

2013

and Risk Decision

Evaluating Pesticide Approval in California

Review
of the
Methyl Iodide
Registration Process

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The Sustainable Technology and Policy Program, a joint undertaking of the UCLA Schools of Law and Public Health, is an interdisciplinary research and education program. Its mission is supporting the development of effective, balanced chemical policies, and the spread of safer chemicals and alternative manufacturing processes in the marketplace. STPP brings together researchers from across the UCLA campus and beyond with non-governmental agencies, policymakers and businesses in a unique, action-oriented initiative.

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I Introduction

Fumigant pesticides are widely used in agriculture in California and other states to control soil pests for high-value crops such as strawberries, peppers, tomatoes, and stone fruits. These fumigants essentially sterilize the soil and permit the same crop to be planted year after year on the same land. Before they can be used in California, new pesticides generally must be approved by the California Department of Pesticide Regulation (DPR) in a process known as registration. This report focuses on one fumigant—methyl iodide—and the story of its registration in California.

Most new pesticides are typically less toxic than their predecessors. Methyl iodide was different. It is a neurotoxicant, known to cause lasting neurological damage, including psychiatric symptoms and chronic movement disorders resembling Parkinson's disease. It is a developmental toxicant, impairing fetal development and causing structural abnormalities and functional deficiencies in the offspring, as well as fetal death, all observed at relatively low doses. It causes DNA damage and mutations and is listed as a Proposition 65 carcinogen by the state of California. It vaporizes readily at ambient temperature, and when used as a soil fumigant at several hundred pounds per acre as proposed, forms a gaseous plume of methyl iodide that drifts away from the application site.

In December 2010, DPR approved methyl iodide (MeI), as a replacement for the widely used fumigant methyl bromide. Methyl bromide is being eliminated globally because of its stratospheric ozone depleting properties. This approval followed the conditional registration of methyl iodide as a pesticide by the United States Environmental Protection Agency (EPA) in 2007. Due in large part to the questions regarding the toxicity of methyl iodide, the registrations of methyl iodide by EPA and DPR were highly contested, and there was controversy surrounding its approval including a law suit.

After the spotlight on the toxicity of methyl iodide, farmers were reluctant to adopt the new fumigant. Five methyl iodide fumigations on fewer than 20 acres were conducted in California after the registration was finalized. On March 21, 2012, citing economic reasons, Arysta Life Science voluntarily withdrew all methyl iodide-containing products from the U.S. market. In November 2012, EPA announced that Arysta Life Science had voluntarily requested cancellation of its

methyl iodide product registrations and in January 2013, EPA granted this request.

This report uses methyl iodide as a case study to explore the limitations of the risk governance approach reflected in California's registration process. Risk governance refers to the social, legal and institutional decision-making processes used in identifying and responding to risks facing society. In evaluating the scientific, social, and legal dimensions of registration, the report draws upon reports, letters, hearing transcripts and other documents generated as part of the registration process. From existing literature, it identifies best practices for the relevant elements of risk governance—Problem Identification/Framing; Risk Assessment; Evaluation/Option Selection; and Stakeholder Communication—and assesses the methyl iodide registration process against them.

That assessment identified a variety of deficits in the pesticide registration process, implicating four general themes underlying risk governance. Effective risk governance should be realistic when framing and assessing risk, taking into account multiple and cumulative risks facing individuals. It should be based on the best available science and data, and should deal cautiously and conservatively with data gaps, uncertainty, and variability. It should take the concept of prevention seriously, carefully considering the availability of safer alternatives. Finally, it should be a transparent and interactive process, involving all stakeholders in a meaningful way. The report concludes by presenting recommendations to improve pesticides risk governance in light of these themes, drawing in large part from new approaches offered by the National Research Council (NRC) in 2009¹ as a way forward.

A. The Registration Process

Methyl iodide was introduced as a substitute for methyl bromide, a widely used fumigant slated for phaseout in 2015 under the Montreal Protocol on Substances that Deplete the Ozone Layer and Clean Air Act. Methyl bromide was officially phased out from use in the United States on January 1, 2005 and is now only permitted for use under a Critical Use Exemption (CUE) program, where U.S. EPA allows use because there are no “technically and economically feasible alternatives.”² Growers of high-value crops on which the greatest amounts of methyl bromide are used would thus have been the most likely methyl iodide users: tomatoes,

strawberries, peppers, almonds, tobacco, watermelon, walnuts, and cucumbers. Many of those growers are in California, where approximately 30 million pounds of soil fumigants are used every year. The primary fumigants currently in use in California agriculture are methyl bromide, 1,3-dichloropropene (Telone™), metam salts (sodium or potassium), dazomet, and chloropicrin. Although the mix of fumigants has changed over the years, the total annual use has been relatively constant over time (Figure 1).³

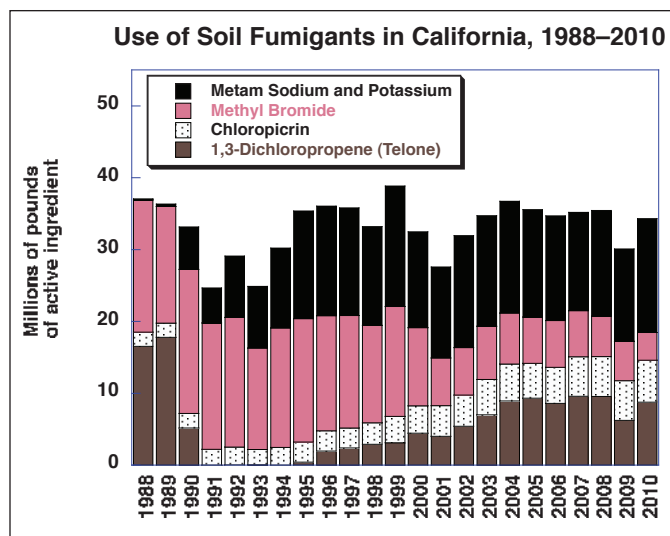


Figure 1: Fumigant use in California has remained relatively constant over the last 20 years. *Data Source:* Reference 3.

With many farmers dependent on methyl bromide and the phase-out deadline fast approaching, research into alternatives accelerated in the early to mid-1990s. Methyl iodide was considered one of the most promising candidates and it is not an ozone-depleting chemical. It controlled the same pests and could be applied using the same equipment and methods used for methyl bromide, so agricultural researchers envisioned the transition as being relatively seamless.

Upon receiving an application for registration, DPR evaluates the product to establish its efficacy and safety. DPR staff scientists evaluate the application and the scientific data concerning the functionality of the product, potential human and ecological exposures, and the human health and environmental effects of its use. If, as in the case of methyl iodide, they conclude that there is a potential for adverse health effects, they perform a risk assessment, with input from outside experts from other agencies. In this case, DPR initiated a peer-review process by establishing an independent Scientific Review Committee (SRC). The SRC was charged with evaluating the methods, content, and

conclusions of the DPR staff risk assessment. The SRC held a two-day public workshop on the draft DPR risk assessment that included presentations from U.S. EPA, DPR, Arysta, and a number of NGOs.⁴ Time was also dedicated to public testimony from a variety of interested parties, including farm workers, farm owners, the methyl iodide patent holder, other scientists, and NGOs.⁵ After extensive review, the SRC submitted a set of critiques and recommended changes for the DPR draft risk assessment. DPR staff made changes to its draft risk assessment documents in response to SRC suggestions.

On April 30, 2010, the Director of DPR recommended the registration of five products containing methyl iodide in a Notice of Proposed Decision. This notice included summary risk calculations and mitigation recommendations to be incorporated in product labeling. As required by law, DPR opened a 30-day public comment period. Due to a high degree of public interest, DPR later provided an additional thirty days for comment. On December 1, 2010, DPR issued the final registration approving methyl iodide for use in California.⁶

B. Overview of Risk Governance

Broadly conceived, risk governance is the manner in which a society identifies and responds to risks facing it. In the context of human health and environmental protection, risk governance has historically been characterized as government-centric, consisting of the two related steps of risk assessment and risk management, both of which are largely conducted or overseen by regulatory agencies following formal legal procedures.¹ More recent literature on risk governance in the area of environmental health expressly acknowledges and incorporates the role of informal actions of, and interactions among, regulators, stakeholders and other interested parties.^{7, 8, 9}

The leading models of risk governance share four central elements: Problem Identification/Framing; Risk Assessment; Evaluation/Option Selection; and Implementation/Monitoring.¹ As set out in Table 1: Elements of Effective Risk Governance, each element includes a set of functional components reflecting the steps or activities included in that element.

This study evaluates the DPR registration process for methyl iodide against the modern risk governance framework. The evaluation covers the formal legal

Table I: Elements of Effective Risk Governance

Element	Functional Components
Problem Identification/Framing	<ul style="list-style-type: none"> • Systematic identification of new risks • Problem definition • Decision rule/process selection • Identification of potential options • Effective communication with stakeholders
Risk Assessment	<ul style="list-style-type: none"> • Risk assessment (quantitative and/or qualitative) • Effective communication
Evaluation/Option Selection	<ul style="list-style-type: none"> • Evaluation of potential options • Option selection • Effective communication
Implementation/Monitoring	<ul style="list-style-type: none"> • Implementation of option, including securing, allocating and deploying resources • Monitoring and evaluation of outcomes • Effective communication

process set out in the relevant California statutes and regulations, as well as informal practices and interactions of the regulatory agencies, industry, non-governmental organizations and other stakeholders and participants. In doing so, this study identifies those areas in which the registration process—including both its formal and informal aspects—is effective in implementing the principles of modern risk governance. It also identifies risk governance deficits in the registration process and develops potential steps for their resolution. A risk governance deficit is defined for these purposes as a failure of a process to effectively implement one of the central risk governance components.⁷

Performing such an evaluation required that the authors articulate more precisely what constitutes “effective” risk governance in practice. With that end in mind, we conducted a survey of the literature on risk governance practices (including recent work by the National Research Council¹ with respect to risk assessment) to identify best practices within a regulatory context. We also reviewed the administrative record for methyl iodide registration, including all available documents generated by DPR and other regulatory agencies involved, public comments, records of the SRC, and records of individual meetings and telephone conversations between DPR staff and other parties. By comparing the registration process as revealed in the documentary and legal research to the best practices, we identified those areas in which that process was effective and where it fell short.

In the sections that follow, we present the results of the evaluation for each of the risk governance elements. Each section provides an overview of the specific element under consideration, a description of best practices and common deficits found in the literature, and ultimately an evaluation of the performance of the methyl iodide registration process regarding that element. The report concludes with recommendations for improvement of the pesticide registration process.

