparable in toxicity to chlorinated dioxins in certain short-term toxicity assays. Polybrominated dibenz-p-dioxins and dibenzofurans have been measured in municipal waste combustors and have been shown to form in the gas phase of laboratory scale incinerators.

An assessment of the fraction of brominated versus chlorinated compounds that are present in the waste feed should be performed for each facility which burns hazardous waste. An uncertainty factor can be added to the estimated or measured chlorinated dioxin emissions to account for the potential impact of brominated and chlorobrominated compounds. Such an approach was utilized in the in-depth risk assessment of an incinerator in East Liverpool, Ohio. The waste feed for the first year of operation was reviewed and the amount of brominated waste was compared to the amount of chlorinated waste. An uncertainty analysis was then performed.

A similar measurement of brominated dioxins and furans in the stack emissions would be difficult at this time since analytical methods are not yet well-defined. The National Risk Management Research Laboratory (NRMRL) of the Office of Research and Development at Research Triangle Park, North Carolina has conducted a preliminary study of chlorinated, brominated and mixed bromochloro dioxins and furans in incinerator stack emissions. However, further research is still necessary to better quantify these compounds and to further develop the appropriate sampling and analytical methodologies.

Issue 4:

The Agency's treatment of putative compound synergistic interactions when applied to the assessment of facility specific risk.

Response:

Because the current scientific database on synergistic effects (or on antagonistic effects) of multiple contaminants in complex mixtures is not complete enough to determine if such effects are occurring, it is EPA's policy to not evaluate such effects at this time. With respect to carcinogens, EPA guidance for assessing risks of complex mixtures is to assume additivity of risks at low doses (Guidelines for the Health Risk Assessment of Chemical Mixtures, 1986). This assumes independence of action by the various carcinogens and is equivalent to the assumption of dose addition as well as response addition. The combined effects of antagonism and additivity are assumed to balance the possible effects of synergism. This assumption is believed to be protective of human health. Should sufficient verified data become available on the interactions of the chemicals in a given complex mixture, then such results could be used to evaluate the cancer risks of that mixture.

For systemic toxicants, the assumption of dose addition is most properly applied to compounds that induce the same effect by similar modes of action such that a separate hazard index is generated for each endpoint of concern. Dose addition for dissimilar effects does not have strong scientific support and, if done, needs to be justified on a case-by-case basis in terms of biological plausibility. The assumption of dose addition is most clearly justified when the target organs or tissues and the mechanisms of action of the compounds under consideration are known to be the same (Guidelines for the Health Risk Assessment of Chemical Mixtures, 1986). Since the mechanisms of action for most compounds are not well understood, the justification of the assumption of dose addition will often be limited to similarities in pharmacokinetic and toxicologic characteristics. Where it is made, the assumption of dose additivity is generally believed to be protective of human health.

Issue 5:

The Agency's position on "endocrine disrupting" compound(s) in the context of site specific risk evaluations.

Response:

The term endocrine disruptor applies to any number of a broad class of compounds with the ability to perturb or interfere with the finely-tuned endocrine system that is fundamental to normal function and homeostasis in cells, tissues, and organisms. Examples of chemicals suspected of being environmental endocrine disruptors are DDT, chlordane, polychlorinated biphenyls, and polychlorinated dioxins and furans. The evidence of adverse health effects resulting from exposure to endocrine disruptors stems from a body of diverse historical information, augmented by new findings. This evidence, however, lacks sufficient detail and precision to be used in a site specific risk assessment. Indeed, empirical data to support the designation of specific chemicals as endocrine disruptors is limited and in some cases conflicting. Given the current limited state-of-the-science, it is premature to attempt to evaluate the potential risks from human exposures to chemicals from the standpoint of endocrine disruption. Therefore, EPA has not yet developed a methodology for the quantitative assessment of risks due to exposures to potential endocrine disruptors.

I hope that the above responses provide sufficient clarification of the Agency's position on the issues raised. Should you have any additional questions or comments, please feel free to contact James Michael or Rosemary Workman, at (703) 308-8610 and (703) 308-8725 respectively, concerning chemical demilitarization issues or Dorothy Canter, at (202) 260-3100, concerning risk assessment issues.