Building Capacity for Robust Pesticide Regulation

Part I: Cumulative Impacts

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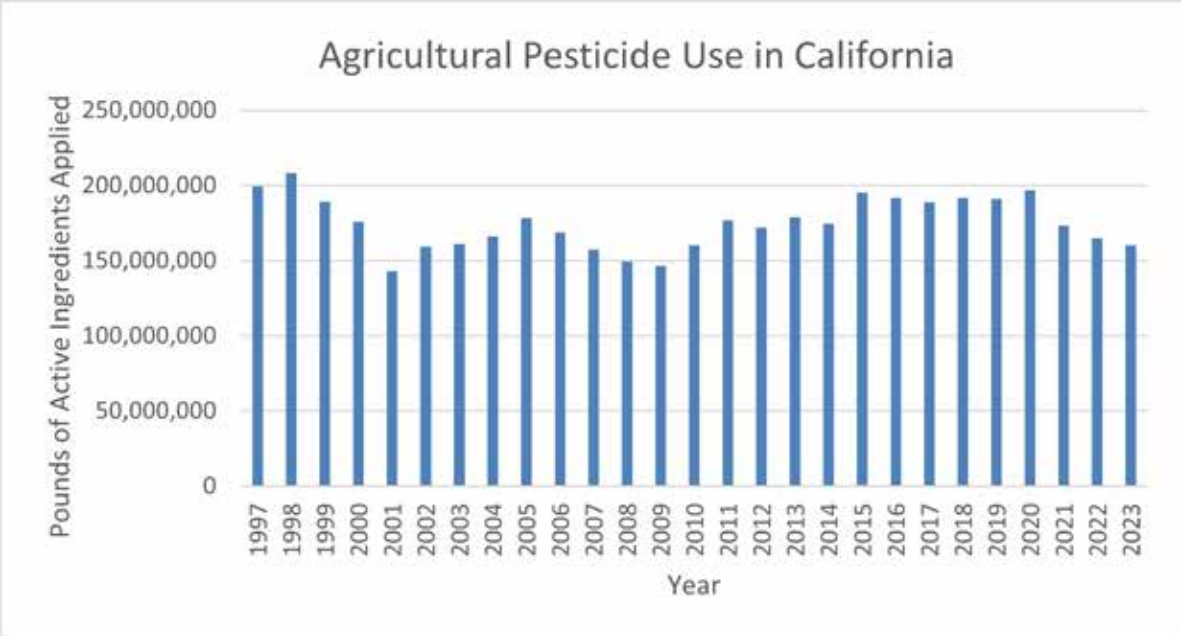
KEY TERMS AND ACRONYMS

CAC	County Agricultural Commissioner
CEQA	California Environmental Quality Act
CIA	Cumulative Impact Assessment
CalCAT	Cumulative Risk Assessment Tool
CalCB	Qualitative Cumulative Risk Assessment Tool
DPR	California Department of Pesticide Regulation
EPA	United State Environmental Protection Agency
IPM	Integrated Pest Management
NOI	Notice of Intent
OEHHA	Office of Environmental Health Hazard Assessment
PCA	Pest Control Advisor
PUR	Pesticide Use Reporting
UCANR	University of California Agriculture and Natural Resources

1 INTRODUCTION

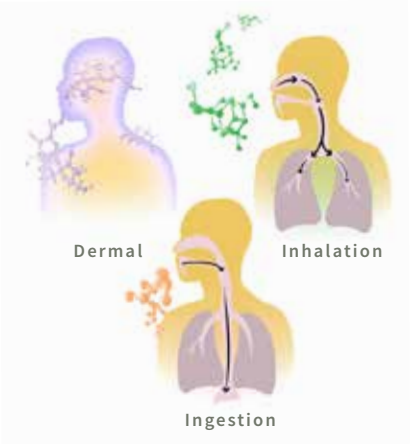
The agricultural industry in California and other states relies heavily upon chemical pesticides for a range of high-value crops to control pests, such as insects, weeds, and other problems. Many of these pesticides contain toxic active ingredients which evaporate into the air, seep into the soil and groundwater, or remain as residue on crops. In California, this usage is pervasive; in 2022 more than 160 million pounds of pesticide active ingredients were applied to land in California for agricultural purposes (see Figure 1). Farm workers, residents near or around farms, and consumers are all at risk of being exposed to pesticides. In many instances people are exposed to multiple pesticides at once, potentially increasing the health risks they face.

Figure 1. Agricultural Pesticide Use in California
(Derived from DPR Summary of Pesticide Use Report Data—2023 Data Summary)



Currently, in California, there are 12,793 pesticide products registered, with 1,047 different active ingredients.[1] Cumulative exposures to these pesticides are occurring on a regular basis.[2] For purposes of this report, we define cumulative exposure as the combined exposure to multiple chemical or non-chemical stressors that affect people or the environment.[3] A stressor can be a chemical released into the environment, such as a pesticide. Or it can be physical (*e.g.* heat or noise), or psychosocial (*e.g.* poverty or fear of crime).[4] The exposures can occur through different pathways and routes, sometimes referred to as "aggregate" exposure. "Pathway" generally refers to the manner by which the chemical or other stressor reaches the individual, for example a chemical moving through air or surface water. "Route" involves the way in which the receptor is ultimately exposed to the chemical.[5] For example, as Figure 2 illustrates, an individual could ingest, inhale, and touch several different chemicals, resulting in a cumulative exposure to multiple chemicals via three different routes.

Figure 2. Routes of Exposure



In this report, we identify and evaluate several regulatory approaches for addressing cumulative exposures associated with the use of pesticides in agriculture. The report recommends a path forward for addressing cumulative exposures under existing law, with emphasis on pesticide registration at the state level and permitting at the county level. The recommendations provide a conceptual roadmap for state agencies and stakeholders, acknowledging that resolution of numerous specific scientific, technical, institutional and funding issues must be addressed in implementing the roadmap.

We distinguish between cumulative risk and cumulative impacts. Cumulative risk refers to combined risk from aggregate exposures to multiple chemicals, in this case pesticide products. Cumulative impact is a broader concept which considers the combined effects of chemical and non-chemical stressors on health, well-being, and quality of life.[6] We focus primarily, but not exclusively, on chemical stressors and cumulative risk, and particularly on three types of cumulative exposures to pesticides used in the agricultural setting.

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1 https://www.cdpr.ca.gov/docs/label/actai.htm (last accessed March 11, 2024).

2 See, *e.g.*, Shiwen Li, et al., Proximity to Residential and Workplace Pesticides Application and the Risk 0f Progression of Parkinson's Diseases in Central California, 864 Sci. Total Env. 160851 (2023); Timothy F. Malloy, et al., GOVERNANCE ON THE GROUND: EVALUATING THE ROLE OF COUNTY AGRICULTURAL COMMISSIONERS IN REDUCING TOXIC PESTICIDE EXPOSURES (2019) (hereinafter, Malloy, et al., GOVERNANCE).

3 Virginia Zaunbrecher, et al., EXPOSURE AND INTERACTION: THE POTENTIAL HEALTH IMPACTS OF USING MULTIPLE PESTICIDES (2016) (hereinafter, Zaunbrecher, et al., EXPOSURE AND INTERACTION).

4 U.S. EPA, FRAMEWORK FOR CUMULATIVE RISK ASSESSMENT 3 (EPA/600/P-02/001F 2003).

5 Id. at 26.

6 See Susan Julius, et al., CUMULATIVE IMPACTS: RECOMMENDATIONS FOR ORD RESEARCH 4-5 (EPA/600/R-22/014a 2022).

PRODUCT MIXTURES

Many pesticide products are themselves mixtures of chemicals, such that exposure to the pesticide product is by definition exposure to a mixture.[7] A conventional formulated pesticide may consist of one or more active ingredient(s). It may also include adjuvants (that is, substances like emulsifiers or wetting agents meant to enhance the pesticide's effect, considered as pesticides under the Food & Agricultural Code) and "inert" ingredients.[8] Consider Pic-Clor 60 EC, a fumigant pesticide used for the control of parasitic worms and soil-borne diseases. The product label states that Pic-Clor 60 EC consists of Chloropicrin (56.6%), 1,3-Dichloropropene (37.1%), and other unidentified ingredients (6.3%).[9]

FIELD MIXTURES

Intentional mixtures often occur in the field, as growers or their contractors purposefully combine different pesticide products in what is known as tank or field mixing, and then apply the mixture on farm land.[10] For some pesticide products, the application instructions on the product label require or encourage mixing with other pesticides or with materials such as emulsifiers or wetting agents.[11] Labels for other pesticide products are silent with respect to mixing, leaving that decision to the grower or applicator.[12] In some cases, pesticide product labels prohibit mixing generally or with specific types of other pesticides or materials.[13]

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7 California Department of Pesticide Regulation (DPR), A GUIDE TO PESTICIDE REGULATION IN CALIFORNIA 70 (2017). (https://www.cdpr.ca.gov/docs/pressrls/dprguide.htm (hereinafter DPR, GUIDE)). John Froines, et al., RISK AND DECISION: EVALUATING PESTICIDE APPROVAL IN CALIFORNIA (2013) (hereinafter, Froines, et al., RISK AND DECISION).

8 DPR, GUIDE, *supra* n.7, at 22.

9 Letter from Hope Johnson, US EPA to Mardel Rose Belotinsky, Soils Chemicals Corporation dated November 13, 2017.

10 See EPA, PRN 82-1: Revised Policy on Label Claims for Tank Mixing (1982); Elizzandra Marta Martins Gandini, et al., Compatibility of Pesticides and/or Fertilizers in Tank Mixtures, 268 Journal of Cleaner Production 122152 (2020); Andrea Wade, Combined Toxicity of Insecticides and Fungicides Applied to California Almond Orchards to Honey Bee Larvae and Adults, 10 Insects 20, 23, 26 (2019).

11 See, *e.g,* EPA, Notice of Pesticide Registration for Helm Nicosulfuron 75, EPA Reg. No. 74530-26 (Feb. 7, 2008). Under California law, adjuvants such as emulsifiers and wetting agents are considered pesticides and subject to registration. Food & Agricultural Code Sections 12753(a), 12758.

12 EPA, PRN 82-1.

13 Id.

COINCIDENTAL MIXTURES

Mixing of pesticides in the environment may also occur as an consequence of local agricultural operations. For example, different growers located in proximity to one another (or a single grower) may apply different pesticide products close in space. Those pesticides may mix in the air, soils, or water, exposing workers, bystanders, residents, and/or environmental receptors to the mixture.[14]

Cumulative exposures to product, field, and coincidental mixtures raise substantial concerns regarding human health and the environment. The joint effect of chemicals in mixtures may be additive, meaning that the mixture's effect reflects the joint action of its individual components. In other cases, the joint effect may be interactive, such as a greater-than-additive effect where the toxic effects exceed those predicted by models of additivity. (This is sometimes called a synergistic effect.) Or the interactive effect may be less-than-additive, where the mixture's effects are less toxic than those predicted under an additivity model. (This is sometimes described as an antagonistic effect.[15])

Disadvantaged communities bear a greater burden from cumulative exposures, whether additive or interactive.[16] To some degree, this is related to greater use of agricultural pesticides in the vicinity of those communities as well as occupational exposures among farm workers.[17] Also, these same communities are typically burdened by higher levels of exposure to other chemical and non-chemical stressors.[18]

This report is the fourth in a series of UCLA reports on pesticide regulation in California. The first, *Risk and Decision: Evaluating Pesticide Approval in California*, identified a variety of strengths and weaknesses in the state registration process used by the Department of Pesticide Regulation (DPR). In addition to highlighting deficits

14 Aude Kienzler, et al., Regulatory Assessment of Chemical Mixtures: Requirements, Current Approaches and Future Perspectives, 80 Regulatory Toxicology and Pharmacology 321, 322, 328 (2016); Malloy, et al., GOVERNANCE, *supra* n.2; Zaunbrecher, et al., EXPOSURE AND INTERACTION, *supra* n.3.