II Problem Identification/Framing

A. Overview of Best Practices

The Problem Identification/Framing element involves the detection and definition of a risk facing society, and articulation of the process for assessing and responding to that risk. It includes four components:

- **Early identification of new risks.** This component consists of the initial identification of the relevant risks as well as initial efforts to generate data regarding the scope, nature and likelihood of the potential harms associated with those risks. In the case of commercial products subject to regulatory oversight, detection of the

risk often occurs when the manufacturer notifies the regulatory agency of the planned use.⁸

- **Problem definition.** This component involves articulating the specific health, environmental and other risks of concern. It is critical to establishing the appropriate scope of the risk assessment—the hazards, pathways of exposure and populations to be addressed. Contemporary formulations of risk governance emphasize the value in thinking broadly in this regard—putting the problem in a realistic context. For example, contextual problem definition in pesticide regulation would consider other associated risks faced by the relevant population, such as exposure to other chemicals the population faces.⁸ Problem definition also includes identifying and obtaining the information needed to engage in meaningful assessment of the problem. Lastly, establishing the goals of the risk governance process is part of problem definition as well.
- **Decision rule selection and risk manager/ stakeholder identification.** This component establishes the standards by which decisions will be made, and the parties who will be involved. In part, this imperative is driven by pragmatic concerns of efficiency and rigor. This component is also important in that it enhances the legitimacy of the risk governance process by providing a measure of transparency and coherence to the process. Clear decision rules at the outset coupled with early stakeholder participation signals to all interested parties that the process will be open and principled, both important aspects of legitimacy.^{10,11}
- **Option Identification.** Recent formulations of risk governance particularly stress the need to identify the range of potential management options early in the process.^{1,8} From a practical standpoint, delay in identifying options can result in insufficient information at the evaluation stage.⁸ Early identification of options is important as a substantive matter as well. Exclude potential options early on, and risk managers may be left with inadequately protective responses when it comes time for evaluation. In particular, knowledge regarding management options can shape other activities in risk governance, such as the scope and nature of the risk assessment and identification of relevant stakeholders.¹

B. Positive Aspects of the Methyl Iodide Registration Process

The DPR risk governance process for pesticides exhibits a number of positive features in terms of problem identification and framing. Most notably, regarding *early identification of risks*, DPR's program adopts a pre-market review approach, meaning that it restricts the introduction of new pesticides into commerce without prior review and approval by the regulatory agency.¹² This provides an opportunity for systematic identification of risks associated with new fumigants and other pesticides before their general use. This is in contrast to the process for introducing non-pesticidal chemicals into the marketplace, which requires no review.

The DPR registration process also provides an opportunity for careful evaluation of *problem definition*, including identifying specific risks of concern, data generation and collection, and goal setting. Regarding specific risks of concern, the agency follows a methodical approach making use of the wide range of expertise and disciplines represented among its professional staff. A decision options memorandum prepared for top managers at DPR described the input received from staff in these areas, and explained how the staff concerns were addressed.¹² Concerning data generation and collection, the statute and associated regulations provide DPR with clear authority to require the registrant to engage in toxicological and ecological testing and monitoring to inform the registration process,^{13,14} including mandatory health effects studies¹⁵ and studies regarding groundwater impacts.¹⁶ Goals are well defined also. The California Food and Agricultural Code identifies the specific goals of the pesticide registration program.¹⁷ In its regulations DPR identifies a goal of registration to be selection of “a risk-reduction strategy of integrated measures that are scientifically sound and cost-effective, and that reduce or prevent risks while taking into account social, cultural, ethical, political and legal considerations.”²⁰ In practice, DPR does not consider promotion of nonchemical or least-toxic methods in farm fields as a specific goal of the registration program; i.e., it does not use its regulatory authority to mandate use of safer alternatives.¹⁸ Instead, the agency relies upon a combination of voluntary programs and incentives (such as expedited review of reduced-risk pesticides) to encourage development and adoption of safer chemical alternatives.^{18,19}

Decision rule selection and risk manager/ stakeholder identification. Section 12825(a)–(h) of the California Food and Agricultural Code provides a set of factors that may be considered by DPR in evaluating a pesticide registration application. A finding that any one of these Section 12825 factors exists provides grounds for denial of the registration.²⁰ DPR regulations establish specific criteria based on the Section 12825 factors,²¹ requiring the DPR director to give special attention to them in reaching a decision to register or not register the pesticide. The criteria include acute and chronic health effects, environmental impacts, efficacy and the availability of alternatives.²² Neither the regulations nor DPR guidance documents describe how the (a) through (h) factors were to be applied or set out their importance *vis-à-vis* each other.

The DPR review process has no formal means for identifying relevant stakeholders in the registration process, apart from inviting public comment on its risk assessment and on its proposed registration decision.^{23, 24} In the case of methyl iodide, DPR convened an independent *ad hoc* Scientific Review Committee (SRC) to review the risk assessment. The SRC held a two-day public meeting, hearing presentations from government, industry and NGO stakeholders. Perhaps most notably, the SRC also opened the meeting for public comment.²⁵

C. Governance Deficits in the Methyl Iodide Registration Process

Here we focus only upon the deficits relating to problem definition, decision rule/stakeholder selection, and option identification in the methyl iodide registration process. Early identification of risks is excluded because we did not identify deficits associated with that component. As identified in Table II, the DPR registration process exhibits governance deficits in five areas:

1. Demand Pressure Coupled with Risk Research Gaps

Substantial pressure for access to a new technology can create a crisis-like environment that shapes the problem definition process in ways that facilitate registration. The record in this case supports the conclusion that there was a strong demand pressure for registration of methyl iodide, and that DPR staff and management were acutely aware of that pressure. This perceived pressure was expressed by numerous industry speakers at the public hearing held by the SRC, and in written comments received by DPR industry-related stakeholders in response to its proposed registration decision.^{30, 31, 32, 33} A major pressure was the perceived need to rapidly replace methyl bromide.

Table II: Problem Identification/Framing Governance Deficits in DPR Registration Process

Affected Component	Governance Deficit	Description
Problem Definition	Demand Pressure	This deficit focuses on whether the pressure for quick access to the new technology impacts the problem definition process, creating an atmosphere conducive to other deficits. ²⁵ For example, in cases in which there is strong perceived desire for a transformative technology (such as cell phones) or replacement of a critical existing technology, risk managers may be more apt to frame issues narrowly or forgo or postpone risk research.
	Risk Research Gap	This deficit refers to the failure to engage in necessary risk research during early stages of development and diffusion of a new technology, and during problem definition. ²⁶ The resulting gap in relevant information can undermine comprehensive framing of the problem to be addressed in the governance process.
	Narrow Framing	Narrow framing can lead risk managers and stakeholders to develop less effective responses than if all relevant dimensions of the problem are articulated. ⁸ Narrow framing can also lead to unintended consequences and create conflict among risk managers and stakeholders. ^{10, 26, 27}
Decision rule selection and risk manager/ stakeholder identification	Limited Stakeholder Group	This deficit refers to the failure to identify the full set of relevant stakeholders early in the risk management process. The deficit may spring from inadequate effort by the risk managers, or flow from a lack of interest, capacity or resources of the stakeholder group. ^{28, 29}
Potential option identification	Narrow Alternatives	This deficit concerns the failure of the governance process to identify a full range of potential reasonable alternatives. ^{9, 10}

The Registration Branch established an ambitious schedule for the review process, especially with the added step of SRC review. The decision occurred immediately prior to the inauguration of a new governor and likely change in leadership at DPR. Staff appeared to be aware of the pressure for prompt action; in one internal memorandum the DPR Assistant Director reminded them that “we are on a very tight time frame for this pesticide.”³⁴

The characterization of methyl iodide registration as a response to the impending phaseout of methyl bromide thus created an atmosphere conducive to another deficit: the failure to engage in necessary risk research. This effect is most apparent with respect to gaps in information regarding the lack of testing for the developmental neurological toxicity of methyl iodide identified by the SRC. Methyl iodide causes fetal death in laboratory animals at relatively low doses, interferes with thyroid function, and is a neurotoxicant. For chemicals with these characteristics, the SRC noted that there was a very high probability that exposures to even lower doses of methyl iodide would impair fetal neurological development, resulting in developmental disabilities in the offspring of exposed mothers. DPR did not require Arysta to submit a developmental neurotoxicity study.

The second major gap in research was in the estimation of potential groundwater impacts. The application of methyl iodide to farm fields raised significant concerns regarding contamination of groundwater with methyl iodide’s degradation product—iodide. The exposure assessment in DPR’s final risk assessment noted that iodide is particularly mobile in types of soils to which methyl iodide would be applied.³⁵ DPR’s risk assessment concluded that DPR needed additional information regarding groundwater contamination if methyl iodide was to be used for soil fumigations.³⁶ Indeed, before and after the completion of the risk assessment, DPR staff consistently expressed the opinion that there were insufficient data to predict how iodide might dissipate through the soil and into the groundwater.^{35, 37, 38} Ultimately, no dissipation study was required and the registration moved forward. While the administrative record is silent on why DPR did not require the study, testimony of a manager from the Environmental Monitoring Branch during the SRC’s public hearing suggests that DPR adopted an “approve first, monitor and mitigate later” approach. Such an approach is inconsistent with the principles of effective risk governance. In this case, there was a clear and significant

data gap, and well-established methodologies in the form of groundwater studies for closing that gap.³⁹

The final significant risk research gap was in the modeling of anticipated emissions of methyl iodide from farm fields. An individual’s potential exposure to a fumigant is dependent upon, among other things, the emission rate or “flux” of methyl iodide vapors after application, which in turn depends on the type of tarp used to cover the soil. Flux values are typically calculated using data generated from air monitoring of fumigant concentrations for a period of time after application up to and including the point at which tarps are removed (“tarp cutting”). Arysta submitted a number of studies calculating flux at test fields. DPR concluded that the studies were incomplete and deficient in that they used poor methodology, did not include measurements during tarp cutting or removal, and likely underestimated the air concentrations and flux.^{38, 40} Despite the lack of data regarding flux and emissions, DPR staff developed “worst case” calculations of emissions in a memorandum dated one day prior to the announcement of the proposed registration.⁴⁰

2. Narrow Framing

Effective risk governance seeks to place the issues of concern in a realistic context in an attempt to understand and address the issues meaningfully. For example, when a consumer or worker uses a product containing multiple chemicals, that consumer is exposed to all of the ingredients at once. Regulatory programs tend to take a chemical-by-chemical approach, examining the health risks of one chemical in isolation and essentially ignoring the others. The DPR methyl iodide registration process was just such a case.

