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To California Department of Pesticide Regulation and the External Science Advisory panel,

I am a postdoctoral fellow at the Program for Reproductive Health and the Environment at UC-San Francisco. I understand the current step in this process is for the science advisory panel to comment on the CDPR's assessment of MeI, which I will discuss later in this letter. I am also writing today to highlight not only reproductive development and neurotoxicity concerns of methyl iodide, but to speak as a chemist. I am very concerned with the replacement of methyl bromide with methyl iodide. I agree with the 1986 decision to phase-out methyl bromide because of its reactivity with the ozone layer, but methyl iodide doesn't impact the ozone as much as methyl bromide not because it's *less* reactive, but because it's actually *more* reactive and will interact with humans, animals and the environment before reaching the upper atmosphere.

I received my PhD in Chemistry from UC-Berkeley a year and a half ago and when I speak to fellow chemists about the possibility of replacing something as toxic as methyl bromide with an even more reactive compound, they often laugh at me and think I'm not being serious. And since most chemists are unfamiliar with pesticide practices, when I tell them that we spray hundreds of pounds of methyl bromide on soil at a time, they are shocked. When I tell them methyl iodide is the proposed replacement for methyl bromide, they are stunned.

Methyl iodide is a registered carcinogen in California (prop 65) and is known to cause serious health effects such as thyroid hormone and central nervous system disruption, and neurotoxicity in addition to cancer.

Synthetic chemists use methyl iodide in their reactions because it is an extremely reactive alkylating agent, but we use it only under extremely protective conditions – in a fume hood, with appropriate personal safety equipment, and only then do we handle this liquid via a syringe in a sealed container to prevent exposure because we know it's an efficient DNA methylator that will increase our likelihood of cancer. And we use these precautions for when we are working with very small amounts—a few drops to a few milliliters. The USEPA has determined it safe to spray up to 175 pounds PER ACRE, 40 acres at a time of this compound onto fields with a buffer zone of 500 feet. The buffer zone is only 25 feet if you spray fewer acres.

At UCSF, a major focus of our group's research is how environmental factors may affect reproductive health and development. The thyroid hormone system regulates not only reproductive development, but also general metabolism, growth and neurodevelopment. The structure of the main thyroid hormone contains iodine, and is the reason iodine is an essential micronutrient. However, too much iodide exposure leads to suppression of thyroid hormone synthesis, and severe perturbations in the endocrine system. These can cause serious consequences on neurologic development and have long-term adverse reproductive health outcomes.

One of the toxicity endpoints of greatest concern to CDPR is perturbation of thyroid hormones of adults and fetus. (pg. 172, vol I) During fetal development, the mother is the only source of thyroid hormones for the baby and therefore, a perturbation in the mother can also lead to an imbalance in the fetus. Fetal development

is a period of rapid growth and development of essential organs and internal systems and very small perturbations can lead to severe adverse effects months and years down the road. Moreover, the populations that are most likely to be exposed to MeI are already exposed to other pesticides in their daily lives, and this leads to higher chemical body burdens and should be considered in the risk assessment.

In pregnant rats and rabbits, methyl iodide causes thyroid hormone disruptions, fewer viable fetuses, lower birth weight, and increased fetal death, especially during late pregnancy. According to its MSDS sheet, it's also a neurotoxicant that can be absorbed through the skin as well as inhaled. The USEPA's website states "short-term exposure may depress the central nervous system, irritate the lungs and skin, and affect the kidneys. While "long-term exposure may affect the central nervous system and cause skin burns."

While there is a high rate of volatilization (or evaporation into the air), and our low-organic matter soils in California have higher rates of volatilization compared to higher-organic matter soils, there are other degradation routes for MeI that are known to occur in the soil-water environment, and they all yield an iodide ion (pg. 6, vol 3). Iodomethane is also more persistent than methyl bromide in soil and water, which early investigators who studied the environmental fate & transport, suggested would lead to more groundwater contamination from methyl iodide. (Gan, Yates, et al, J. of Env. Qual., 26, 4, 1107-1111, 1997). The CDPR estimates that inhalation exposure for bystanders and groundwater exposures together would surely exceed safety limits for iodide set by the National Academy of Science and ATSDR.