15 Cynthia V. Rider and Jane E. Simmons, Introduction, in Cynthia V. Ryder and Jane E. Simmons (eds), CHEMICAL MIXTURES AND COMBINED CHEMICAL AND NONCHEMICAL STRESSORS (2018); National Research Council, ASSESSING RISKS TO ENDANGERED AND THREATENED SPECIES FROM PESTICIDES (2013).

16 Alexis Temlin, et al., Racial and Social Disparities in Ventura County, California Related to Agricultural Pesticide Applications and Toxicity, 853 Science of the Total Environment 158399 (2022)

17 Nicole C. Deziel, et al., A Review of Nonoccupational Pathways for Pesticide Exposure in Women Living in Agricultural Areas, 123 ENVIRONMENTAL HEALTH PERSPECTIVES 515 (2015); Michael Gochfeld and Joanna Burger, Disproportionate Exposures in Environmental Justice and Other Populations: The Importance of Outliers, 101 AMERICAN JOURNAL OF PUBLIC HEALTH S53 (2011).

18 Lara Cushing, et al, Racial/Ethnic Disparities in Cumulative Environmental Health Impacts in California: Evidence from a Statewide Environmental Justice Screening Tool (CalEnviroScreen 1.1), 105 American Journal of Public Health 2341 (2015).

in DPR's process, the report made a number of recommendations aimed at better protecting public health, including performing cumulative risk assessments to consider all active ingredients in the pesticide formulation.[19]

The second report, *Exposure and Interaction: The Potential Health Impacts of Using Multiple Pesticides*, investigated the interactive effects of widely used pesticides, evaluated the extent of exposure, determined the populations most at risk, and developed policy recommendations to ensure public health protection. The report recommended that DPR evaluate pesticide mixtures and implement regulations to protect human health more adequately.[20]

In 2019, *Governance on the Ground: Evaluating the Role of County Agricultural Commissioners in Reducing Toxic Pesticide Exposures* evaluated the restricted material permitting process used by County Agricultural Commissioners (CACs) across the state. The report revealed that CAC staff receive no guidance from DPR regarding cumulative impact assessment and do not consider cumulative exposure during the permitting process.[21]

In sum, these three prior reports raised significant questions about the capacity of DPR and the CACs in pesticide governance, particularly with respect to cumulative impacts. While the legal mandates for these considerations are now clear, state and county officials assert, among other things, that no practical methods for cumulative impact assessment (CIA) are available. This project aimed to address this point, exploring existing and emerging frameworks (including methods and tools) for cumulative impact assessment.

Section II of the report presents our research goals and methods. Section III examines cumulative impact assessment, providing an overview of the state of the law, science, and current practice by DPR and CACs. Section IV identifies and evaluates candidate cumulative impact assessment frameworks relevant to the California regulatory context and offers a set of recommendations for relevant stakeholders.

19 Froines, et al., RISK AND DECISION, *supra* n.7.

20 Zaunbrecher, et al., EXPOSURE AND INTERACTION, *supra* n.3.

21 Malloy, et al., GOVERNANCE, *supra* n.2.

2 PROJECT GOALS AND METHODS

This project aims to catalyze use of CIAs in California pesticide regulation by generating a toolbox of sorts, a set of practical but sufficiently rigorous methods and tools fit for use in this context. The project used a mixed methods approach, including convening an advisory committee; conducting a literature review of cumulative risk assessment tools, methods, and frameworks; seeking expert and stakeholder consultation; organizing a stakeholder workshop; and evaluating potential approaches for cumulative risk assessment.

- The Advisory Committee consisted of relevant stakeholders from academia, non-governmental organizations, government, and the agricultural sector. Three full committee meetings were held during the project period, and smaller groups and individual members were consulted throughout. Committee members provided guidance on the design and implementation of the literature review and regarding the structure and content of the workshop. They provided peer review of the pre-workshop background papers and assisted in the identification and recruitment of workshop participants. Lastly, committee members reviewed a draft of this report. A list of Advisory Committee members is in Appendix A.
- The literature review surveyed and categorized academic literature and grey literature regarding existing and emerging frameworks, methods, and tools for cumulative risk assessment. (By grey literature we mean documents produced by governments, academics, businesses, or industry rather than by commercial publishers and collected and preserved by libraries and institutional repositories.[22])
- The project team consulted with experts from the United States and Europe and stakeholders from government, industry, and civil society regarding potential frameworks, methods, and tools that may be a fit for the California pesticide regulatory context. In particular, we worked closely with Dr. Thomas Backhaus (University of Gothenburg), Dr. Cynthia Rider (US National Institute of Environmental Health Sciences), and Dr. Allison Phillips (US Environmental Protection Agency) to identify potential workshop participants and to develop case scenarios, background readings, and presentations for the workshop approaches for California CIA.
- Prior to the workshop sessions, we circulated background white papers on the California pesticide regulatory program and on cumulative risk assessment methods. We also circulated three specific fictional discussion scenarios regarding product mixtures, field mixtures, and coincidental mixtures, providing realistic context for examination of potential methods and tools. Each scenario illustrated a different potential approach to addressing cumulative risk in the pesticide regulatory context.

22 Twelfth International Conference on Grey Literature (2010).

- The workshop consisted of two virtual sessions spaced one week apart. It was designed to facilitate in-depth discussions among the 25-30 participants regarding scientifically rigorous, practical, and effective methods and tools. It was structured as follows:
  - The workshop began with introductory overviews of the workshop, California pesticide regulation, and cumulative risk assessment, followed by time for clarifying questions. These overviews were meant to provide a common basic understanding of those topics.
  - Following the introductory presentations, participants considered three simulated discussion scenarios, each presenting a different approach to CIA. Participants discussed the relative benefits and challenges presented by these sorts of approaches and were invited to offer revisions or propose alternatives.
  - Two project team members took notes of the discussion. Following the workshop, we analyzed the notes to identify common themes, concerns, and disagreements from the discussions.
- Based upon the literature review, consultation with experts and stakeholders, and discussions during the workshop, we evaluated each of the candidate approaches. The evaluation identified the benefits and issues presented by each and considered potential solutions to those issues. It also assessed each approach against a set of five guiding principles described in Section IV, below. Members of the Advisory Committee and external reviewers provided review and comment on a draft report setting out that evaluation.

3 CUMULATIVE IMPACTS: LAW, PRACTICE, AND SCIENCE

THE STATE OF THE LAW

In the United States, the sale and use of pesticides is primarily regulated by the federal Environmental Protection Agency (EPA). (For our purposes, a pesticide is a substance or mixture of substances intended to prevent, destroy, repel, or mitigate pests.) Under the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA), EPA must ensure that pesticides are safe when used in accordance with label instructions. To that end, pesticides must be registered with EPA prior to sale. During the registration process, EPA evaluates the health and environmental effects of the candidate pesticide and imposes conditions, directions, and precautions on its use which must be displayed on the product label approved by EPA.[23]

FIFRA preserves the right of individual states to regulate federally registered pesticides "to the extent that regulation does not permit any sales or uses prohibited by FIFRA."[24] California has a robust pesticide regulatory program that, like the federal program, requires pesticides to be registered by the state Department of Pesticide Regulation. California's program has three important features relevant to this project. First, unlike the federal system, California has a dual system of regulation, with product registration at the state level and a pesticide use permitting process at the county level. Second, California explicitly requires both the state and county regulators to consider cumulative impacts in registration and permitting decisions, respectively. Third, unlike the federal government and other states, California has an extensive, publicly accessible reporting system for pesticide use which provides a trove of historical data regarding patterns of pesticide use statewide.

> The European Union has a similar system of dual regulation. Active ingredients are registered at the European Community level. Subsequently, the pesticide products incorporating registered active and inert ingredients must be authorized by individual member states. Commission Regulation 1107/2009, 2009 O.J. (L309)

23 See 40 CFR Section 156.10.

24 7 U.S.C. Section 136v(a). However, the state may not impose any labeling requirements in addition to or different from those required by EPA. 7 U.S.C. Section 136v(b).

DUAL REGULATION

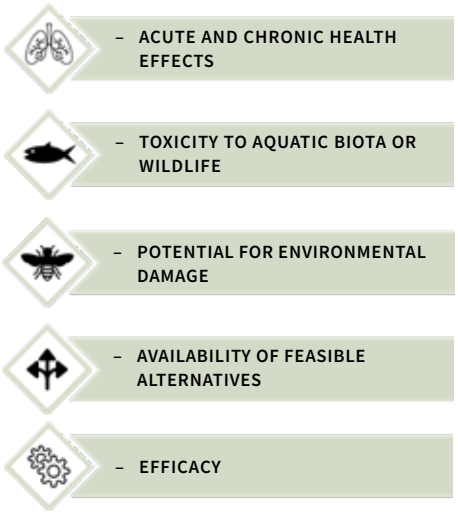
At the state level, the California Department of Pesticide Regulation (DPR) uses the registration process to evaluate new pesticide products. A pesticide product may not be sold or used in California until DPR issues a registration for it. DPR classifies registered pesticides of significant concern as restricted materials. Growers must obtain a restricted material permit from their local County Agricultural Commissioner (CAC) before using a restricted material pesticide in their fields. This dual system is depicted in Figure 4 and described in detail below.

The Registration Process. Upon receiving an application for registration, DPR staff scientists collect and review available data (including required data submitted by the registrant) regarding potential human and ecological exposures and human health and environmental effects. Among other information, registrants must submit test results regarding acute toxicity of the pesticide product.[25] If the product contains a new active ingredient, the registrant must also submit data regarding the chronic toxicity of that active ingredient.[26]

Based on the collected data, DPR scientists evaluate the risks presented by specific uses of the pesticide. They also determine whether the label warnings and handling directions for the pesticide product are appropriate. If DPR concludes that there is a potential for adverse health effects, it may propose that the product be designated as a "restricted material," triggering permitting requirements discussed below. DPR may also perform a more extensive risk assessment with input from outside experts from other agencies.

Following the premarket evaluation (and risk assessment if required), DPR management determines whether the pesticide should be registered based on a number of factors set out in its regulations. Where the pesticide presents health or environmental concerns (see Figure 3), DPR may require mitigation measures intended to protect the environment or the health of agricultural workers and of other individuals who live, work, or engage in activities nearby (sometimes called "bystanders"). Mitigation measures, such as buffer zones, use limits, and personal protective equipment, may be established in labeling requirements (with EPA approval), regulations, or recommended restricted material permit language. After registration, all pesticides are subject to continuous reevaluation by DPR.[27] In particular, revaluation is appropriate where new information suggests a significant adverse risk resulting from the use of a registered pesticide.[28]

Figure 3: Registration Factors



25 Acute toxicity refers to effects from short term exposure to the substance.

26 Chronic toxicity refers to effects from longer term exposure to the substance.

27 Food and Agriculture Code section 12824 (requiring a program that calls for informal, continuous evaluation of all registered pesticides); 3 CCR 6226: Product Evaluation.

28 3 CCR 6221(j): Reevaluation Criteria.