The registration application submitted by Arysta covered methyl iodide itself, but also included registration of products marketed under the name of Midas. Three Midas formulations contained methyl iodide and a second fumigant—chloropicrin—as active ingredients, with chloropicrin percentages of 2%, 50% and 67% respectively. A 2010 DPR risk assessment of chloropicrin concluded that the weight of the available evidence supports classifying chloropicrin as a potent carcinogen and a glutathione depletor, similar to methyl iodide.⁴¹ Given those existing conclusions, one would expect the cumulative impacts of a mixture of the two chemicals to be of substantial concern in the registration process. In response to concerns raised by the SRC, DPR staff included explicit discussion of the methyl iodide/

chloropicrin mixture issue, but did not modify the risk analysis methods or conclusions.

3. Limited Stakeholder Group

Section VIII below (Effective Communication) describes in detail the manner in which DPR substantively dealt with the expressed concerns of the stakeholders. This deficit addresses the specific issue of the efforts made by the agency to capture the broad range of the interested stakeholders.²⁹ Generally speaking, DPR makes minimal effort to engage public stakeholders other than the registrant in the process of registering new pesticides. In the case of methyl iodide, the public participation process was enhanced due to DPR's request for expert review by the SRC.

The pesticide registration stakeholder process also includes mandatory consultation with a variety of other agencies. By statute, DPR must consult with the Office of Environmental and Human Health Assessment (OEHHA) on human health risks⁴² and in developing regulations intended to ensure worker safety.⁴³ Also DPR was required to consult with the California Department of Food and Agriculture (CDFA) pursuant to a legally mandated memorandum of understanding between the two agencies.⁴⁴ Through that consultation vehicle, CDFA is able to provide insights regarding, among other things, (1) impacts on agriculture resulting from the proposed action, (2) benefits derived from the use of the pesticide, and (3) any recommended alternative action.⁴⁴

While DPR met its obligation to obtain OEHHA input on the risk assessment, it did not allow OEHHA to participate in the development of the worker safety mitigation measures included in the registration decision, as required by law. DPR also limited CDFA's participation by providing late notice of the possibility of denial of registration.⁴⁵

4. Narrow Alternatives

As noted above, the early identification of potential alternatives allows for the development of sufficient data regarding and assessment of those alternatives. This enables risk managers to meaningfully evaluate the candidate pesticide as against potential alternatives as required by principles of effective risk governance and, in California, as required by law. See Section VIII (Evaluation/Option Selection (Risk Management)). The record is devoid of evidence of any effort by DPR to identify the nature or impacts of alternatives to registration. This includes the rather straightforward

question of whether existing fumigants could serve the same purpose with less significant human health or environmental impacts, as well as whether any safer, viable emerging technologies or cultural practices were available.

III Best Practices in Risk Assessment in the Scientific Community

A. Background

Risk assessment has formed the basis of environmental decision-making for the last 30 years and is considered to be the most quantitative approach to determining the risks associated with chemical exposure. Faustman and Omenn⁴⁶ and the National Academy of Sciences (NAS) have defined risk assessment as:

“the systematic scientific characterization of potential adverse health effects resulting from human exposures to hazardous agents or situations. This type of assessment includes qualitative information on the strength of the evidence and the nature of outcomes, quantitative assessment of the exposure and the potential magnitude of the risks and a description of the uncertainties in the conclusions and estimates. Risk is defined as the probability of an adverse outcome.”⁴⁷

Numerous efforts have been undertaken by the NAS and federal and state agencies to strengthen the technical content and utility of risk assessment and to ensure its scientific integrity. Most recently, the NAS published *Science and Decisions: Advancing Risk Assessment*,¹ a report that concluded that risk assessment is now at a crossroads, with its value and relevance increasingly questioned. The NAS believes that a newly modified risk assessment methodology is the most appropriate available method to measure the relative benefits of the many possible interventions available to improve human health and the environment.

DPR employed traditional risk assessment methods for methyl iodide. However, there was considerable controversy over their selected methods. This section is a review of what may be considered “best practices”

for modern chemical risk assessment. We place special emphasis on the recommendations in the 2009 NAS report, which created a new paradigm for risk assessment.

Risk assessment first became an issue of attention in the Food Section of the Food, Drug and Cosmetic Act.⁴⁸ In carrying out the Act, the Food and Drug Administration (FDA) had to develop criteria, semi-quantitative in nature, to address questions, such as “How many insect parts or rodent pellets in breakfast cereal constitute filth?” and, “when is a food unfit, filthy and adulterated, or wholesome and safe?” These issues were addressed in a qualitative context and were not adequate to quantitatively address the complex issues of chemical toxicants.

In 1961 Mantel and Bryan developed a mathematical model to determine when a level of exposure to a chemical would not constitute a cancer risk greater than one in a million.⁴⁹ Probabilistic methods have been developed since Mantel/Bryan, and a range of options are available.⁵⁰ Given the limits of epidemiology and toxicology, these models reflect mathematical extrapolations from experimental data to low dose regions of exposure.

The historical approach to risk assessment for non-cancer agents derives from a fundamental paradigm that assumes chemical toxicity is based on dose, but there is a threshold for effects. If there are thresholds for toxicity, then the risk assessment process should seek to identify the No Observed Adverse Effect Levels (NOAEL). It is clear today that this approach is an oversimplification of the mechanisms of toxicity, because evidence exists for effects occurring with no threshold.

B. Best Practices as Envisioned by the National Academy of Sciences

The NRC, in its report entitled *Risk Assessment in the Federal Government, Managing the Process* (1983), referred to as the Red Book, detailed the steps that defined the risk assessment process as hazard identification, exposure assessment, dose-response determination, and risk characterization.^{47, 51} The Red Book also emphasized the need to separate risk assessment from risk management in order to maintain the integrity of the scientific process. In contrast, risk management was tied to issues such as development of regulatory options, which includes public health evaluation, economics, social, and political consequences as factors.

Until recently, the Red Book represented the paradigm for best practices. The tools to address these elements included:

- **Hazard identification:** Epidemiology, *in vivo* toxicology, *in vitro* tests, structure-activity analysis, individual susceptibility, potency, and case studies to determine the adverse effects that may be caused by a chemical agent.
- **Exposure assessment:** Determination of likely exposures of different populations (workers, consumers, children) based on use patterns, occupation and task, behaviors, chemical properties, environmental monitoring, and computer modeling.
- **Characterization of risks:** Comparison of predicted exposures from allowed uses to doses known to cause adverse effects.

The ideas set forth in the 2009 NAS report¹ represent a significant improvement in risk assessment using a new framework for risk-based decision-making consisting of three phases:

- Enhanced Problem Formulation and Scoping
- Planning and Conduct of Risk Assessment
- Risk Management

Sections III through VI of this report focus on the second phase: risk assessment. The first phase of problem formulation and scoping was covered in Section II, above. The last phase of risk management will be discussed in Section VII.

Phase II of the NAS framework requires improvements in uncertainty and variability analysis and a unified approach to dose-response assessment that will result in more accurate risk estimates for both cancer and non-cancer endpoints. The risk assessment should provide sufficient information and technical analyses to fully inform the risk management options developed in Phase I. Ensuring that the technical analyses supporting a risk assessment are supported by the best science and are relevant to the problem is critical, as is the elimination of data gaps that would preclude a comprehensive analysis. Peer review of the work provides additional expert feedback on the technical and scientific issues that comprise the risk assessment.

C. Office of Environmental Health Hazard Assessment Methods

In addition to the best practices outlined in the 2009 NAS report, the State of California Office of Environmental Health Hazard Assessment (OEHHA) has developed risk assessment guidelines that represent the state of the art. These guidelines have been approved by the SRP which is chaired by Dr. Froines who also chaired the SRC, the body of scientists appointed by the State to ensure the scientific adequacy of the risk assessments at the State level. The OEHHA guidelines are unique in the U.S. They do not encompass the scope of the ideas developed in the NAS recommendations, but it is anticipated that OEHHA will move to further update its guidelines.

D. Conclusions

Traditional risk assessment practices are now being scrutinized for their scientific validity. The NAS (2009) report,¹ along with the procedural input of OEHHA,⁵² forms the basis for the best practices for risk assessment in the future. The new approaches to best practices for risk assessment are based on significant advances in the science of toxicity testing as exemplified by the 2007 NRC toxicity testing report, the development of Tox21 and Toxcast for *in vitro* testing, the development of the paradigm for using upstream *in vitro* data for downstream policy considerations, and new considerations of dose-response relationships. These innovative changes, when combined with the recommendations of the 2009 NAS report on new risk assessment methodologies, illustrate that we are at a fundamentally new era in addressing toxic chemicals in the environment. These new methodologies were relevant to the risk assessment prepared by DPR for methyl iodide, but they were not addressed.

The approaches recommended in this section represent changes that will enhance confidence in the risk assessment process and its outcomes. The best practices described in this study are somewhat general in their descriptions, with the exception of the OEHHA guidelines. A major task for the agencies charged with conducting risk assessment will be to define specific criteria for practice of the NAS recommendations. This represents a challenge yet to be addressed in California.

IV Hazard Identification

Hazard identification is the first step in risk assessment, where toxicological data from *in vivo* animal studies, *in vitro* laboratory tests, human poisoning incidents, and epidemiological studies are evaluated to determine the types of toxic effects associated with exposure to a particular chemical. In this section, we review the primary hazard identification issues for methyl iodide that formed the basis for the DPR risk assessment. We shall explore the basis for the toxicity of methyl iodide, identify the relevant adverse effects that were key to the overall findings in the risk assessment, identify scientific issues that represented differences in findings between the DPR and the SRC, and draw conclusions about the adequacy of the toxicological data and study design. In developing this review, we will highlight chemical reactivity, human case studies, *in vitro* assays, and animal studies as the crucial data elements for evaluation. We shall address the mechanisms of toxicity as they relate to ultimate risk management decisions. There were no epidemiological studies identified in the risk assessments for methyl iodide.

A. Chemical Reactivity of Methyl Iodide

The chemical properties of methyl iodide affect how it interacts with biological systems. Methyl iodide (CH₃I) is a highly reactive molecule that has characteristic and predictable interactions with biomolecules such as DNA and proteins. These interactions result in the formation of chemical bonds that disrupt DNA replication and protein function and serve as a distinct starting point for toxicity.