I agree that the CDPR's assessment is an improvement over the USEPA's assessment, and now I'll discuss some of the specific parts of the risk assessment I found important.

- CDPR more appropriately used a directional wind parameter in their calculations and found that estimated exposures for bystanders were 375 times higher than the determined safety limit and 3000 times higher than the limit for workers. Clearly, this is an additional reason to look carefully at allowing such a potent toxicant into our environment in such large amounts. The model used by EPA to calculate wind drift and bystander exposures did not take into account directional wind, which is most often the case in reality.
- CDPR recommends an extra 10-fold uncertainty factor because of the absence of sufficient pre-and post-natal developmental neurotoxicity data. This would result in an even higher benchmark dose as well as proportionally lower calculated reference concentrations. USEPA argues that MeI is a non-food use pesticide and consequently is not subject to the 10x safety factor required under the Food Quality Protection Act (appendices pg. 64 or C-4). Nevertheless, children will be exposed and they are more sensitive to carcinogens. CalEPA's OEHHA has published a detailed analysis of the greater sensitivity of children to carcinogens. Children are also more susceptible to thyroid hormone disruptions, as they are growing and developing faster. Additionally, children receive a higher dose because they breathe about twice as much air per pound of body weight than adults.
- The uncertainty factor CDPR recommends is 300—10 times larger than USEPA. However, even if you only apply the 30x uncertainty factor to the USEPA 24-hour HEC for fetal death endpoint, the estimated excess iodide burden would be up to 10,400 ug/day. This is 30-90 times higher than tolerable upper limits set by the National Academies of Science and the ATSDR for iodide exposure.
- CDPR more correctly estimates exposures to iodide by including water sources as well--USEPA only considers exposure to MeI from air. CDPR found that "From both water and air, the calculated iodide

intakes under most cases are higher than established health standards for iodide. Thus, the recommended MeI RfCs for any duration should be much lower, at levels not to exceed 1ppb, for the protection of young children”(pg. C-4 and C-5 of appendices). The CDPR’s assessment of groundwater fate discusses the lack of data on fate of iodide ions after application. The only studies in California show low levels of iodide in the soil but did not determine the ultimate fate of the iodide. Additionally, this study did not address long-term repeated application situations, which are typical for annual crops and how this might affect groundwater contamination.

- Determining a lower NOAEL for fetal death than USEPA is an improvement, but the more scientifically appropriate method is to use a benchmark dose model. These linear models are much better representations of the dose-response behavior. By using NOAEL methods, USEPA ignored the large percentage of fetal deaths during mid-range dose experiments.
- Rather than using overt health outcomes such as thyroid hormone tumors and fetal death to calculate reference concentrations, CDPR should use the doses that indicate earliest observed adverse endpoints such as the glutathione depletion seen in these experiments. The USEPA actually recommends this method of risk assessment, but the pesticide office does not use it.
- There is no safety factor considered or discussion of, background chemical exposures or co-exposure incidences—populations living in agricultural areas are also exposed to other pesticides year-round and these contribute to higher body burdens and increased overt health outcomes in these groups.
- The formulation of this pesticide is such that is mixed with another highly toxic fumigant, Chlorpicrin. I’m told this is because chlorpicrin is a strong lachrymator and this will aid workers in determining if they have been acutely exposed because methyl iodide has very little smell. There is nothing in the risk assessment that addresses the fact there will be simultaneous exposures to both of these chemicals.

In summary, California Department of Pesticide Regulation has done an improved risk assessment, but it’s still incomplete. I encourage the science advisory panel to support their findings and even though I believe some improvements could be made in their findings that would probably lower reference concentrations, and there are a couple areas where there are some gaps in the data, I do not think more data or toxicity tests will somehow find this chemical safe to use as a soil fumigant. It is more toxic than the MeBr it’s replacing and since CDPR concludes that people will most likely be exposed at levels much higher than the reference concentrations, allowing MeI to be used as a pesticide *will* have adverse effects on public health.

Sincerely,

Amber R. Wise, PhD