Restricted Materials Permitting. At the county level, "on the ground" implementation of the pesticide regulations is performed by the 56 CACs. (Two of the CACs serve two counties each.) The Board of Supervisors in each county appoints that county's CAC. Growers or their licensed pest control advisor (PCA) wishing to use a restricted pesticide for agricultural uses at a particular location must first obtain a permit from the relevant CAC.[29]

In deciding whether to use a restricted material for agricultural uses, PCAs and growers must consider and adopt any feasible alternatives and mitigation measures to the proposed pesticide use.[30] The permit application for restricted material use typically does not specify the precise timing of the use, and the permit is usually effective for one year.[31]

When a grower who has obtained a permit is ready to apply the restricted pesticides, the grower submits a notice of intent (NOI) at least 24 hours (48 hours for fumigants) prior to application, providing CAC staff with the chance to assess the site prior to or during application. The NOI describes the particular location, pesticides, and manner of application. In most counties, the NOI is submitted through CalAgPermits, a statewide web-based pesticide permitting and reporting program, which allows CAC staff to manage restricted material permits and NOIs and to view boundaries and features of the subject sites.

In evaluating a permit application, the CAC must determine if a substantial adverse environmental impact may result from the proposed use, and if so, must consider whether feasible alternative pesticides or mitigation measures would substantially reduce that impact.[32] In addition to the requirements mandated on pesticide use by DPR, the CACs have broad authority to include additional restrictions in the permit based on local conditions.

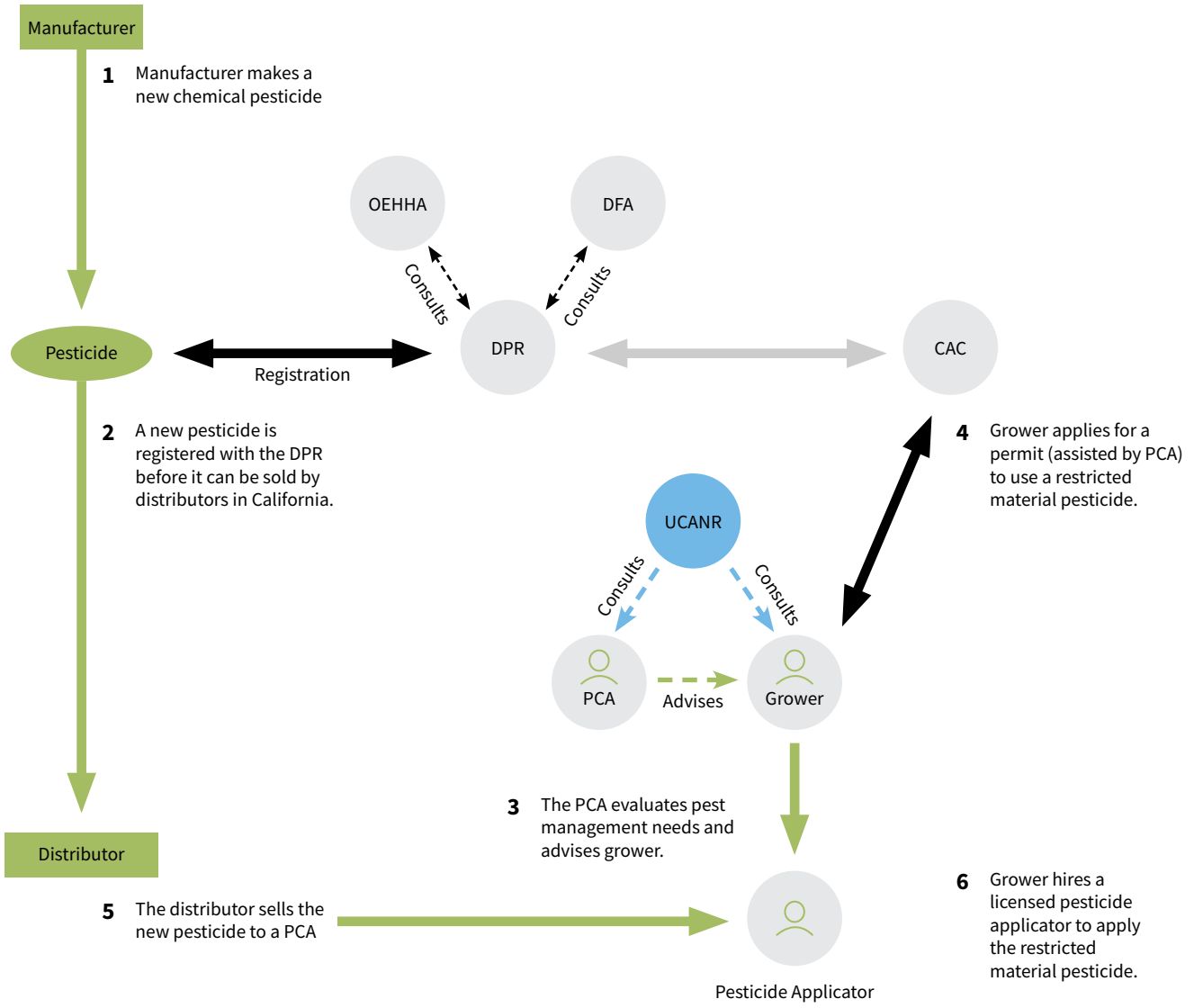
29 Food and Agriculture Code Section 14006.5. Professional structural pest control applicators do not need to obtain permits to use restricted material permits, for example, to fumigate buildings.

30 3 CCR Section 6426: Alternatives and Mitigation Measures.

31 3 CCR Section 6422: Permit Duration.

32 Food and Agriculture Code Section 14006.5 (incorporating Food and Agriculture Code Section 12825(c)); CCR Section 6432: Permit Evaluation.

Figure 4: Life Cycle of Pesticide Regulation



OEHHA - Office of Environmental Health Hazard Assessment
DFA - Department of Food and Agriculture
DPR - Department of Pesticide Regulation
CAC - California Agricultural Commissioner (56 in CA)
UCANR - University of California Agriculture and Natural Resources
PCA - Pest Control Advisor (The PCA may be affiliated with the distributor or independent.)

legal (regulatory) process
pesticide cycle
pest management technical support
legal consultation
consultation

CONSIDERATION OF CUMULATIVE IMPACTS

State law mandates that DPR and the CACs consider cumulative impacts (including chemical and non-chemical stressors) as part of registration and permitting, respectively. DPR's obligation to consider cumulative impacts in the registration process flows from two sources. First, the governing statute explicitly defines "pesticide" to include any *mixture* of substances intended to be used for preventing, destroying, repelling, or mitigating any pest. Accordingly, registration of a pesticide necessarily includes evaluation of the *mixture* rather than just the active ingredient.

Second, the California Environmental Quality Act (CEQA) requires DPR to consider the cumulative impacts of its registration decision.[33] Under CEQA, cumulative impacts refers to "two or more individual effects which, when considered together, are considerable or which compound or increase other environmental impacts."[34] CEQA establishes procedural requirements and substantive standards for public agency decisions regarding projects conducted, financially supported, or approved by those agencies. Procedurally, unless a covered project has no significant adverse environmental impacts, the agency must prepare an environmental impact report (EIR) evaluating the project. As a substantive matter, the EIR must consider certain core issues, including significant cumulative impacts of the project and feasible mitigation measures and project alternatives.

In 1980, acknowledging that procedural aspects of CEQA were impractical for pesticide regulation, the California legislature allowed the department to implement a "functionally equivalent" but more expeditious process; namely, the registration and permitting programs. In 2017, in *Pesticide Action Network North America v. California Department of Pesticide Regulation* (PANNA), the California Court of Appeals concluded that registration must nonetheless meet the substantive aspects of CEQA review, including consideration of alternatives and evaluation of cumulative impacts.[35]

A CAC's obligation to consider cumulative impacts as part of the restricted materials permitting process likewise flows from two sources. First, DPR's regulations establishing the restricted material permitting program require that the CAC take into account "local conditions" in determining whether a proposed pesticide use may result in substantial adverse environmental impact.[36] Second, CEQA's substantive requirements—including the obligation to evaluate cumulative impacts —apply to CACs directly as covered public agencies.[37]

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33 Public Resources Code §§ 21000-21177.

34 CCR Section 15355: Guidelines for Implementation of the California Environmental Quality Act.

35 *Pesticide Action Network North America v. California Department of Pesticide Regulation*, 16 Cal. App. 5th 224, 245 (2017).

36 CCR Section 6432: Permit Evaluation.

37 *In the Matter of the Agricultural Commissioner of the County of Monterey*, Permit Appeal No. A-0002 at 17 (March 6, 2024).

PESTICIDE USE REPORTING

California is unique in that it maintains extensive, publicly available pesticide use reporting (PUR) data dating back decades. Mandatory pesticide use reporting, which originated in 1934, took many forms through the years.[38] In its current iteration, in place since 1990, growers are required to report specified pesticide use information to their CAC on a monthly basis.[39] The CACs submit the PUR data to DPR. DPR assembles, curates, and maintains the PUR data and makes it available to the public through the online California Pesticide Information Portal (CalPIP). The reporting requirements are extensive, providing DPR with a relatively finely grained picture of pesticide use over time and place. That said, PUR does have significant limitations. For example, grower reports for large operations may not specify the particular location of pesticide application.

PUR DATA REPORTING INCLUDES:

- Name, registration no., and amount of product applied
- Date and time of application
- Site location by:
  - Physical Address
  - County assigned site ID no.
  - Public Land Survey System Section (1x1 mile sections)
  - Type of crop treated
  - Application method
  - Operator name and address

DPR and other state and federal agencies use the PUR data for a variety of purposes, including evaluating trends, identifying potential enforcement cases, and prioritizing air and water quality issues.[40] Researchers and non-profit organizations have also made substantial use of the PUR data, often in combination with Geographic Information System (GIS) methods, to evaluate various impacts of pesticide use.[41] For example, a number of epidemiological studies have relied upon PUR data in estimating pesticide exposures and risk.[42]

THE STATE OF PRACTICE IN CALIFORNIA

State law requires evaluation of cumulative impacts during registration and restricted material permitting of pesticides. Bear in mind that such cumulative impacts could occur from exposure to product mixtures, intentional

38 DPR, GUIDE, *supra* n.7, at 74.

39 Food Safety Act of 1989 (Chapter 1200, AB 2161); see also https://www.cdpr.ca.gov/pesticide-use-in-california/pesticide-use-reporting/.

40 Nino Yanga, et al., Pesticide Use Reporting Data in Pesticide Regulation and Policy: The California Experience, in Minghua Zhang, et al. (eds.), MANAGING AND ANALYZING PESTICIDE USE DATA FOR PEST MANAGEMENT, ENVIRONMENTAL MONITORING, PUBLIC HEALTH, AND PUBLIC POLICY (2018) (hereinafter Zhang, PESTICIDE USE DATA).

41 See Michael L. Grieneisen and Minghua Zhang, et al., The Extensive Use of Pesticide Use Report (PUR) Data in Scholarly Scientific Research, in Zhang, PESTICIDE USE DATA, *supra* n.40; Alexis M. Temkin, et al., Racial and Social Disparities in Ventura County, California Related to Agricultural Pesticide Applications and Toxicity, 853 SCI. TOTAL ENV'T 158399 (2022); Caroline Cox and Michael Zeiss, Health, Pesticide Adjuvants, and Inert Ingredients: California Case Study Illustrates Need for Data Access, 130 Environmental Health Perspectives 085001-1 (2022); Ashley E. Larsena, D. Nakoa Farranta, and Andrew J. MacDonald, Spatiotemporal Overlap of Pesticide Use and Species Richness Hotspots in California, 289 AGRICULTURE, ECOSYSTEMS AND ENVIRONMENT 10674 (2020).