B. Neurotoxicity of Methyl Iodide

Neurotoxicity is the result of exposure to neurotoxicants—either natural or synthetic—resulting in damage to the central, peripheral, and autonomic nervous systems. There is substantial evidence from case reports that methyl chloride, methyl bromide and methyl iodide are all neurotoxic, with some of the symptoms of exposure quite profound in their severity. Symptoms include ataxia (inability to coordinate movements) and dysarthria (impairment of motor function of the face musculature), impairment of vision, psychiatric symptoms such as agitation, delusions, hallucinations, insomnia and depression, mild to permanent loss of cognitive abilities, and changes in

personality. Often the effects are delayed, taking several days to appear after exposure. Return to full function can take weeks to months.

1. Case Studies Highlight Neurotoxic Effects

DPR initially addressed five case studies that demonstrate the outcomes associated with known human exposure to methyl iodide.³⁶ The SRC identified a total of fifteen studies, some of which were added to the second draft of the DPR risk assessment. In standard risk assessments, case studies are often given inadequate attention because there is rarely specific information on the levels of exposure and timeframe associated with the exposure conditions. For purposes of hazard identification, the information derived from case studies can be crucial. The case studies associated with methyl iodide showed clear evidence of both acute and chronic neurotoxicity. The number and type of neurotoxic insults were extensive and devastating in nature and clearly justify the conclusions that methyl iodide causes neurotoxic effects on both a chronic and acute basis that appear in a large number of material safety data sheets. The case studies reveal the need for carefully designed animal studies that address a range of neurological endpoints and evaluate dose-response relationships, particularly for susceptible subgroups (e.g., children).

2. *In vivo* Studies Inadequate for Characterizing Neurotoxicity

The data DPR used for characterizing the neurotoxicity of methyl iodide consisted of a single EPA guideline animal study, the Neurotoxicity Screening Battery.⁵³ It is remarkable that EPA required only a single study for its registration of methyl iodide, given the known neurotoxicity of methyl iodide based on the evidence from earlier case studies. The SRC found that in addition to the paucity of data, the current EPA guidelines for conducting neurotoxicity studies are inadequate for identifying known neurotoxicants.^{54, 55, 56} The one-time, six-hour exposure required by the guidelines is not consistent with the anticipated worker or bystander exposure that occurs over several days to several months and will not be predictive of the irreversible neurologic damage caused by longer-term exposures. These studies would not be accepted in the scientific community as a valid assessment of neurotoxicity.

The Neurotoxicity Screening Battery for methyl iodide showed statistically significant decreases in activity for exposed rats, concurrent with clonic convulsions and hypothermia. The DPR toxicologists had concerns about

the study design for activity monitoring because of the “unusually large data variability” and the practice of combining two different types of activity observations such that the differences were averaged out rather than clearly grouped by category.³⁶

Microscopic examination of nervous system tissues was also conducted on the control and high-dose groups. The laboratory conducting the study indicated that there were no significant treatment-related effects. An SRC expert questioned the conclusion that methyl iodide did not cause neuropathology, noting the absence of documentation of how the results were interpreted. Basic information was non-existent, including the criteria used to evaluate effects, comparisons of neurons versus glial cells that are typically used in standard examinations of neuropathology, and even the types of tissues examined. The SRC panel also noted that the pathology laboratory from which the study was reported was insufficiently skilled in conducting neuropathology tests, with earlier results indicating that the laboratory had a high rate of false negatives.

The SRC expert pointed out that neurotoxicity typically develops over a period of days to weeks, which indicates that examinations at one time point shortly after exposure are not really definitive in assessing the complex group of endpoints in this category. For example, a child poisoned by ingestion of small amounts of lead would not necessarily exhibit observable symptoms of poisoning within 24 hours. Neurotoxicants in general produce adverse effects at much lower exposures when the exposure is chronic or repeated.⁵⁵

3. Conclusion

With only a single questionable acute neurotoxicity study available for a chemical that is decidedly a neurotoxicant, DPR was left with inadequate information for risk assessment, considering that acute and subchronic exposures to methyl iodide were likely to occur for workers and bystanders. In the absence of sufficient data to assess risk, an additional uncertainty factor should have been used, but was not.

C. Developmental and Neurodevelopmental Effects of Methyl Iodide

Developmental toxicity is defined as adverse health effects derived from exposure to agents or conditions that affect normal development. Developmental toxicity results in structural malformations, growth

retardation, functional impairment, and/or death of the fetus. Thalidomide is an infamous developmental toxicant. Used as a sedative prescribed to pregnant women in the late 1950s and early 1960s, thalidomide caused fetal death or limb and other malformations in 100% of fetuses exposed during first trimester of pregnancy. The list of developmental toxicants has grown dramatically since the 1960s and includes alcohol, cocaine, retinoids (excess vitamin A), and valproic acid (an anti-seizure drug).

The effect of greatest concern with methyl iodide is developmental toxicity, in the form of late-term fetal death. This outcome was observed in animal studies at low doses of methyl iodide, comparable to exposures people living or working near a fumigated field would experience. This endpoint—late term miscarriage—is severe, and developmental toxicity was a major focus of both the DPR toxicologists and the SRC.

1. Fetal Death

There is no question that methyl iodide is a developmental toxicant, and the most sensitive endpoint identified was fetal death in rabbits. With such a severe outcome, it seems critical to have sufficient information to adequately evaluate the cause of this effect and the doses at which it may occur. The developmental toxicity data provided by Arysta were inadequate and did not provide a reasonable certainty that pregnant women and the fetus would be protected from harm if methyl iodide were to be used as a soil fumigant.

The inhalation exposure of pregnant rats and rabbits to methyl iodide during gestation produced a number of effects. In the rabbit study, there was reduced litter size, fetal weight, and viability, with increased incidence of late fetal death. There was a dose-related decrease in the number of viable fetuses associated with post-implantation fetal loss due to late resorption and fetal death. Both the numbers of fetuses resorbed and the number of affected litters increased with higher doses. Damage to the thyroid was observed in both maternal and fetal rabbits. From the standpoint of risk, fetal death was the most important endpoint in the methyl iodide risk assessment.

2. Neurodevelopmental Toxicity

Neurodevelopmental disorders are the impairment of the growth and development of the central nervous system. Causes may include genetic disorders, immune dysfunction, infectious diseases, metabolic disorders,

malnutrition, and environmental exposures. The mechanistic details of these disorders are still being investigated. Based on the evidence of neurotoxicity and fetal death endpoints associated with methyl iodide exposure, it is crucial to address developmental neurotoxicity (DNT), for which no studies have been done whatsoever.

DPR recognized the potential of methyl iodide to cause developmental neurotoxicity and should have required a DNT study prior to approving the registration. This was one of the key issues in the SRC's evaluation of the toxicity of methyl iodide and represents a major failing on the part of both EPA and DPR. Methyl iodide is clearly neurotoxic. The fetal deaths in rabbits demonstrate developmental toxicity. If one were to present the methyl iodide studies showing neurotoxicity, developmental toxicity and endocrine disruption to a wide range of academic scientists, they would undoubtedly conclude this compound is highly likely to be a developmental neurotoxicant.

Throughout the DPR risk characterization document, DPR scientists pointed out the lack of adequate information on developmental neurotoxicity. In the Hazard Identification section of the risk assessment, staff scientists explain:³⁶

For Methyl iodide, studies which examine the developmental neurotoxicity for animals exposed in utero, as well as those examining the postnatal effects of Methyl iodide on the nervous system of young animals are not available. The absence of such studies can lead to the underestimation of the toxicity based on the current database.

In recent years there has been a significant increase in the incidence of neurodevelopmental disorders, including learning disabilities, conduct disorders, autism spectrum disorders, and ADHD. When a compound is known to be neurotoxic as well as developmentally toxic, it would seem prudent to err on the side of caution, and demand that a developmental neurotoxicity test be done. This critical test was not required by EPA or DPR and represents a major failure of the pesticide registration process.

D. Carcinogenicity of Methyl Iodide

The animal test data indicate that methyl iodide causes thyroid tumors, brain tumors (astrocytomas), lung tumors, and urinary and cervical tumors.³⁶

The reaction between methyl iodide and DNA results in the formation of DNA adducts that cause genotoxic changes, including mutagenesis, that ultimately could lead to cancer. The evidence is incontrovertible that methyl iodide is genotoxic. The final approved regulatory target levels of 96 ppb and 32 ppb for workers and bystanders, respectively result in significantly increased cancer risks for those exposed, 24–56 times higher than the standard one in one million risk for workers and 32–800 times higher for bystanders.

1. Genotoxicity

In evaluating cancer risk, the focus is generally on the chemical initiation of mutagenesis that is a result of changes in DNA structure, and clastogenesis, or damage to chromosomes, collectively referred to as genotoxicity. Two appendices to the SRC report described in depth the genotoxicity of methyl iodide and cited the scientific work that demonstrates that it is tumorigenic, mutagenic, clastogenic, or an alkylating agent. Twenty-two of 24 published, peer-reviewed studies demonstrate at least one of these effects. As a result of the efforts of the SRC, DPR staff scientists included a summary of these studies in the final risk assessment, a review that U.S. EPA had not conducted in its evaluation.

2. Tumorigenicity and Mechanism

Methyl iodide is an alkylating agent that reacts with DNA. This mode of action is analogous to a variety of other direct acting methylating agents that are known mutagens and carcinogens. IARC has classified numerous alkylating agents as “human carcinogens.”

The animal carcinogenesis study conducted by Arysta and addressed in detail in the DPR risk assessment indicated that methyl iodide produced a variety of tumors. Inhalation exposure to methyl iodide produced thyroid follicular cell tumors in male rats and astrocytomas in male rats. Oral exposure produced thyroid follicular tumors in male mice. Female mice developed cervical adenomas/carcinomas. Intraperitoneal injection of methyl iodide induces lung tumors in mice.⁵⁷ In light of the evidence examined, DPR concluded:

There is concern for lifetime exposure to methyl iodide because of the weight of evidence showed that methyl iodide is oncogenic causing thyroid tumors and tumors in other tissues from laboratory animal studies.

In summary, a genotoxic MOA for methyl iodide-induced thyroid tumor is plausible because methyl iodide is an alkylating agent with genotoxic properties in vitro and in vivo assays. It has been demonstrated to form adducts (Gansewendt et al, 1991; Cloutier et al., 2001), which has been implicated in carcinogenesis. . . . methyl iodide is also an oncogen resulting in thyroid tumors in rats, and humans should be assumed to be more sensitive to the oncogenicity of methyl iodide than laboratory animals.³⁶

The SRC similarly concluded: “Unresolved issues of mechanism and toxicokinetics, in addition to the exposure scenarios issues can also lead to underestimation of methyl iodide-associated risk.” Regarding oncogenicity, the SRC concluded the genotoxicity of methyl iodide should be highlighted, given its potency as a methylating agent. The SRC agreed with DPR that the final cancer risk assessment should be based on the more likely mechanism with the more significant risk, i.e., a linear exposure response and no threshold level.

3. Astrocytomas

Astrocytomas are a relatively common type of brain tumor affecting the glial cells. One of the studies evaluated by DPR and the SRC demonstrated that exposure to inhaled methyl iodide resulted in statistically significant increases in these tumors. Arguments suggesting that astrocytomas in rats were methyl iodide-induced are compelling. Not all genotoxic alkylating agents induce brain tumors; this is usually thought to be determined by how well the genotoxin can pass the blood-brain barrier. Methyl-nitrosourea (MNU) crosses the blood-brain barrier and is a well-established brain carcinogen in rats. MNU is a simple methylating agent that induces the same spectrum of DNA adducts as methyl iodide. These adducts are likely to be the pre-mutagenic lesions for both MNU and methyl iodide. Because methyl iodide passes the blood-brain barrier, it would be expected to be mutagenic in the brain by analogy to MNU. The probability is low that the four astrocytomas observed in male rats exposed to methyl iodide happened by chance.^{57, 58}

E. Conclusions

The SRC and DPR toxicologists concluded methyl iodide is a highly toxic chemical, with any anticipated agricultural or structural fumigation use scenario

likely resulting in exposures to the public that would have an adverse impact on public health. Due to the inherent volatility of methyl iodide and ready transport by prevailing winds away from the application site, adequate control of human exposure would be difficult, if not impossible.

Methyl iodide is a potent developmental toxicant, causing fetal death in the late stages of pregnancy through one or more possible MOAs. It is also a neurotoxicant, with neurological outcomes possible for people exposed at the high end of the exposure spectrum such as farm workers and applicators. Methyl iodide reacts readily with DNA with potential for genotoxic outcomes at much lower exposures.

An important element in the DPR review was the lack of critical studies that should have been performed prior to consideration of registration of pesticides using this toxic chemical. There appears to be a strong consensus within both the toxicology staff at DPR and the SRC, that the database of studies on methyl iodide had very severe deficiencies that left key questions unanswered. The standard scientific approach is to identify these data shortcomings and discuss their potential implications for any presumed findings. DPR did not discuss such matters extensively. In this case where there are clear data inadequacies, such detailed discussions are quite important.

The lack of sufficient data and methodological inadequacies in the studies submitted by Arysta raise serious doubts about the validity of the risk assessment. The gaps in our knowledge about methyl iodide are particularly deep in relation to the toxic effects observed at the lowest doses, such as neurotoxicity and developmental toxicity. This lack of toxicologic information makes the use of case reports even more important, as they demonstrated acute and chronic neurotoxic effects.

If appropriate studies had been conducted, they would likely show methyl iodide to be a potent developmental neurotoxicant at exposures well below those required for overt signs of acute exposure. Methyl iodide concentrates in the fetal brain to levels well above those in the mother. The DPR document did acknowledge this data gap and does include an additional uncertainty factor in its modeling of the chronic neurotoxicity and fetal death endpoints, but it was deleted in the final risk management decision.

With input from the SRC, DPR effectively summarized the available scientific data and gaps on the potential health effects of methyl iodide. By doing so, DPR took a highly appropriate public health protective approach throughout the risk assessment. Unfortunately, the final decision by DPR management to register methyl iodide for use did not include these analyses.

V Exposure Assessment

An analysis of the risks associated with using methyl iodide requires not only identification of the inherent hazards associated with exposure, but also an assessment of the extent of exposure anticipated for different populations. Methods have been developed to estimate exposures for different scenarios and populations, including workers and bystanders.

Exposure assessment utilizes information regarding the source of the chemical, the route of exposure (oral, dermal, or inhalation), the location of the exposed individual and the concentration at this location, and the duration and frequency of exposure. Both the duration and frequency of exposure are dependent on a person's task and habits during the time of exposure.

For inhalation exposure to a chemical like methyl iodide, the actual dose absorbed into the body is less than the amount a person is exposed to, due to the physiological processes that govern the uptake of gases from the lungs into the bloodstream. The actual amount absorbed (the absorbed dose) is dependent on the concentration of the chemical during the exposure period, breathing rate and body weight of the person, and the duration of the exposure.

A. Estimating Methyl Iodide Concentrations in Air Near Application Sites

A person's potential exposure to methyl iodide vapor is dependent on the concentration of methyl iodide in the ambient air after an application. The concentration depends on several key factors: application rate, area treated, application method, distance between the application site and the exposed person, and wind and weather conditions.

In conducting the risk assessment for methyl iodide, DPR staff estimated exposures for farmworkers involved in the application, worker bystanders in adjacent fields, and bystanders in areas near the fumigation site using the Probabilistic Exposure and Risk Model For Fumigants (PERFUM) model. This model was calibrated with actual air monitoring data from methyl iodide and other fumigant applications, and provided a range of methyl iodide concentrations in air near an application site as a function of application conditions, distance and prevailing winds. For workers, DPR's calculations assumed that respiratory personal protective equipment (PPE) and engineering controls for applicators were being used correctly.²

There were concerns about the adequacy of the PERFUM model to accurately predict exposures to methyl iodide. One of the significant variables not well accounted for by the PERFUM model is weather. The PERFUM model does a poor job of accounting for poisoning incidents from off-site drift of fumigant vapors, primarily because it sets concentrations to zero when winds are calm. Periods of calm winds define temperature inversion conditions most likely to lead to high concentrations of fumigant in the air. Inversion conditions, where little vertical mixing of the air mass occurs, are the most likely to concentrate the fumigant vapors close to the ground. Most documented fumigant poisoning incidents have occurred under such conditions.⁵⁹

An assessment of past poisoning incidents to determine the failure modes of fumigant dispersion models should have been conducted as part of the methyl iodide risk assessment, since these incidents occur regularly and are realistic high-dose exposures that often result in illness and hospitalizations. During the September 25, 2009 public SRC meeting on methyl iodide, several field workers testified about poisoning incidents during application of methyl bromide that they were involved in.¹² Many of these exposures led to immediate and severe health effects. DPR did not analyze fumigant poisoning incidents, which would have allowed them to better characterize the concentration of fumigant vapors in the air under inversion conditions.

The use of a 24-hour average exposure also led to an underestimate of acute exposures that could cause adverse effects. The rate of methyl iodide loss from the soil changes over time, with the maximum rate of loss (the flux) observed soon after the application

and decreasing over time. A 24-hour average does not accurately estimate the initial spike in concentration that occurs soon after application of the fumigant, yet this exposure is toxicologically significant because of the rapid uptake of methyl iodide and onset of adverse effects.

B. Use of Exposure Modeling to Determine Buffer Zones

One mitigation measure used to reduce the impact of fumigant drift is to require a buffer zone between the treated area and sensitive sites such as homes, schools, workplaces, and other locations where people spend time. There were major differences between U.S. EPA and DPR in the methods used to determine buffer zones.

In modeling exposure for methyl iodide, U.S. EPA used a "whole field" method of estimating buffer zones that assumes the fumigant moves off of the field equally in all directions. DPR rejected U.S. EPA's "whole field" approach and instead estimated the maximum methyl iodide air concentrations that would be predicted downwind in the fumigant plume. DPR's approach correctly addresses the fact that prevailing winds often exist at a given location. EPA's "whole field" approach will not protect the stay-at-home mother and her small children or an elderly home-bound person or an entire school full of children in an area with a prevailing wind pattern that results in fumigant drift in their direction.

C. Estimating Inhalation Exposure

One of the most important steps in a risk assessment is to determine the absorbed dose of the chemical. The amount of methyl iodide actually absorbed through the lungs depends on the concentration of methyl iodide in the air, the effectiveness of any protective gear in limiting the amount of methyl iodide that is inhaled, the breathing rate of the individual, the surface area of the lungs, and how long the air stays in the lungs with each breath. There was substantial disagreement between Arysta/U.S. EPA and DPR/SRC with regards to the assumptions made in the calculation of the absorbed dose. The SRC also disagreed with DPR on its estimates of worker exposure.

1. DPR Rejects Arysta's PBPK Model for Uptake of Methyl Iodide

The estimate of the absorbed dose of methyl iodide used in the DPR risk assessment was based on animal studies. Because there are differences in the rates at which animals and humans absorb inhaled toxicants, there must be a conversion between the concentration that produces a measurable toxic effect in the animal and the human-equivalent concentration (HEC). Arysta developed a Physiologically Based Pharmacokinetic (PBPK) model to estimate the absorbed dose, which U.S. EPA used in their determination of the HEC in preference to the standard U.S. EPA method. DPR toxicologists and the SRC disagreed with their methodology, noting a number of concerns about the validity of the model. The primary issues were the use of incorrect breathing rates for both the pregnant rabbits and pregnant humans, the lack of concordance of model results with experimental data, and the failure of the model to account for multi-day exposures to methyl iodide that may occur in an area where fumigations are frequent. DPR went to great lengths to explain why the PBPK model was inappropriate and led to an underestimate of the human-equivalent dose.³⁶

2. DPR Underestimates Worker Exposures

DPR estimated inhalation exposures for applicators during pre-plant fumigation, applicators working in a field adjacent to a previously treated field, and worker bystanders. In total, six occupational exposure studies were conducted and used in the exposure assessment. The SRC highlighted four components of exposure that DPR underestimated—breathing rate, workday length, work season length, and use of respirators.⁶⁰

Breathing rate. The breathing rate is the volume of air inhaled per minute per pound of body weight and is a critical component of estimating the dose of an inhaled substance. Breathing rates vary with age, body weight, and activity level. Field workers doing strenuous work, recreational athletes and children receive the highest doses because their respiration rates are high. Pregnant women also have higher breathing rates than non-pregnant women.⁶⁰ When estimating methyl iodide exposure to workers and bystanders, DPR used a default breathing rate of 0.83 cubic meters of air per hour. This is a 24-hour average and includes sleeping time, when respiration rates are much lower than that for an awake and active adult.⁶¹ This breathing rate is appropriate when calculating lifetime chronic exposure; however,

for a field worker doing hard labor, DPR should have used a breathing rate consistent with heavy activity, with standard values ranging from 1.2–1.7 cubic meters of air per hour. The result of DPR's selection of breathing rate was underestimation of worker exposure by a factor of 1.5 to 2.