42 H. Yang, et al., Residential Proximity to a Commercial Pesticide Application Site and Risk of Chronic Rhinosinusitis, 149 JAMA Otolaryngol Head Neck Surg. 773 (2023); Christina Lombardi, et al., Residential Proximity to Pesticide Application as a Risk Factor for Childhood Central Nervous System Tumors, 197 ENVIRONMENTAL RESEARCH 111078 (2021); Beate Ritz and Fei Yu, Parkinson's Disease Mortality and Pesticide Exposure in California 1984–1994, 29 INTERNATIONAL JOURNAL OF EPIDEMIOLOGY 323 (2000).

field mixtures, and coincidental mixtures resulting from application of different pesticides close in space and time. And ample evidence exists that such exposures do occur.[43] All this begs the question of whether DPR or the CAC evaluate the cumulative impacts of their regulatory decisions allowing the application of pesticides.

With very limited exceptions described below, DPR does not evaluate the impacts of any of the three cumulative exposures scenarios.[44] DPR guidance and website statements do not discuss the agency's approach to cumulative exposures. Indeed, in evaluating the DPR's risk assessment process, the National Research Council concluded in 2015 that "[t]he extent to which DPR has considered such cumulative risk assessments is unclear".[45]

With respect to product mixtures, it appears from a review of selected DPR risk assessments that DPR typically treats cumulative effects of exposure to the candidate active ingredient and its co-formulants as an uncertainty. For example, in the 2019 risk assessment of propanil, DPR noted:

> In California, some propanil formulations also contain the herbicidal [active ingredients] bensulfuron methyl (BSM) and halosulfuron methyl (HSM) (NPIRS, 2012). The characterization of risk from exposures to mixtures containing propanil and BSM or HSM is beyond the scope of this assessment. Nevertheless, co-exposure to these chemicals is likely and presents an additional layer of toxicologic uncertainty. The development of newer technologies and methods (*e.g.*, in vitro methods like those in ToxCast) may be needed to gain a greater understanding of the toxicity of mixtures of this type.[46]

Nor does DPR perform cumulative risk assessment of intentional field mixing or coincidental mixing of different pesticides.[47]

There are two primary exceptions to this pattern. First, DPR does require limited toxicity testing of the product mixture during registration. In particular, registrants must provide whole product toxicity data for acute inhalation, ingestion, and dermal contact.[48] This data is typically used to determine toxicity categories reflected on product labels but is not used to determine acute thresholds for the risk assessment. Determination of acute thresholds in the risk assessment relies upon testing of the single active ingredient being registered rather than the whole product.[49]

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43 Malloy, et al., GOVERNANCE, *supra* n.2; Zaunbrecher, et al., EXPOSURE AND INTERACTION, *supra* n.3.

44 Zaunbrecher, et al., EXPOSURE AND INTERACTION, *supra* n.3 ; Froines, et al., RISK AND DECISION, *supra* n.7. Outside of the registration and permitting contexts, DPR has engaged in ambient air monitoring for pesticides, in part to study cumulative exposure to a small set of pesticides exhibiting a common mode of action for toxic effects. DPR, AIR MONITORING NETWORK RESULTS FOR 2018 (November 2019).

45 National Research Council, REVIEW OF CALIFORNIA'S RISK-ASSESSMENT PROCESS FOR PESTICIDES (2015).

46 DPR, FINAL PROPANIL RISK CHARACTERIZATION DOCUMENT (2019) (emphasis added). See also, DPR, 1,3-DICHLOROPROPENE RISK CHARACTERIZATION DOCUMENT (2015) ("Finally, it is worth mentioning that most 1,3-D-containing formulations sold in California also contain the fumigant chloropicrin, which is not only a severe irritant, but also may be carcinogenic. That the two chemicals could have synergistic toxicity or carcinogenicity is not known, but is considered at least a plausibility.").

47 Zaunbrecher, et al., EXPOSURE AND INTERACTION, *supra* n.3.

48 3 CCR Section 6172: General Toxicity Data.

49 See DPR, FINAL PROPANIL RISK CHARACTERIZATION DOCUMENT (2019).

Second, in limited circumstances DPR has considered impacts from the sequential or simultaneous application of the same or even different active ingredients as part of risk management. For example, in issuing new regulations effective in 2024 for the application of 1,3-Dichloropropene (1,3 D), DPR established special setback distances where there were "overlapping" applications of 1,3 D on adjacent or nearby fields. These steps were intended to ensure that the resulting aggregate air concentrations were below the 55 ppb regulatory target concentration for acute exposure to non-occupational bystanders.[50] Similarly, in 2023 DPR issued regulations establishing a combined seasonal application rate when multiple neonicotinoid active ingredients are used by a grower.[51]

THE STATE OF THE SCIENCE

This section provides an introduction to risk and risk assessment, followed by an overview of well-established approaches for evaluating cumulative risk.

Risk has different definitions in different settings, but generally speaking, risk is the likelihood that humans or ecological systems will be harmed by exposure to a "stressor." A stressor can be a chemical released into the environment, such as a pesticide. Or it can be physical (*e.g.* heat or noise) or psychosocial (*e.g.* poverty or fear of crime.) In chemical regulation, risk is typically described as having two components—hazard (how toxic the substance is) and exposure (how much contact the affected person or ecosystem has with the substance.)

CONVENTIONAL RISK ASSESSMENT

Broadly defined, risk assessment is a process for evaluating the extent and nature of risk. Risk assessment can take many forms. In some cases, it is a formal, quantitative process relying heavily upon numerical data and mathematical models. When DPR determines that risk assessment of a pesticide product is needed during registration, DPR uses quantitative risk assessment. In other situations, risk assessment may be qualitative, incorporating categorical measures and various rules of thumb. For example, in the industrial setting, qualitative and semi-quantitative risk assessment methods are often used to evaluate the risks associated with industrial processes. Risk assessment generally involves five steps, as illustrated in Figure 5.[52] (The discussion below focuses on assessment of risks to human health. Environmental risks are also assessed with consideration of both exposure and effects thresholds.)

Risk assessment typically begins with **problem formulation**, in which the specific focus and goals of the risk assessment are articulated, and the nature of the analysis identified. It essentially sets the stage for the remaining steps:

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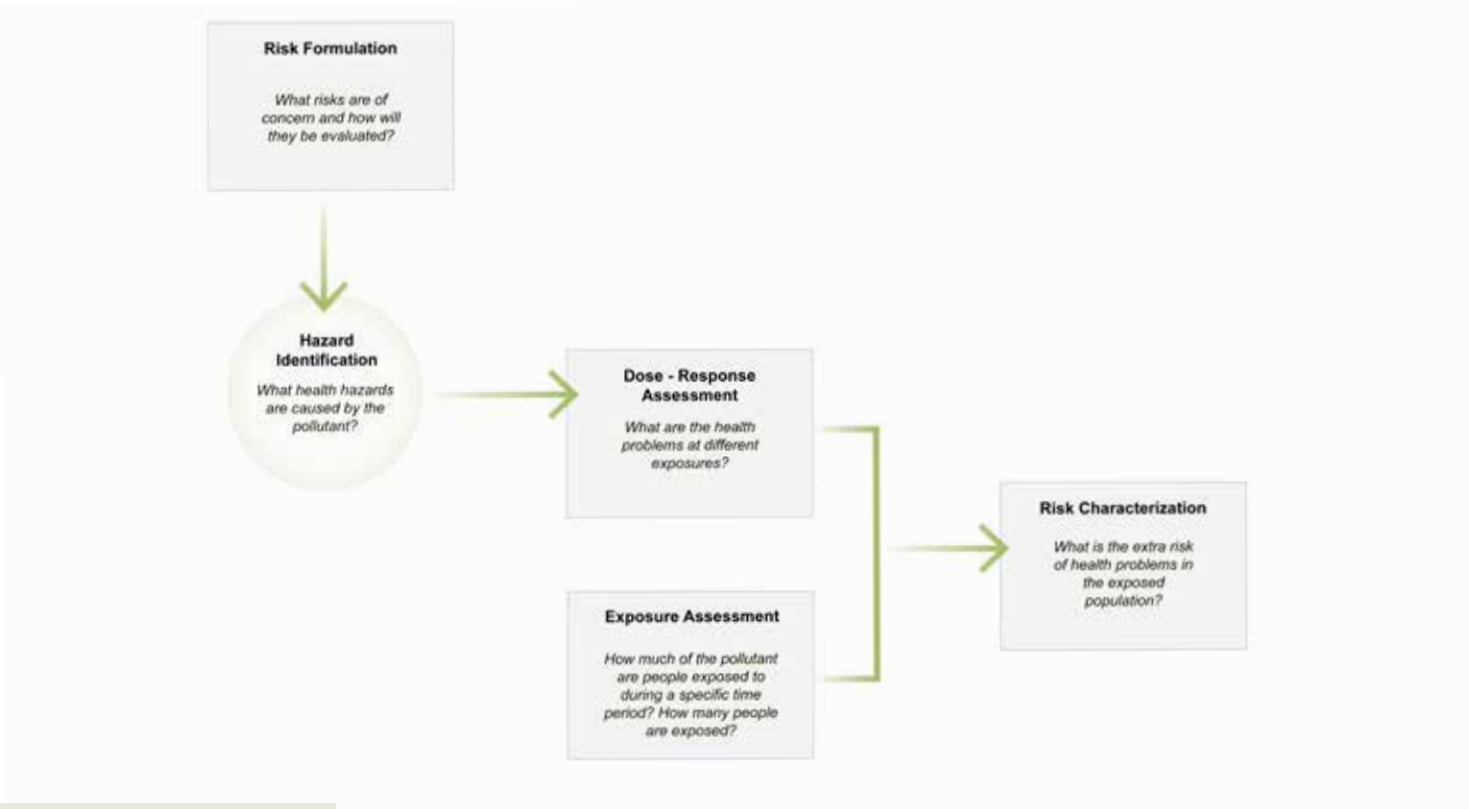
50 3 CCR Section 6448: 1,3-Dichloropropene Field Fumigation – General Requirements; DPR, INITIAL STATEMENT OF REASONS AND PUBLIC REPORT, HEALTH RISK MITIGATION AND VOLATILE ORGANIC COMPOUND EMISSION REDUCTION FOR 1,3-DICHLOROPROPENE.

51 3 CCR Section 6990 et seq.

52 Adapted from https://www.epa.gov/risk/conducting-human-health-risk-assessment.

Figure 5. Risk Assessment Steps



SOME HAZARDS THAT RISK ASSESSMENT CONSIDERS:

- Breathing problems
- Immune system problems
- Reprodcution
- Cancer
- Hormone functions
- Brain and nervous system

• **Hazard identification** determines the harmful effects inherently associated with the chemical, such as respiratory problems, kidney damage, or even death. Some of these effects may be acute, meaning the effects arise quickly after short term exposure. Other effects may be chronic, resulting from long term exposure and developing over time. Risk assessors rely on a variety of data to identify pesticide hazards, including in vivo animal studies, in vitro laboratory tests, human poisoning incidents, and epidemiological studies. In many cases, the results of animal studies and in vitro tests are the primary sources of information. There are standardized testing methods for a range of harmful effects, providing procedures for exposing laboratory animals (*e.g.*, mice, rats, rabbits, or fish) to the chemical and for collecting the resulting data. Many of the testing methods call for exposing test animals to increasing doses of the chemical and observing the resulting effects. (New non-animal testing methods that take advantage of advances in genomics, big data, and other innovations are being developed.)