Workday and work season length. In order to calculate an absorbed dose of methyl iodide, an assumption must be made for the exposure time. DPR assumed that the workday for farm workers involved in fumigation and other farm work is eight hours long. However, there are reports of fumigations taking as long as eight hours, with workers needing to stay longer than the fumigation period to secure tarps, water in the fumigant, monitor drift, or conduct other tasks. In recognition of the typical farm workday, overtime pay for farmworkers does not take effect until they have worked at least 10 hours, a fact that DPR did not incorporate into their dose calculation. For example, if a workday is 10 hours long, workers may be exposed to 25% more methyl iodide than during an 8-hour day. A 12-hour workday could lead to 50% greater exposure.⁶⁰ DPR's assumption of an 8-hour workday neglects the reality of field work, resulting in an underestimate of worker exposure. Similarly, DPR assumed a 3-month work season, when some workers are involved in fumigation work for five to six months of a year.

Since workers often live in close proximity to the fields where they work, it is also important to estimate the contributions of both on-the-job exposure and potential subsequent exposure to the drifting vapors. DPR did do these exposure calculations, and they were incorporated into the risk assessment.

Effectiveness of respirators. Worker exposure to methyl iodide vapors was estimated assuming that respirators are used and used properly. By having respiratory protection built into the dose calculation for the risk assessment, DPR made an implicit assumption that respirators are not a mitigation strategy, but are assumed to always be used. In fact, the SRC noted that respirators should be used as a last resort, not incorporated as mitigation, since there are so many ways for them to fail.⁶⁰

The most important aspect of respirator use is fit testing to get a good seal. Respirators are quite uncomfortable, especially when doing strenuous work on hot days. It is not possible to talk, eat, drink, or smoke while wearing them. These limitations lead to the frequent

nonuse of respirators for at least portions of the workday. Professor Katherine Hammond of the SRC put this in clear perspective: If one removes the respirator for 53 minutes of an otherwise perfect 8-hour day (equivalent to a 5–10 minute break every hour during work), the protection factor attributable to respirator use is cut in half.⁶⁰

Another problematic issue with the worker exposure assessment was that DPR assumed a 90% efficiency of respiratory protection and only estimated exposure for workers who were always wearing proper PPE. This is an unrealistic assumption that usually leads to underestimation of worker exposure. The SRC asserted that a 50% protection factor, while not entirely sufficient, would better address variability inherent in respirator use.⁶¹ The use of the 50% protection factor still does not address the issue of whether respirators are effectively worn, if the correct respirator is used, if there is any attempt at quantitative fit testing, or if it is practical to consider a highly efficient protection factor in hot and dry climates, where wearing the respirator is uncomfortable for the user.

Conclusion. Underestimation of exposure due to inaccurate breathing rates, workday and work season length, and inappropriate respirator protection factors is multiplicative. According to the SRC, the inhalation rate for children should have been at least 2–4 times higher if they are playing outdoors; the inhalation rate for workers should have been increased by at least a factor of 1.5; the length of the workday should have been increased by an appropriate amount, perhaps to a 10-hour workday; and the protection factor for respirators should have been decreased to fifty percent or less. Implementing these changes would have increased DPR’s estimated dose of methyl iodide to children and workers by factors of 2–4.⁶⁰

D. Exposure through Groundwater Contamination

Because methyl iodide is partially water-soluble, it poses a significant risk to groundwater supplies. Work by Yates *et al.* indicates that methyl iodide moves downward through the soil column, with greater downward movement observed when the soil is tarped.⁶² Irrigation or rainfall soon after tarp removal can cause further downward movement of methyl iodide into groundwater aquifers, with shallow aquifers most at risk. Methyl iodide can degrade in the soil to form iodide,

which is stable and highly mobile in soils. Iodide is of concern, since consumption of excess iodide causes thyroid disruption. The exposure to methyl iodide or its degradation product iodide from contaminated groundwater was a topic of some discussion among the SRC and DPR staff, with concerns about long-term contamination of drinking water supplies in vulnerable areas.

The SRC advised DPR that agricultural use of methyl iodide could allow unacceptably high levels of iodide to accumulate in water supplies and found it “alarming that there were no reliable data on the potential of methyl iodide to contaminate groundwater” in DPR’s risk assessment. California’s Pesticide Contamination Prevention Act requires a data set on the physical properties and field dissipation studies. The law provides that DPR “shall not register or renew the registration of a pesticide intended to be applied or injected into the ground” if any of these data are absent or if DPR determines that a study is not “valid, complete, and adequate.” By DPR’s own admission, the field dissipation study was inadequate, and soil adsorption data for iodide were missing.

VI Risk Characterization

The final step in the process of conducting the methyl iodide risk assessment was the characterization of risk in the context of its associated toxic effects and the anticipated exposures based on the intended use as a soil fumigant. The “Red Book”⁴⁷ describes risk characterization as the final integrative step in which the likely exposures are compared to the Reference Doses to determine if adverse effects may occur from the use of the pesticide. Risk characterization consists of a relatively detailed description of the nature of the hazard to be incurred, its seriousness and the likelihood of its occurrence.⁶³

In the methyl iodide risk assessment, the endpoint of greatest concern was fetal death. This severe outcome occurred in animal studies with exposure to relatively low concentrations of methyl iodide in air. The SRC indicated that other serious outcomes such as neurodevelopmental toxicity were likely at even

lower concentrations, but data gaps precluded further knowledge about the extent and magnitude of such effects. The use pattern for methyl iodide, in which it is injected into the soil at high application rates, combined with its high volatility, together ensure that relatively high concentrations of methyl iodide will be found in the air downwind of treated fields. Indeed, the risk characterization demonstrated that the anticipated exposures were much higher than the Reference Concentrations determined by DPR staff, which prompted the SRC to conclude in its findings:

Based on the data available, we know that methyl iodide is a highly toxic chemical and we expect that any anticipated scenario for the agricultural or structural fumigation use of this agent would result in exposures to a large number of the public and thus would have a significant adverse impact on the public health. Due to the potent toxicity of methyl iodide, its transport in and ultimate fate in the environment, adequate control of human exposure would be difficult, if not impossible.⁵⁴

In this section, we describe the risk characterization process that led to this conclusion.

A. Determination of a Reference Concentration for the Critical Endpoint, Fetal Death

As described in the Hazard Identification section above, exposure to methyl iodide causes a number of adverse effects, including fetal death, neurological damage, developmental toxicity, thyroid hormone disruption, and benign and malignant tumors. Fetal death is the acute effect that occurs at the lowest dose and was therefore the primary consideration in conducting the methyl iodide risk characterization for bystanders and for workers.

The NOAEL/LOAEL approach was used by U.S. EPA to characterize fetal death in animals, and the NOAEL was set at a concentration of 10 ppm. But when the DPR toxicologists evaluated the incidence of fetal death per litter, there was a statistically significant dose-related decrease in the number of viable fetuses per litter at all doses tested. Figure 2 shows the percent of fetuses affected per litter as a function of dose. The nearly linear curve fit is remarkable for a toxicological study, and the data indicate that 10 ppm was far from being a No Effect level; one could reasonably expect to see fetal death even below 2 ppm.

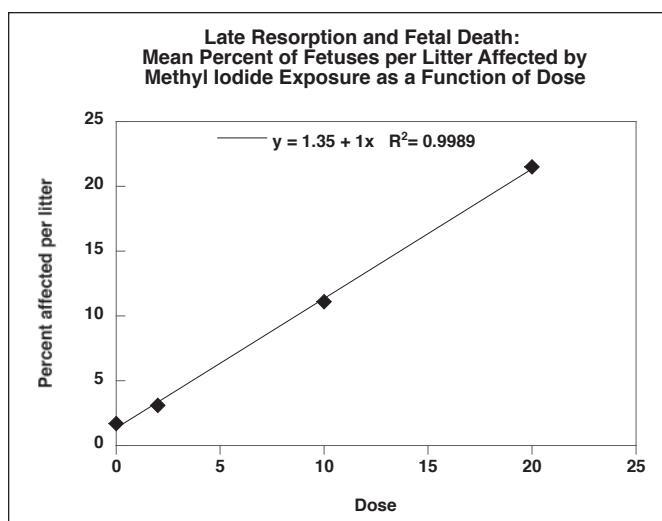


Figure 2: The trend observed in the percent of fetuses affected by methyl iodide as a function of dose is unmistakably linear and indicates that neither 10 ppm nor 2 ppm are NOAEL doses. *Data Source:* Table 34b in Reference 36.

An improved estimate of a No Effect dose for the fetal death endpoint can be obtained using the Benchmark Dose (BMD) approach, a method in wide use by U.S. EPA that is generally accepted as superior to the NOAEL/LOAEL approach for obtaining accurate NOAELs. The BMD approach also allows setting an “acceptable” rate of the critical effect. In consideration of the fact that there are few effects more serious than fetal death, the SRC recommended using a 1% incidence of fetal death in the animal studies as the Lower Effective Dose, the LED₀₁. Below this level, fetal death caused by methyl iodide is not distinguishable from other causes of fetal death in animal studies. DPR’s resulting analysis produced an LED₀₁ of 0.5 ppm. This concentration is a factor of 20 lower (more protective) than the NOAEL of 10 ppm selected by U.S. EPA and a factor of four lower than the NOAEL of 2 ppm selected by DPR management in the final registration decision.

The SRC made extensive commentary, critique and suggestions to DPR staff regarding the use of the BMD approach. DPR staff acceded to the recommendations of the SRC and used the BMD approach for their determination of dose-response for these endpoints in the final risk assessment.

B. Determination of Appropriate Uncertainty Factors

In every risk assessment there is uncertainty. Animals and humans are different in the way they absorb, metabolize and excrete toxicants; humans have differing abilities to detoxify chemical substances because

of differences in genetic makeup; children and the developing fetus are typically more sensitive to toxic insults than adults; and the available data are frequently inadequate to definitively characterize the hazards and the anticipated exposures. Standard risk assessment methodology utilizes an interspecies uncertainty factor of 10 to account for differences between animals and humans and an intraspecies uncertainty factor of 10 to account for differences between different humans. The interspecies factor of 10 is frequently reduced to a factor of three in inhalation studies.