• **Dose-response assessment** determines the relationship between the amount of exposure (the dose) and the severity of the resulting effect (the response). Typically, but not always, as the dose increases, the observed response also increases. Generally speaking, for each hazard of concern, toxicologists determine the lowest level at which no toxic effects are seen. A critical effect (*e.g.*, the adverse effect that occurs at the lowest dose to the most sensitive species) is identified, and then this level is decreased to take into account various scientific uncertainties, such as differences between the laboratory animals and humans

or the variability in expected human responses. That adjusted level is used to establish an acceptable exposure level.

- **Exposure assessment** estimates the size and nature of the dose humans would receive when the pesticide is used. It considers how the chemical moves through the air, water, and other pathways to reach human receptors, as well as how it enters the body—whether through breathing, ingestion, or even through the skin or eyes. And exposure will vary depending upon who the receptor is; for example, a worker applying the pesticide will interact with the pesticide very differently than a nearby resident or children playing in an adjacent schoolyard. Exposure can be measured through environmental monitoring or directly through body fluid levels but is more often calculated using modeling of air, water, and other environmental media. Exposure assessment also considers how the chemical may be transformed in the environment, such as by breaking down into degradation products.[53]

- **Risk characterization** combines information from the exposure assessment with information from the dose-response assessment to determine the likelihood that use of the pesticide could harm exposed people. It also explains how the risk was assessed, describes any assumptions underlying the analysis, and discusses uncertainties in the analysis. Uncertainties arise in each of the prior three steps; for example, there may be uncertainty regarding the reliability of particular animal studies used in hazard assessment or concerning the quality or representativeness of data used for exposure assessment.

RISK MANAGEMENT

The risk assessment is used to support risk management decision-making. The goal of risk management is to identify a set of options that can reduce hazard and exposure. It also aims to evaluate those options to determine if they provide acceptable protection of human health and the environment. Risk management often presents trade-offs that complicate decision-making. Effective risk management must craft a combination of mitigation measures that reduce hazard and exposure to acceptable levels, are enforceable in the field, allow for effective pest management, and do not result in other unacceptable health or environmental impacts.

RESTRICTED MATERIAL PERMITTING:

DPR can manage risks by designating a pesticide as a "restricted material." Use of such a pesticide requires a permit from the local County Agricultural Commissioner (CAC). Permits can include permit conditions developed by DPR or by CACS.

Mitigation measures can include, among other things, controls on timing and frequency of application; limits on crops to be treated; use of feasible, safer alternatives; use of personal protective equipment by workers; and required buffer zones to protect people or wildlife near the application site. If mitigation measures cannot reduce the risk to acceptable levels, DPR can deny registration of the pesticide product. Mitigation measures may be implemented through regulations, permit conditions, or labels (in conjunction with the United States EPA).

53 Dick Sijm, et al., Transport, Accumulation and Transformation Processes, in C.J. van Leeuwen and T.G. Vermeire (eds.), RISK ASSESSMENT OF CHEMICALS: AN INTRODUCTION 73 (2007).

CUMULATIVE RISK

For the most part, conventional risk assessment evaluates one chemical at a time. But humans and ecological systems are typically exposed to multiple chemicals and other stressors at any given time. People can be exposed to multiple chemicals in a variety of ways. In this project, we will consider three scenarios. In the first, the pesticide product itself consists of an intentional mixture of chemicals. When the product is applied in the field, workers, bystanders, and nearby residents could be exposed to that mixture. The second scenario involves intentional mixtures created by field mixing. Third are coincidental mixtures that occur when growers apply different pesticides on adjacent or nearby cropland close in time. To varying degrees, the chemicals in those pesticides can mix in the environment and cumulative exposures can occur.

In many cases, the effects of the multiple chemicals are **additive**, meaning that the chemicals can act jointly to produce a common adverse effect such as a disease. Additive effects of similar chemicals are often estimated by dose addition (or concentration addition). Components of the mixture may cause a particular disease or other toxic effect through the same molecular mechanism, or they may act through different mechanisms to cause a similar effect on a particular target organ. In dose addition, the risk of a mixture can be estimated by scaling the doses of the mixture components for their differences in potency and then summing the scaled doses. The sum of the scaled doses is considered the dose of the mixture, which can be mapped to a response. Consequently, exposure to the mixture could cause adverse health effects even though exposure to any one of the component chemicals at the concentration present in the mixture would not.

In other cases, chemicals may have interactive effects. That is, two or more chemicals can interact with each other to either intensify the toxic effect (known as a more-than additive effect or synergism) or reduce it (less-than-additive effect or antagonism). Where a mixture exhibits more-than-additive effects, the toxic effects of the mixture are greater than those predicted by dose addition or response addition. More-than-additive human health and ecological effects have been demonstrated in some studies.[54] Citing the high doses administered in such studies and other factors, systematic reviews of the literature conclude that more-than-additive effects are uncommon at the relatively low doses to which humans and environmental receptors are exposed in practice.[55] When they consider cumulative risk, US and EU regulators apply

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54 Olwenn Martin, Ten Years of Research on Synergisms and Antagonisms in Chemical Mixtures: A Systematic Review and Quantitative Reappraisal of Mixture Studies, 146 ENVIRONMENT INTERNATIONAL 106206 (2021). See, *e.g.*, Lingyun Mo, et al., Quantitative Characterization of the Toxicities of Cd-Ni and Cd-Cr Binary Mixtures Using Combination Index Method, BIOMED RESEARCH INTERNATIONAL Art. 4158451 (2016)(endocrine disrupting compounds and metal compounds); Nina Cedergreen, Quantifying Synergy: A Systematic Review of Mixture Toxicity Studies within Environmental Toxicology, 9 PLOS ONE e96580 (2014) (triazine, azole and pyrethroid pesticides); Hisham El-Masri, et al., Physiologically Based Pharmacokinetic/Pharmacodynamic Modeling of the Toxicologic Interaction between Carbon Tetrachloride and Kepone, 70 ARCHIVES OF TOXICOLOGY 704 (1996) (carbon tetrachloride and kepone).

55 Martin, Ten Years of Research, *supra* n. 54; Alan Boobis, et al., Critical Analysis of Literature on Low-Dose Synergy for use in Screening

approaches based on dose addition, unless the weight of evidence in a specific case indicates that synergistic effects may be occurring.[56]

CUMULATIVE RISK ASSESSMENT

EPA has defined cumulative risk assessment as "an analysis, characterization, and possible quantification of the combined risks to health and/or the environment from multiple agents and/or stressors."[57] (As noted above, this report will focus primarily on pesticide chemical stressors.) There are a variety of approaches that have been used or proposed for cumulative risk assessment. We focus on two in particular: the whole mixture approach and the component-based approach.

Whole mixture approaches deal with the mixture as a whole. In the pesticide registration setting, this could involve performing a risk assessment on the formulated product rather than a single active ingredient. Accordingly, hazard characterization (including toxicity testing), dose response assessment, and exposure assessment would all evaluate the entire pesticide product, while taking into account potential differences in the fate and transport of the components after application in the field.

Component-based approaches rely primarily on information for the respective component chemicals rather than the whole mixture. Such approaches generally assume that if there is evidence that individual chemicals are "similar," the effects of the chemicals are additive. That said, some component-based approaches attempt to factor in potential interactions among the components.[58] The component-based approach assumes that there is sufficient data availability for each relevant component. Component-based approaches are widely used and proposed for regulatory purposes, such as in EPA's Superfund cleanup and pesticide programs and the Euromix project in the European Union.[59]

For our purposes, there are two central questions regarding the implementation of a component-based approach. The first question is which components of the mixture are grouped together for cumulative risk assessment. Dose additive methods assume toxicological similarity of component chemicals.[60] In some

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Chemical Mixtures for Risk Assessment, 41 CRITICAL REVIEWS IN TOXICOLOGY 369 (2011).

56 US EPA, DRAFT PROPOSED PRINCIPLES OF CUMULATIVE RISK ASSESSMENT UNDER THE TOXIC SUBSTANCES CONTROL ACT (EPA-740-P-23-001 February 2023); 84 Fed. Reg. 4787 (Sep. 9, 2019); Stefanie Rotter, et al., Overview on Legislation and Scientific Approaches for Risk Assessment of Combined Exposure to Multiple Chemicals: The Potential Euromix Contribution, 48 CRITICAL REVIEWS IN TOXICOLOGY 796 (2018).

57 EPA, FRAMEWORK FOR CUMULATIVE RISK ASSESSMENT (2003).

58 See Richard C. Hertzberg, et al., Evaluation of the Interaction-Based Hazard Index Formula Using Data on Four Trihalomethanes from U.S. EPA's Multiple-Purpose Design Study, 12 TOXICS 305 (2024).

59 Anna Beronius, et al., Methodology for Health Risk Assessment of combined Exposures to Multiple Chemicals, FOOD AND CHEMICAL TOXICOLOGY 111520 (2020); Richard C. Hertzberg and M. Moiz Mumtaz, Component-Based Risk Assessment Approaches with Additivity and Interactions, in Rider and Simmons, CHEMICAL MIXTURES, *supra* n. 15, at 369.

60 Hertzberg and Mumtaz, Component-Based Risk Assessment, *supra* n. 59. Glenn E. Rice, et al., Assessing Human Health Risks Using

dose additive approaches, chemicals are grouped together only if it is clear that they share a "common mechanism of action," essentially meaning that they cause toxicity through the same process at the molecular level. Identifying common mechanism groups is extremely data and resource-intensive.[61] For example, EPA relies upon a common mechanism of action to group pesticides for cumulative risk assessment under the 1996 Food Quality Protection Act. To date, the agency has identified just five chemical groups. Other dose additive approaches are less restrictive, such as grouping together chemicals that affect the same organ or cause the same disease.[62]

The second question is how the toxicological data on component chemicals are combined to estimate mixture risk. Here again there are a variety of methods, some of which have been used for decades by EPA and other agencies. These methods include the hazard index (HI), relative potency factors (RPFs), and combined margin of exposure approaches. Each method presents its own benefits, uncertainties, and limitations.[63] Identification of the optimal method is beyond the scope of this project. For our purposes, it is enough that these well-established options are available for use in California's program.

Information on Whole Mixtures, in Rider and Simmons, CHEMICAL MIXTURES *supra* n. 15, at 421. Response additive methods assume independent action of component chemicals and have typically been used to estimate mixture risk for carcinogens.

61 Cynthia V. Rider, Mixture Math: Deciding What to Add in a Cumulative Risk Assessment, 31 CURRENT OPINION IN TOXICOLOGY 100358 (2022).

62 Anna Beronius, et al., Methodology, *supra* n. 59.

63 EFSA Scientific Committee, Guidance on Harmonized Methodologies for Human Health, Animal Health and Ecological Risk Assessment of Combined Exposures to Multiple Chemicals, 17 EFSA JOURNAL 5634 (2019); Hertzberg and Mumtaz, Component-Based Risk Assessment, *supra* n. 59, at 369.

4 IDENTIFICATION AND EVALUATION OF CIA OPTIONS

In this section we identify and evaluate potential approaches to cumulative risk assessment and, to some degree, cumulative impact assessment for product, field, and coincidental mixtures, respectively. The section begins with a brief discussion of four features common to all approaches. Next, for each respective mixture type, we evaluate the benefits and limitations of the candidate approaches and offer a recommendation for the most promising approach or set of approaches. Our recommendations are guided by five fundamental principles:

- **Implement What is Possible, Now**. Cumulative risk assessment has been performed in various ways in diverse programs for over forty years. Recognizing that the perfect should not stand in the way of the good, the project aims to identify approaches that can significantly improve California's treatment of cumulative risk in the near term, while pursuing enhancements over the mid and long term. This principle recognizes that risk assessment and risk management are not limited to quantitative methods typically used in registration and similar regulatory programs. Qualitative and semi-quantitative approaches are widely used in a variety of settings and can provide improved and meaningful protection.