Data gaps in the hazard identification (especially the lack of developmental neurotoxicity data) and the severity of the fetal death endpoint raised concerns among the SRC about the adequacy of the final Reference Concentration (RfC) used by DPR as an acceptable level of exposure. Fetal death and impairment of growth are extreme outcomes, which raises the question of what happens to the fetus at lower doses.

The SRC indicated that the appropriate UF to use in determining an RfC is 300, which includes an additional data gap uncertainty factor of 10, instead of the conventional value of 30. The additional uncertainty factor was deemed necessary to address concerns about methyl iodide causing potential developmental neurotoxicity and post-natal death, as well as iodide toxicity.

DPR staff used a UF of 300 in their risk assessment, calculating RfC values of 0.8 ppb (for an 8-hour exposure) for workers and 0.3 ppb for residential bystanders (for a 24-hour exposure). Exposure estimates for different scenarios were compared to the RfCs, with sobering results. Even with buffer zones, worker bystanders (i.e., workers with no respiratory protection in fields adjacent to the fumigated field) were anticipated to be exposed to an 8-hour average concentration of methyl iodide of 1,600 ppb, a level that is 2,000 times higher than the RfC of 0.8 ppb, and higher even than the LED₀₁ benchmark dose of 500 ppb for the fetal death endpoint. The worker bystander cancer risk is 9,600 per million people, much higher than the one in one million risk traditionally deemed acceptable by regulatory authorities. For residents living near a treated field, the 24-hour average concentration was calculated to be 300 ppb, a level that is 1,000 times higher than the RfC of 0.3 ppb. The SRC noted that gaps in the available data on neurotoxicity raise *“serious doubts about the adequacy of any risk assessment to fully estimate the risks*

that would be associated with the introduction of methyl iodide into the general environment.”

An additional uncertainty in the methyl iodide risk assessment is the fact that two of the three Midas™ products to be sold contained a substantial percentage of chloropicrin. Chloropicrin is a severe irritant, and clinical experience with human exposures demonstrates unequivocally that respiratory tract injury can occur from chloropicrin exposure. DPR’s recent risk assessment of chloropicrin conducted under the Toxic Air Contaminant program also concluded that the weight of the available evidence supports classifying chloropicrin as a potent carcinogen and a glutathione depletor, similar to methyl iodide.⁴¹ DPR noted that toxic effects from exposure to a mixture of methyl iodide and chloropicrin were likely to be observed at lower doses than those determined in a risk assessment that accounts for exposure to only methyl iodide. The co-application of two chemicals, each of which by itself is quite toxic, warrants the inclusion of additional uncertainty factors because of potential for interactive effects that result in synergistic or multiplicative outcomes.

C. Failure to Use Best Practices Contributes to Unacceptable Risk

A fundamental issue associated with the methyl iodide risk assessment is whether DPR used best practices in its development of the risk characterization. This section addresses the underlying flaws in U.S. EPA’s science and the alterations made to DPR’s risk characterization by DPR’s risk managers that led to the final DPR registration decision. Interestingly, the findings described by DPR staff in the risk assessment document are substantially different than those that formed the basis of the risk management process as discussed in Section VII.

Was the risk assessment document developed by DPR staff adequate? In general the answer is a qualified yes. The SRC agreed in general with the endpoints selected, and with DPR’s use of the benchmark dose approach. The potential carcinogenic risk determined by DPR is important, and the SRC agreed that the mode of action for carcinogenesis should be based on a genotoxic approach.

The lack of information on neurotoxicity and neurodevelopmental toxicity was a major gap in the database of studies and precluded a more comprehensive

analysis; in light of the data gaps, the SRC indicated that additional uncertainty factors were necessary.

The DPR staff toxicologists were very responsive to the SRC’s suggestions for improving the science of the risk assessment and overall, the work of the staff was laudable. They took a highly appropriate public health protective approach throughout the process, reasonably summarizing the available scientific data on the potential health effects of methyl iodide and attempting to systematically account for scientific uncertainties and data gaps that affected the determination of risks to human health. In each instance where the DPR findings differed from the U.S. EPA risk assessment for methyl iodide, the difference was attributable to the scientifically rigorous approach used by DPR.

The risk management process that followed completion of the risk assessment was highly unsatisfactory. DPR management agreed to a number of changes suggested by the SRC in their final document (as described in Appendix 3 of the SRC report and the transcript), but never adopted them. The quality of the subsequent decision-making was wholly inadequate, as will be described in Section VII.

VII Evaluation/Option Selection (Risk Management)

A. Overview of Best Practices

The ultimate purpose of the Evaluation/Option Selection element of risk governance is to reach a decision, taking into account the information and conclusions provided by the risk assessment.^{1,8} This element is often referred to as risk management. In this part of the process, risk managers evaluate the candidate options (including no action, risk management and risk prevention options) against specific decision criteria and rules.^{1,9}

As noted above, Section 12825 of the CA Food and Agricultural Code establishes a set of decision criteria (the “Section 12825 factors”) for pesticide registration. The DPR regulations elaborate upon these criteria. There are also several principles for effective evaluation/selection commonly found in the risk governance

literature that provide additional guidance in evaluating the DPR registration process in this case:

- *Risk management should be based on the best available scientific and technical information.*⁸
- *Risk managers should not manipulate the risk assessment process or alter the ultimate risk assessment outcomes to match the risk managers’ policy preferences.*¹
- *Risk management should be transparent in the sense that information regarding the basis of risk management decision is available to the stakeholders and the public.*^{1,9,64}

B. Risk Governance Deficits in the Methyl Iodide Decision

Table III describes each of the evaluation and option selection governance deficits of concern in DPR’s risk management process.

1. Lack of Transparency

Transparency enhances the legitimacy of the registration process, ensuring that the public will view the process as objective and fair.⁶⁶ It also acts as a deterrent against the improper manipulation of the risk assessment to support particular risk management outcomes.⁶⁵ Such transparency was almost completely lacking from DPR’s evaluation process. Neither the Proposed Decision nor Final Decision documents provided a clear, complete

Table III: Risk Management Governance Deficits in Methyl Iodide Registration

Governance Deficit	Description
Lack of Transparency	This deficit relates to whether the underlying assumptions and judgments made by the risk managers have been sufficiently documented and explained.
Strategic Behavior	This deficit occurs where the risk managers shape the evaluation/option selection process so as to favor a preferred alternative. It may include manipulation of the risk assessment, undervaluing disfavored alternatives, or exaggeration of the adverse consequences of taking protective measures. ^{1,65}
Narrow Alternatives	This deficit occurs where the risk managers do not consider the full range of feasible alternatives. ¹⁰

description of how the risk managers balanced the Section 12825 factors in reaching the decision to register methyl iodide, with one exception. The Proposed Decision clearly states that DPR did not consider one of the Section 12825 factors; namely, the availability of feasible alternatives.

This lack of transparency was perhaps most striking with respect to DPR's selection of acceptable exposure levels. DPR used these "reference concentrations" to develop mitigation measures, such as tarp requirements, personal protective equipment and buffer zones, to ensure that the workers and bystanders were not exposed to unacceptable levels of methyl iodide. The reference concentrations were substantially higher and thus less protective than the values calculated by DPR staff toxicologists and supported by OEHHHA and the SRC as marginally protective. The Proposed Decision contained a one-paragraph explanation of how the numbers were derived,⁶⁷ which one of DPR's staff toxicologists described as so vague as to require her to "read between the lines" to understand how the values were calculated.⁶⁸ In response to comments, DPR provided some additional detail regarding its reasoning.⁶⁹ Beyond the reference concentration issue, the record regarding the development of the mitigation measures is also sparse, with the exception of the calculation of buffer zones.

2. Strategic Behavior Used in the Methyl Iodide Risk Management Decisions

Strategic behavior occurs where the risk managers slant the outcome of a risk assessment to obtain a particular result. Such behavior undermines the relationship between risk assessment and risk management. The record in the case of methyl iodide registration strongly suggests that strategic behavior may have occurred in the selection of the reference concentrations. As discussed above, the public record regarding selection of the reference concentrations was largely opaque. Internal DPR documents create the appearance that DPR risk managers selected the reference concentrations based upon which concentrations supported economically acceptable mitigation measures.

An April 15, 2010 internal document titled "Iodomethane Registration Decision Options" evaluates a range of potential reference concentrations. Some were developed by the SRC and DPR risk assessors, but most appear to have been generated by DPR risk managers themselves. The document next considers six reference concentration scenarios, evaluating the mitigation

measures necessary to achieve those levels and the likely impact of those measures on the applicant. The document concludes by recommending adoption of 32 ppb and 96 ppb as the reference concentrations for bystanders and workers, respectively.⁶⁹

On its face, the document appears to be an exercise in balancing protectiveness against the economic and practical aspects of potential mitigation measures. Such an exercise is inconsistent with the decision rules set out in the statute, and DPR's own pronouncements which preclude economic analysis as part risk management.¹⁹ It is possible instead to view this document as simply an attempt to understand the implications of the different reference concentrations. If that were the case, however, one would expect to see some evidence in the document or elsewhere that the risk managers engaged in a scientific or policy analysis of which reference concentration was appropriate. However, the contrary is true as other documents appear to support the notion that the reference concentrations were selected so as to match the mitigation measures that would be acceptable to growers, in this case buffer zones of less than 100 feet.

The first is a memorandum dated February 16, 2010 prepared by Arysta titled "Rationale for establishing alternative HEC and RfC values for MIDAS in California." The stated purpose of the memorandum was to "suggest ways in which the current [draft] DPR risk assessment may be modified, or how Risk Management decisions can be made that would still offer a high degree of protection while resulting in a manageable label."⁷⁰ The memorandum recommends RfC's of 34 ppb and 96 ppb for bystanders and workers, respectively.⁷⁰ These values are quite close to the values of 32 ppb and 96 ppb adopted by DPR just two and a half months later.

The second is an internal memorandum from the Assistant Director of DPR to a Supervising Toxicologist dated just four days before the Proposed Decision was issued. That memorandum sought assistance in crafting language for the Proposed Decision justifying the deletion of a safety factor applied in calculating the reference concentrations, noting that "I tried to explain it with the conservatism of the HEC calculation but [the DPR Director] wants to be able to explain it further."⁷¹ The development of the final reference concentrations raised significant objections from staff toxicologists. In a draft memorandum prepared for the Supervising Toxicologist, the staff toxicologists observed that the toxicological assumptions "appear to

have been extracted from different MeI risk assessment methodologies that are not interchangeable. Each approach is made up of a series of interrelated values and assumptions: one value or assumption is predicated on the preceding one. It is not scientifically credible to select a value or assumption from one and combine it with a value or assumption from another.”⁷²

Taken as a whole, the documentary record raises substantial questions regarding the basis of DPR’s reference concentrations and thus the mitigation measures that were predicated upon them. As one member of the SRC observed, “This does seem to be a case where management has messed with the detailed technical conclusions rather than playing their more accepted role of rendering [sic] drawing risk management decisions based on multiple value-related circumstances.”⁷³

3. Narrow Alternatives

DPR’s obligation to consider alternatives flows from two sources. First, the statute and its own regulations require that the agency give special attention to the availability of feasible alternatives in reaching a decision to register or not register the pesticide.^{21,22} Second, the California Environmental Quality Act (CEQA) likewise imposes an obligation to consider alternatives.⁷⁴ The regulations implementing CEQA in this context mandate that public reports “contain a statement and discussion of reasonable alternatives which would reduce any significant environmental impact.”⁷⁵

DPR took the position that it did not consider alternatives to registration for two reasons. First, it concluded that alternatives analysis should be performed by the county agricultural commissioner in connection with site-specific permitting for application of the fumigant.⁶⁹ This justification lacks legal support. Neither the DPR regulations nor CEQA contemplate delegation of DPR’s obligation to consider alternatives to the county agricultural commissioners.

Second, in its Final Decision, DPR contended that the only alternative to registration is “to refuse to register the product.”⁷⁰ This is a misreading of CEQA, which requires consideration of a range of reasonable alternatives, including a “no action” alternative.⁷⁶ Moreover, the governing pesticide registration statute and DPR’s own regulations independently require consideration of whether there are feasible, safer alternatives to registration. In this case, DPR could have evaluated a range of different alternatives, including

continued use of the existing chemical fumigants, and emerging non-chemical alternatives (such as solarization or steam treatment) or cultural practices such as crop rotation. Also, DPR could have examined a hybrid approach, allowing the use of methyl iodide in some areas, while refusing registration for areas in which risks were too high or other alternatives would suffice.

VIII Effective Communication

A. Overview of Best Practices

Effective communication is an important component of all elements of risk governance (i.e., identification of new risks; problem identification/framing; risk assessment; and risk management).^{9,77} In the context of pesticide regulation, the term “communication” refers to dialog between the agency charged with identification, assessment and management and the relevant stakeholders, rather than a one-way flow of information from the agency outward. The dialog serves three important functions in this case. First, the local knowledge and “on the ground” perceptions of stakeholders can improve assessment and decision-making by providing additional salient information and a highly contextualized frame for the decision. Second, it gives life to the democratic ideal of citizen participation, allowing stakeholders to express their own concerns and interests and participate in the outcome. Third, effective communication enhances the legitimacy of the ultimate decision, and reduces the likelihood of future legal and political challenges.⁷⁸

B. Effective Communication Governance Deficits

Table IV identifies the governance deficits in effective communication in DPR’s risk management process.

1. Undervaluing Information

DPR gave inadequate consideration to “non-expert” information provided by stakeholders in two instances. The first relates to the realities of agricultural work. As part of its exposure assessment, DPR assumed that workers would be exposed to fumigants eight hours per day over a three-month growing season. Numerous

Table IV: Risk Management Governance Deficits

Governance Deficit	Description
Undervaluing Information	This refers to the tendency to undervalue public perception and local knowledge as being less relevant, less informed or less rational/objective than expert knowledge or knowledge contributed by the sector(s) that may benefit from the decision. ^{79, 80}
Non-Interactive Communication	This deficit occurs where the risk governing body fails to engage in a deliberative and interactive process with stakeholders, such as limiting interaction to “one way” risk communication, ^{80, 81} or not meaningfully interacting in an ostensibly consultative or collaborative process. ⁸⁵

commenters explained that agricultural workers are on the job well beyond eight hours and move from county to county over a five-month period rather than three months.^{82, 83, 84} Rather than engaging with the stakeholders to investigate the accuracy and implications of the information, DPR dismissed the information.⁷⁰

The second instance highlights concerns resulting from tarp failures, tarp placement and removal, and improper fumigant application. Here again, numerous commenters in the SRC public hearing and in written comments (including agricultural workers and residents living near agricultural fields) described incidents of pesticide exposures and pesticide drift.^{25, 82, 84, 85, 86} The records of the registration process provide no evidence that DPR seriously considered or investigated these claims, either by contacting local county agricultural commissioner offices, reviewing records or consulting with agricultural works or residents. DPR’s responses instead largely dismiss the comments, relying instead upon its own technical assumptions and modeling.

2. Non-Interactive Communication

This deficit goes to the question of whether the agency has engaged with stakeholders in a proactive and meaningful way. In this case, DPR was interactive with the registrant, Arysta. To some extent, this interaction was required by law; for example, provision of required notices to the registrant.⁸⁷ Other interactions were more extensive. DPR staff and managers apparently met with Arysta on several occasions to discuss issues as they arose in the registration process, and received substantive input in the risk assessment and

risk management process.^{70, 88, 89} It also appears that DPR interacted to some degree with growers and industry task forces when questions arose regarding working conditions.⁹¹

DPR was not sufficiently interactive with other stakeholders. It appears that neither agricultural workers nor their representatives were consulted with respect to working conditions such as the length of the application season, the length of the workday, or the efficacy of personal protective equipment. Likewise, there was no evidence in the record that the agency actively sought out substantive interaction with the broad range of non-governmental organizations that were active in the registration process. Likewise, the interactions between DPR and other agencies with interest in the outcome—such as the Department of Food and Agriculture, the Office of Environmental Health Hazard Assessment, and Central Coast Regional Water Quality Control Board—were largely limited to formal notices and comments rather than collaborative exchanges.

IX Conclusion and Recommendations

At the outset this report described four themes that underlie effective risk management: realistic framing and assessment of the risks presented; use of best available science and data coupled with caution in the face of uncertainty; thorough identification and evaluation of safer chemical and non-chemical alternatives; and transparent decision-making including meaningful engagement with stakeholders. It then identified a series of risk governance deficits in the pesticide registration process that undermined these themes. The following recommendations respond to the specific deficiencies and advance the four themes of effective risk governance. The recommendations assume that the basic structure of pesticide regulation and agricultural policy more generally in California remains essentially intact. The pervasive use of chemical fumigants is a consequence of modern conventional agriculture, going hand in hand with such elements as intensive tillage, monoculture, and the application of inorganic fertilizer.⁹⁰ Achieving sustainable agriculture which, among other things, would likely minimize the dependence on chemical pesticides would require more

fundamental changes that are beyond the scope of this report.⁹¹

A. Realistic Framing and Assessment of Risk

Develop realistic framing of the problem taking into account the actual context. DPR framed the problem as exposure of workers and residents to methyl iodide, when in fact those individuals would be exposed to mixtures of methyl iodide and chloropicrin. This frame drove the data collection, risk assessment and ultimately the registration decision.

Perform cumulative risk assessments taking into account all active ingredients in the pesticide under review, as well as exposures affecting the relevant population. Implement a phased-in approach to consider chemicals under a unified dose-response assessment framework that includes a systematic evaluation of background exposures and disease processes, possible vulnerable populations and modes of action that may affect human dose-response relationships.

B. Use of Best Available Science/Data and Exercise of Caution

Develop procedures for early identification of mandatory testing. DPR had ample authority to require the necessary testing for neurodevelopmental toxicity, groundwater dissipation and methyl iodide flux. Moreover, at least with respect to the latter two gaps, DPR staff was well aware of the need for the testing early on. The decision regarding specific testing was dealt with iteratively, allowing submission of tests from other jurisdictions over time, leading to an artificial crisis at the end of the DPR review process. To minimize this problem, DPR should identify data gaps and the necessary testing early in the process, requiring a comprehensive data generation plan from the applicant.

Improve uncertainty and variability assessment to accurately reflect all known factors. This would include the context in which the chemical is intended to be used, and would account for unknowns by increasing uncertainty factors. It is particularly important to address exposure assessment and dose-response in the context of uncertainty and variability.

Develop a robust, conflict-free peer review process to ensure the best science is used in developing risk assessments. The peer review process should include scientists with particular knowledge of the most important toxicological and health endpoints.

Incorporate state of the art risk assessment methods into the registration process. Going forward, DPR should take full advantage of OEHHA's expertise to help integrate new risk assessment methods into DPR's registration process. This would include making use of advanced methods for dose-response assessment including the benchmark dose approach, and considering linear dose response models as representative of the most health protective approaches.

Develop procedures for consultation and concurrence of risk assessors. In this case, DPR's risk managers revised scientific conclusions of the risk assessment without participation from or agreement by the DPR scientists who conducted the risk assessment. To prevent similar issues in future cases, DPR policy should be modified to require consultation with and concurrence of the Medical Toxicology and Worker Health and Safety branches on any revisions to the conclusions of the risk assessment.⁹² This recommendation is consistent with existing policy that prevents registration where any reviewing DPR branch recommends against registration because of inadequate data, unacceptable studies or unmitigated adverse effects.¹⁹

C. Embracing Prevention of Risk

Include identification and evaluation of chemical and non-chemical alternatives as part of the registration review. The registration statute and regulations, as well as CEQA, require consideration of alternatives as part of the registration decision. Failure to include the existence and viability of alternatives as part of the problem undermines DPR's ability to do so. DPR should rather require the applicant to provide such information, or independently generate the information as part of the review process.

Develop guidance on alternatives analysis. California statutes and DPR's own regulations require that DPR consider the availability of safer alternatives. DPR policy should be modified to explicitly integrate analysis of alternatives—either by the applicant or the agency—into the registration process. As part of these modifications, DPR should develop standard methodologies for

performing alternatives analyses, and include relevant stakeholders and experts in alternatives analysis in the development process.

D. Engaging in Transparent, Interactive Decision-Making

Review Public Participation Practices. DPR should engage in a structured review of its public participation process, identifying additions and modifications intended to enhance meaningful participation by all relevant stakeholders in the registration process.

Develop requirements for record of decision providing more extensive description of the basis of decision. DPR should address the lack of transparency in the decision-making by fully documenting and explaining the bases of its decisions in the publically available Notice of Proposed Decision and Notice of Final Decision. Agency guidance should be modified to articulate specific performance standards for the notices providing for specific discussion of the assumptions, data and reasoning relied upon in approving registration, setting exposure levels and establishing mitigation measures.⁹³

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