- **Align Responsibilities with Institutional Capacities**. DPR has scientific, administrative, and legal capacities and knowledge that can be supported by the scientific capacities, knowledge, and experience of OEHHA, the UC Agriculture and Natural Resources division, and other entities. The County Agricultural Commissioner offices have limited scientific and regulatory capacities but have close connections to and knowledge about the grower and pest control advisor communities. Recognizing that all these institutions are subject to institutional, budgetary, and other limitations, approaches to cumulative risk assessment should mindfully integrate their respective capacities.

- **Make Full Use of Existing Resources**. DPR has access to useful resources that can support meaningful assessment. For example, the PUR system provides rich information regarding historical practices, allowing DPR to identify common use patterns for existing pesticides and to predict likely use patterns of new pesticides. Likewise, OEHHA's CalEnviroScreen uses environmental, health, and socioeconomic information to generate scores reflecting relative cumulative burden experienced by communities at the census tract level. As discussed below, these and other existing resources can be adapted to support cumulative impact assessment within the pesticide regulatory program.

- **Optimize Protection of Public Health and the Environment Through Cost-Effective Means**. Under California law, DPR and the CACs are required to consider cumulative impacts in decision-making regarding registration and restricted materials permitting, respectively. The costs of enhancing the registration and permitting processes will, to various degrees, increase the costs to industry, the agencies, and

consumers. Principles of good regulation and of state administrative law emphasize the importance of ensuring that regulation achieves its goals in a cost-effective manner.[64]

- **Establish Sustainable and Sufficient Funding**. As discussed below, implementation of some aspects of these recommendations will require additional funding for DPR, CACs, OEHHA, and other entities. The legislature and administration should take steps to identify and implement stable funding strategies to support these efforts. By way of example, in 2021, Senate Bill 158 established the Board of Environmental Safety in the Department of Toxic Substances Control (DTSC), mandating that the Board, among other responsibilities, conduct an analysis of the fee structure funding DTSC's activities and develop recommendations for sustainable funding of those activities. Similarly, development of sustainable funding strategies is critical for meaningful efforts in this area by DPR and its partners.

COMMON FEATURES

All of the approaches discussed below share four common features. First, each approach requires a clear trigger for when cumulative risk assessment is required. Cumulative risk assessment may not be necessary for pesticide products whose ingredients are not expected to exhibit additive or greater-than-additive effects.[65] Thus, each of the approaches should have a mechanism that alerts regulators to the need for a cumulative risk assessment. For example, in the registration process, the problem formulation step of the risk assessment should include such an evaluation. Likewise, in restricted material permitting, a screening step should be used for this evaluation.

We propose that OEHHA, with support from DPR, develop cumulative assessment groups (CAG) which group together known and proposed pesticide ingredients based upon similar toxicological effects on specific organs. The presence of two or more members of the same CAG in a mixture (whether a product, field, or coincidental mixture) would trigger cumulative risk assessment. A variety of approaches to group chemicals into CAGs exist. For example, chemicals may be grouped together when they (1) exhibit any of a number of toxicological effects on the same organ, such as the liver or reproductive system, or (2) are linked to a common effect on one organ, or (3) act through a common mechanism of action at the molecular level.[66] Generally speaking, grouping based on a common mechanism of action at the molecular level provides a more rigorous measure

64 Office of Technology Assessment, ENVIRONMENTAL POLICY TOOLS: A USER'S GUIDE (1995); CA Gov. Code Section 11346.3 (calling for "the most cost-effective set of regulatory measures that are equally effective in achieving the purpose of the regulation in a manner that ensures full compliance with the authorizing statute. . . .")

65 As noted above, ingredients may have independent toxicological effects of concern which DPR should consider even absent additive or greater-than-additive effects. Response addition, which often applies concepts of probability theory in assessing responses, is commonly used in this context. Hertzberg and Mumtaz, Component-Based Risk Assessment Approaches, *supra* n. 59.

66 EFSA Scientific Committee, Guidance on Harmonized Methodologies, *supra* n. 63; Cynthia V. Rider, et al., Predicting Mixture Toxicity with Models of Additivity, in Rider and Simmons, CHEMICAL MIXTURES, *supra* n. 15, at 235; EPA, SUPPLEMENTARY GUIDANCE FOR CONDUCTING HEALTH RISK ASSESSMENT OF CHEMICAL MIXTURES (2000).

of toxicological similarity than a standard based on common effects on a target organ.[67] EPA uses such an approach as part of its program regulating pesticide residues on raw agricultural commodities or processed foods.[68] However, grouping based on common target organ effects is substantially less data- and time-intensive and more conservative from a human health and environmental perspective. (The CAG should also be based upon similar ecological effects.)

The second common feature is the use of tiered approaches to critical decisions. Recognizing the need for scientifically-supported and timely risk evaluation and management, each approach utilizes default assumptions and rules in various ways discussed further below to guide decisions where certain relevant data or more sophisticated analysis are not available. Each approach also provides the opportunity for further data generation and analysis, where practicable and appropriate, to alter the default. Tiered approaches to cumulative risk assessment have been proposed by a variety of regulatory agencies, institutions, and researchers, including the European Food Safety Authority and the World Health Organization.[69]

The third common feature of the approaches discussed below is leveraging existing data, including the comprehensive information on pesticide use maintained by the PUR program. By applying powerful data analytic techniques, DPR can generate information regarding pesticide use patterns that is critical to implementing the cumulative risk assessment approaches. For example, DPR can use PUR data and pesticide product label information to identify commonly occurring intentional mixtures resulting from field mixing. Likewise, OEHHA and DPR can draw upon PUR data to uncover common coincidental mixtures that historically occur, which could guide development of cumulative assessment groups for such mixtures.

The fourth common feature is the integration of the CalEnviroScreen tool into the registration and restricted material permitting process. CalEnviroScreen is a community-based cumulative impact assessment tool developed by OEHHA that synthesizes environmental, health, and socioeconomic data using quantitative and semiquantitative methods.[70] It generates scores at the census tract level across the state, allowing communities, state and local governments, and regulators to comparatively evaluate cumulative chemical and non-chemical impacts burdening communities. A high score reflects a much higher burden than a low score.[71] CalEnviroScreen is used by different stakeholders for a variety of purposes. For example, the California Department of Toxic Substances Control has used it to prioritize facilities for compliance inspections.[72]

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67 Rider, et al., *supra* n. 66.

68 EPA, GUIDANCE ON CUMULATIVE RISK ASSESSMENT OF PESTICIDE CHEMICALS THAT HAVE A COMMON MECHANISM OF TOXICITY (JANUARY 14, 2002)

69 Stefanie Rotter, et al., Overview on Legislation and Scientific Approaches, *supra* n. 56; M.E. (Bette) Meek, Risk Assessment of Combined Exposure to Multiple Chemicals: A WHO/IPCS Framework, 60 REGULATORY TOXICOLOGY AND PHARMACOLOGY S1(2011); European Food Safety Authority, Opinion of the Scientific Panel on Plant Protection Products and their Residues to evaluate the suitability of existing methodologies and, if appropriate, the identification of new approaches to assess cumulative and synergistic risks from pesticides to human health with a view to set MRLs for those pesticides in the frame of Regulation (EC) 396/2005. 704 EFSA J. 1 (2008).

70 Shannon R. Murphy, et al., Community-Based Cumulative Impact Assessment: California's Approach to Integrating Nonchemical Stressors into Environmental Assessment Practices, in Rider and Simmons, CHEMICAL MIXTURES, *supra* n. 15, at 515.

71 https://oehha.ca.gov/calenviroscreen/about-calenviroscreen (last accessed March 18, 2024.)

72 Department of Toxic Substances Control, 2024 DTSC Director's Priorities (July 2023); Murphy, et al., Community-Based Cumulative Impact Assessment, *supra* n. 70.

CalEnviroScreen could be used by DPR to directly address cumulative impacts beyond the particular chemical pesticide exposures addressed in a registration or restricted material permitting decision. For example, under each of the candidate approaches discussed below, cumulative impacts associated with non-pesticide stressors could be taken into account in risk management. In developing mitigation measures for pesticides, DPR could establish more stringent measures for use of that pesticide in or near communities with CalEnviroScreen scores above a particular threshold.[73] These enhanced measures would be set out in regulations and implemented through restricted material permits. CalEnviroScreen could also be used to prioritize application of cumulative risk assessment to particular circumstances.[74] Similar tools also exist for ecosystems, such as the California Department of Fish and Wildlife's California Natural Diversity Database and the San Francisco Estuary Institute's California Aquatic Resource Inventory. While identifying the specific tools and the methods for integrating them into cumulative risk assessment is beyond the scope of this project, it is essential to note the importance of addressing cumulative impacts to sensitive habitats.

PRODUCT MIXTURES

Recall that a product mixture refers to formulated pesticide products in which active ingredients, adjuvants, and other so-called "inert ingredients" are mixed. A particular pesticide product may have several registered formulations consisting of the same ingredients in different proportions. As part of the workshop discussions, we discussed three alternative approaches to product mixtures: whole product assessment, component-based assessment, and hybrid assessment. Regardless of the approach used, product mixture assessment would be performed by DPR as part of registration of new pesticides and reevaluation of existing pesticides.

Whole Product Assessment: Here risk assessment and risk management focus upon the pesticide product as a whole rather than an individual active ingredient. The primary benefit of this approach is its capacity to capture additive and more-than-additive effects of all ingredients. Following a description of whole product assessment, Table 1 identifies issues presented by the approach and potential solutions.

In the problem formulation stage, DPR would review data submitted by the manufacturer and publicly available data in the scientific literature to determine (in consultation with OHHEA) whether the ingredients

73 In practice, this could be implemented by applying an "uncertainty factor" during the dose-response assessment to reflect the increased burdens bourn by the affected communities. DPR, GUIDE, *supra* n. 7; J. R. Varshavsky, et al., Current Practice and Recommendations for Advancing How Human Variability and Susceptibility are Considered in Chemical Risk Assessment, 133 ENVIRON. HEALTH 21 (Suppl. 1) (2023).

74 John Faust, et al., California's Environmental Justice Mapping Tool: Lessons and Insights from CalEnviroScreen, 51 ENVTL. L. REP. 10684 (2021). Of course, use of CalEnviroScreen in these ways would require revisions to the system, for example, to enable it to generate maps and scores at a local scale and to integrate it with CalAgPermits.

are within the same chemical assessment group (CAG). DPR would also determine whether there was a reasonable, scientifically-based hypothesis of interactive effects relying upon available evidence such as mechanistic studies, epidemiological data, and scientific judgment.[75] If either case is true, DPR would require submission of toxicity data sufficient for risk assessment of the formulated product, as well as the product's expected degradation products.

As part of the exposure assessment, DPR would consider how the ingredients will move through the environment to reach human or ecological receptors. Whole product testing will be most relevant where some or all of the ingredients reach the receptor without significant transformation; for example, exposures experienced by pesticide applicators or farm workers. In other cases, the ingredients may move through the environment at different rates or through different pathways such that the receptor is not exposed to the formulated product as a whole.[76] Whole product testing data would be less relevant in such cases, requiring use of data regarding the component substances. (See Hybrid Approach below.) The dose-response and risk characterization steps with respect to the whole mixture would essentially follow the process used in conventional risk assessment, treating the formulated product as a single substance.

Table 1: Whole Mixture Approach: Issues and Potential Solutions

Issues:	Potential Solutions:
Variability in formulations	• Use of representative formulation or sufficiently similar mixture • Implement data bridging strategy where appropriate. See, *e.g.*, Food and Agricultural Organization of the UN, GENERAL GUIDANCE ON BRIDGING OF PESTICIDE RISK ASSESSMENTS (2018)
Differential fate (including transformation and degradation of ingredients) and transport of formulated components	• Perform fate and transport analysis of formulations to establish if there is differential fate. See, *e.g.*, EPA, Fate, Transport and Transformation Test Guidelines: OPPTS 835.6400 Combination and Tank Mixes Field Dissipation (2008)
Increased animal use for toxicity testing in some cases	• Develop and use new approach methodologies • Use screening strategies to reduce testing needs
Increased cost and complexity of risk assessment	• Utilize prioritization processes initially focusing whole product assessment to certain cases; for example, based on total burden using CalEnviroScreen • Secure additional funding and resources through fee increase or other funding devices

75 Zaunbrecher, et al., EXPOSURE AND INTERACTION, *supra* n. 3.

76 EFSA Scientific Committee, Guidance on Harmonized Methodologies for Human Health, Animal Health and Ecological Risk Assessment of Combined Exposures to Multiple Chemicals, 17 EFSA JOURNAL 5634 (2019); L. Blair Paulik and Kim A. Anderson, Considerations for Measuring Exposure to Chemical Mixtures, in Rider and Simmons, CHEMICAL MIXTURES, *supra* n. 15, at 37; EPA, Supplementary Guidance for Conducting Health Risk Assessment of Chemical Mixtures (EPA/630/R-00/002 2000).

Component-Based Product Assessment: Here risk assessment focuses upon the individual product ingredients, with a component-based method used to combine risks to determine cumulative risk and craft risk mitigation measures. Unlike the whole product assessment approach, the component-based approach is unlikely to address interactive effects.[77] Despite that limitation, the component-based approach provides other benefits over whole product assessment, to the extent that adequate toxicity data is available for all ingredients. The component-based approach may avoid expensive and time-consuming testing of the whole product. Also, this approach could allow for less complicated assessment of varying formulations of a pesticide product than whole product testing. Table 2 identifies issues presented by the approach and potential solutions.

As in whole product assessment, during problem formulation, DPR would determine whether the ingredients are within the same CAG. If so, DPR would require submission of toxicity data for each relevant ingredient (i.e., each ingredient in the shared CAG) and their expected degradation products.

Exposure assessment would track the movement of each relevant ingredient in the environment, including scenarios in which exposure to two or more ingredients occurs within the same space and timespan ("co-occurring exposures"). DPR would use existing monitoring and dispersion modeling methods to identify and quantify solitary ingredient exposures and co-occurring exposures, including transformation products as appropriate. For co-occurring exposures, the dose-response and/or risk characterization steps would use the component-based method selected by DPR (for example, the hazard index, relative potency factors, or combined margin of exposure approaches) to determine the cumulative risk.

77 A variety of quantitative and qualitative methods for incorporating interactivity into component-based approaches exist. Since 2000 a component-based approach developed by EPA—the interaction-based hazard index (HIINT)—has been available and has been used for regulatory purposes in limited circumstances. Richard C. Hertzberg, et al., Evaluation of the Interaction-Based Hazard Index Formula Using Data on Four Trihalomethanes from U.S. EPA's Multiple-Purpose Design Study, 12 Toxics 305 (2024).

Table 2: Component-Based Product Approach: Issues and Potential Solutions

Issues:	Potential Solutions:
Misses more-than-additive effects of ingredients	• Screen the ingredients to identify likelihood of more-than additive effects. See, *e.g.*, U.S EPA, Process for Receiving and Evaluating Data Supporting Assertion of Greater than Additive (GTA) Effects in Mixtures of Pesticide Active Ingredients and Associated Guidance for Registrants, August 2019 • If specific data regarding interactive effects are available, consider use of an interaction-based hazard index
Requires toxicity and other data for all ingredients, which may not be available for "inert" ingredients	• Use existing data for ingredients to extent possible • Require generation of necessary data • Develop and use new approach methodologies
May produce conservative results (*e.g.*, false positives)	Use tiered approach allowing for more extensive assessment/testing. Where evidence suggests that the component-based approach outcomes may overestimate risk, more sophisticated component-based approaches or whole product assessment of the formulation may be performed
Transformation and degradation of ingredients in use	• Currently addressed in single ingredient risk assessment; adapt methods to multiple ingredients to identify worst-case co-occurring exposures (defined in text above) • Where appropriate, perform fate and transport analysis of formulations. See, *e.g.*, EPA, Fate, Transport and Transformation Test Guidelines: OPPTS 835.6400 Combination and Tank Mixes Field Dissipation (2008)
Increased cost and complexity of risk assessment	• Utilize prioritization processes initially focusing component-based assessment to certain cases; for example, based on total burden using CalEnviroScreen. • Secure additional funding

Hybrid Assessment: As noted above, whole product assessment and component-based assessment each have significant limitations. Toxicity testing results for the formulated product in whole product assessment may not be relevant in cases where the ingredients dissipate differently in the environment. Although component-based assessment can deal with that concern, it does not necessarily capture more-than-additive effects. Hybrid assessment can harness the benefits of both whole product and component-based assessment.

As in whole product assessment, in the problem formulation stage, DPR would evaluate whether (1) the ingredients are within the same CAG and (2) there was a reasonable, scientifically-based hypothesis of interactive effects. If either case is true, DPR would require whole product testing unless significant differential dissipation of the ingredients is expected. DPR would consider how the ingredients' respective physicochemical properties and other factors may affect their relative movement through the environment. For potential exposure scenarios in which there is significant differential dissipation of ingredients, DPR would apply component-based assessment. Table 3 identifies issues presented by the hybrid approach and potential solutions.

Table 3: Hybrid Approach: Issues and Potential Solutions

Issues	Potential Solutions for Issues
Component-based aspect requires toxicity and other data for all ingredients, which may not be available for "inert" ingredients	• Use existing data for ingredients to extent possible • Require generation of necessary data • Develop and use new approach methodologies
Component-based aspect may produce conservative results (*e.g.*, false positives)	Use tiered approach allowing for more extensive assessment/testing. Where evidence suggests that the component-based approach outcomes may overestimate risk, more sophisticated component-based approaches or whole product assessment of the formulation may be performed
Transformation and degradation of ingredients in use	• Currently addressed in single ingredient risk assessment; adapt methods to multiple ingredients to identify worst-case co-occurring exposures (defined in text above) • Where appropriate, perform fate and transport analysis of formulations. See, *e.g.*, EPA, Fate, Transport and Transformation Test Guidelines: OPPTS 835.6400 Combination and Tank Mixes Field Dissipation (2008)
Increased cost and complexity of risk assessment	• Utilize prioritization processes limiting hybrid assessment to certain cases • Secure additional funding

RECOMMENDATION FOR PRODUCT MIXTURES: HYBRID ASSESSMENT

The hybrid assessment approach offers the best overall approach to cumulative assessment of whole products, capturing the benefits of the other potential approaches in a cost-effective manner.

Like the other approaches, the hybrid assessment approach (1) is grounded in well-established cumulative risk assessment methods and tools, (2) draws upon existing capacities of DPR and leverages OEHHA expertise in the generation of CAGs, and (3) uses the problem formulation step to limit cumulative risk assessment to appropriate cases.

The hybrid assessment approach calls for whole product testing (which would uncover interactive effects) where it is fit for purpose, reducing cost while enhancing protection of human health and the environment. Likewise, the hybrid assessment approach uses component-based methods to evaluate co-occurring exposures not captured by the whole product assessment approach.

FIELD MIXTURES

As discussed previously, field mixing is a common practice in California. In field mixing, one pesticide may be mixed with another or with other products meant to enhance the pesticide's effectiveness. Field mixing may be done to manage multiple pests with a single application, or to manage a single type of pest with multiple products. For some pesticides, the approved label specifically calls for or permits mixing with other specified products or product types. Other pesticide labels may prohibit mixing with other specified products. Absent such a prohibition, growers may engage in mixing even if the label is silent with respect to mixing.[78]

The intentional mixtures resulting from field mixing are essentially product mixtures created in the field. As such, assuming that the common tank mixture formulations can be identified, DPR could assess the cumulative impacts of those mixtures by applying the same assessment method used for formulated products. As for actual product mixtures, hybrid assessment provides the best overall approach for cumulative assessment of field mixtures. Also as with product mixtures, such assessment would be performed by DPR during registration of new pesticides and reevaluation of existing pesticides.[79]

78 See EPA, PRN 82-1: Revised Policy on Label Claims for Tank Mixing (1982); Elizzandra Marta Martins Gandini, et al., Compatibility of Pesticides and/or Fertilizers in Tank Mixtures, 268 JOURNAL OF CLEANER PRODUCTION 122152 (2020); Aude Kienzler, et al., Regulatory Assessment of Chemical Mixtures: Requirements, Current Approaches and Future Perspectives, 80 REGULATORY TOXICOLOGY AND PHARMACOLOGY 321, 322 (2016).

79 Application of the whole product assessment to field mixtures involving two or more products manufactured by different producers raises the question of which parties should bear the responsibility of providing the whole mixture data.

In this context, additional efforts are required to identify field mixtures for assessment. For new pesticides undergoing registration, DPR would require the applicant to identify expected field mixing uses of the proposed pesticide. For currently-registered pesticides, DPR would create an inventory of existing field mixtures used in California by (1) reviewing labels to identify instances of recommended field-mix formulation and (2) relying upon PUR data to identify common patterns of field mixing beyond those mixing scenarios identified under (1). In the event that a grower proposes a field mixture not already listed in the inventory, the CAC would notify DPR for inclusion in the inventory and assessment by DPR.

RECOMMENDATION FOR FIELD MIXTURES: HYBRID ASSESSMENT

Intentional mixtures created through tank mixing should be treated as product mixtures. Accordingly, for the reasons discussed above regarding product mixtures, the hybrid assessment approach offers the best overall approach to cumulative assessment of intentional mixtures.

COINCIDENTAL MIXTURES

Coincidental mixing refers to scenarios in which different pesticides are applied close in time and space. This occurs where an individual grower applies two or more pesticides sequentially. It also results where two or more growers located near one another apply different pesticides close in time. Coincidental mixing is undoubtedly occurring across the state. For example, *Governance on the Ground* identified 61 instances of chloropicrin, Telone, and metam sodium being applied on the same and adjacent fields within a 48 hour period in 15 counties in 2015.[80]

To address coincidental mixtures through the regulatory process, DPR and CACs must first identify the nature and location of such mixtures. They must answer questions such as which pesticides are mixing in the environment, in what proportions, and under what circumstances (such as time and location.) Fortunately, the regulators have several data sources and methods to answer these questions.

First, at the state level, DPR has ample historical data from pesticide use reporting to identify "common mixing patterns," meaning recurring instances in which the same set of pesticides are typically applied close in time and space throughout the state. Working with OEHHA, DPR would screen this set of common

80 Malloy, et al., GOVERNANCE, *supra* n. 2.

mixing patterns to select those involving pesticides that fall within shared CAGs, giving rise to the concern that cumulative effects may occur.

Second, for new pesticides submitted for registration, DPR can predict likely mixing patterns involving that new pesticide by relying upon the historical common mixing pattern data. Taking into account the manufacturer's submission and with support from UC Agriculture and Natural Resources experts, DPR would identify the existing pesticides in lieu of which the candidate will likely be used. Where that existing pesticide is part of a common mixing pattern, DPR would evaluate the mixing patterns to determine whether the candidate pesticide shares a CAG with the other pesticides in the mixing pattern.

Third, the CACs can obtain real time information regarding potential coincidental mixing through the online CalAgPermits system. Currently, growers submit information regarding planned pesticide application, including location and pesticide type, to CalAgPermits when requesting a restricted material permit. This information could be used to identify potential cumulative exposure scenarios at single sites and adjacent sites. (Because adjacent sites will sometimes be located in different counties, CalAgPermits must be revised to provide CACs with access to information from nearby counties.)

Below we discuss three approaches to coincidental mixtures. Recognizing that there is no single formulated "product" to test in this context, each approach relies upon a form of a component-based risk assessment. The first approach would be implemented by DPR at the registration phase and during reevaluation of previously registered pesticides. The CACS would use one of the remaining two approaches, with support from DPR, as part of restricted material permitting.

Extended Component-Based Assessment: This approach is an extension of the component-based assessment discussed with respect to pesticide registration. Recall that in that approach, DPR would track the movement of each relevant ingredient in the environment, identifing co-occurring exposures to substances from the same CAG. Relying upon exposure assessment and dose-response assessment for each ingredient, DPR would use a dose addition method to characterize the risk associated with the co-occurring exposure. For scenarios involving common mixing patterns, the assessment of the new pesticide would be expanded to include the chemicals expected to mix with it (the "coincidental chemicals"). Drawing upon the historical mixing pattern data, DPR would develop default assumptions to model the expected exposure profiles of the coincidental chemicals. In this way, the coincidental chemicals would essentially be treated as additional ingredients of the pesticide under review. (For issues regarding the Extended Component-Based Assessment approach and potential solutions, see generally Table 2.)

This approach would, of course, cover new pesticides seeking registration. It would also be applied to previously registered pesticides during reevaluation. Of relevance here is the fact that addressing coincidental mixtures through the reevaluation of existing pesticides will take a significant period of time. In the interim, some approach is needed to manage ongoing co-occurring mixtures of existing pesticides. Two such interim approaches are described, both of which are grounded in the restricted materials permitting process.

Cumulative Risk Assessment Tool (CalCAT): In this approach, when a grower submits an NOI, the CAC would use an integrated cumulative risk assessment screening tool (CalCAT) to evaluate potential coincidental exposures. CalCAT would be developed and maintained by DPR in consultation with OEHHA.

CalCAT would be integrated with CalAgPermits, allowing it to notify CAC staff when it detects the proposed use of pesticides from the same CAG close in time and space. Using relevant exposure models, it would estimate the amount of each pesticide identified in the NOIs to which workers, bystanders, and residents may be exposed. Many of the input parameters used by the model would be pre-loaded by DPR, leaving a small amount of site-specific information to be input to CalCAT by CAC staff. It would calculate health impacts to the persons most at risk using a component based approach developed by DPR in consultation with OEHHA, identifying whether any exposures exceed acceptable levels. Where necessary, it would display a set of standard risk mitigation measures for that combination of pesticides. CAC staff would choose one or more of these measures to mitigate the cumulative risk. In complex cases, CAC staff would consult with DPR.

CalCAT focuses on the specific location and nature of pesticide applications in real time. It would provide timely assessment of potential cumulative risk and identification of associated mitigation strategies. While development of CalCAT would likely require significant resources, it would be practical. Tools relevant to pesticides that are similar to the proposed CalCAT have been developed by researchers[81]. Table 4 identifies issues presented by the approach and potential solutions.

The CalCAT concept is inspired by the Hotspots Analysis and Reporting Program (HARP2), a software suite developed by the California Air Resources Board for use in the state Air Toxics "Hot Spots" program. HARP2, which assesses air emissions only but can be used for cumulative exposures, is used by regulators and individual facilities for streamlined evaluations. See ARB, User Manual for HARP2 (2015) for more information about HARP2.

81 See, *e.g.*, Julie Boberg, Chemical Mixture Calculator - A Novel Tool for Mixture Risk Assessment, 152 FOOD AND CHEMICAL TOXICOLOGY 112167 (2021); Yu Zhan and Minghua Zhang, Pesticide Use Risk Evaluation (PURE), A Self-Evaluation Tool of Pesticide Use, in Zhang, PESTICIDE USE DATA.

Table 4: CalCAT Approach: Issues and Potential Solutions

Issues:	Potential Solutions:
Misses more-than-additive effects of ingredients	Screen the CAGs to identify likelihood of more-than additive effects. If likelihood found, and specific data regarding interactive effects are available, consider use of an interaction-based hazard index. Alternatively, include more protective mitigation requirements in CalCAT where such likelihood is found
Differential fate (including transformation and degradation of ingredients) and transport of relevant applied pesticides	Currently addressed in single ingredient risk assessment; adapt methods to multiple ingredients to identify worst case co-occurring exposures
Different pesticides could be applied using differing application methods	The CalCAT tool would incorporate appropriate exposure models for the relevant application methods
Increased cost and complexity of risk assessment	• Utilize prioritization processes initially limiting CalCAT use to certain cases, perhaps based on total burden using CalEnviroScreen or on common CAGs of heightened concern • Secure additional funding
May produce conservative results (i.e., false "positives")	Use tiered approach allowing for more extensive assessment/testing
NOI's from which local input parameters are drawn are submitted 24-48 hours prior to application. This leaves little time for evaluation using CalCAT, creating large burden for CACs and great uncertainty for growers	• Make CalCAT available to PCAs and growers to incorporate into their advance planning • Centralize CalCAT at DPR level (see CalCB below)
Regulation of coincidental exposures will lead to unintended consequences: • Strategic behavior among growers in effort to be the first to submit an NOI • Shifting of agricultural operations (and risk) to locations outside California	Make CalCAT available to PCAs and growers to incorporate into their advance planning and to encourage coordination among growers/PCAs

Qualitative Cumulative Risk Assessment Tool (CalCB): In this approach, DPR and OEHHA would develop a web-based expert system that relies on numerical data and qualitative analysis. The system draws upon the concept of control banding, an approach widely used in the area of occupational safety and health.[82] Control banding emerged in the pharmaceutical sector to support decision-making by industrial hygienists in the face of limited data and resources. Over time its use has expanded to other sectors, and most recently a number of control banding tools have been developed for assessment of industrial nanoparticle exposures. Control banding, and therefore CalCB, would assign default protection strategies to groups of chemicals falling into the same "band" based on cumulative exposure and hazard.

Like CalCAT, the CalCB system would be integrated with CalAgPermits so as to access data from NOIs in real time. The system would alert CAC staff to possible cumulative effects from one or more NOIs if it detected the proposed use of pesticides from the same CAG close in time and space. It would categorize the extent of the cumulative exposure according to a five point scale ranging from very low to very high. Categorization would depend upon an algorithm that takes into account the relative location of the pesticide applications, the expected movement of the pesticides through the environment, the location of potentially exposed receptors, and other relevant factors.[83]

CalCB would also classify the extent of the hazard to exposed receptors according to a five point scale ranging from very low to very high. It would rely upon an algorithm that takes into account the relative toxicity of the pesticides, the expected changes to chemical nature and toxicity of the pesticides as they move through the environment, the characteristics of potentially exposed people, and other relevant factors. CalCB subsequently would generate an estimated risk level based upon the exposure and hazard levels on a five point scale ranging from very low to very high. Lastly, if necessary, CalCB would display a set of standard risk mitigation measures for that combination of pesticides based upon the calculated risk level. In complex cases, CAC staff would consult with DPR.

Like the CalCAT tool, CalCB focuses on pesticide applications in real time, providing the CACs with a practical means of addressing potential cumulative risk. This approach would significantly reduce the complexity and resource burden presented by CalCAT. Table 5 identifies issues presented by the approach and potential solutions.

82 David M. Zalk and Deborah Imel Nelson, History and Evolution of Control Banding: A Review, 5 JOURNAL OF OCCUPATIONAL AND ENVIRONMENTAL HYGIENE 330 (2008).

83 For an example of such an exposure algorithm, see H. Marquart, et al., Stoffenmanager, A Web-Based Control Banding Tool Using an Exposure Process Model, 52 ANN. OCCUP. HYG. 429 (2008).

Table 5: CalCB Approach: Issues and Potential Solutions

Issues:	Potential Solutions:
Increased cost and complexity of risk assessment	• Prioritization processes limiting CalCB use to certain cases, perhaps based on total burden using CalEnviro-Screen or on common CAGs of heightened concern • Secure additional funding
NOI's from which local input parameters are drawn are submitted 24-48 hours prior to application. This leaves little time for evaluation using CalCB, creating large burden for CACs and great uncertainty for growers	Make CalCB available to PCAs and growers to incorporate into their advance planning
Use of algorithms and categorical matrix loses resolution available in quantitative assessment and could create disputes regarding "edge" cases	Use tiered approach allowing for more extensive assessment/testing
Regulation of coincidental exposures will lead to unintended consequences: • Strategic behavior among growers in effort to be the first to submit an NOI • Shifting of agricultural operations (and risk) to locations outside California	Make CalCB available to PCAs and growers to incorporate into their advance planning and to encourage coordination among growers/PCAs

RECOMMENDATION FOR COINCIDENTAL MIXTURES: EXTENDED COMPONENT-BASED ASSESSMENT + INTERIM USE OF CalCAT/CalCB

Extended component-based assessment offers the best overall approach to cumulative assessment of coincidental mixtures. It (1) is grounded in well-established cumulative risk assessment methods and tools, (2) efficiently and cost-effectively integrates assessment of coincidental mixtures into the registration process, and (3) draws upon existing capacities of DPR and leverages the PUR data in identifying common mixing patterns. However, given their large number, application of the approach to existing pesticides through the reevaluation process will likely take a substantial period of time. In the interim, another approach is required.

The CalCAT approach offers a streamlined risk assessment tool for CAC staff that enhances statewide consistency while providing timely and cost-effective evaluation of coincidental exposures. The approach builds on the experience of the California Air Resources Board and OEHHA with the Air Toxics Hot Spots program and relies upon existing component based risk assessment methods and well-established exposure models. The approach also draws upon the expertise and resources of DPR and OEHHA while enabling the CAC staff to better exercise their mandate to consider local conditions in restricted material permitting. Yet significant time will be needed to develop, validate and implement a CalCAT software package and associated protocols and supporting data. In the interim, the qualitative CalCB approach should be used by CACs to address cumulative risk.

CONCLUSION

Developing and deploying rigorous, effective, and equitable cumulative assessment methods and policies in the agricultural setting is challenging. Methodological hurdles, resource constraints, and other obstacles face regulators at the state and county level in California. Yet legal mandates and good public policy require cumulative assessment of pesticide use in the state. This project identified well-established, existing approaches that can significantly and quickly improve California's treatment of cumulative risk in the near term, while further improvements over the longer term are developed.

For product and field mixtures in the agricultural setting, we recommend the expeditious adoption of a hybrid assessment approach, which is grounded in well-established cumulative risk assessment methods and tools and draws upon existing capacities and expertise of DPR and OEHHA. For coincidental mixtures, we recommend a component-based assessment approach to be applied by DPR during registration and reevaluation processes. Recognizing that full implementation of that approach will require time, we also propose a near term strategy as part of restricted materials permitting. That strategy provides CAC staff with streamlined cumulative assessment and decision support tools to address coincidental mixtures as part of the permitting process. The strategy enhances statewide consistency while providing timely and cost-effective evaluation of coincidental exposures.

APPENDIX A

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