Department of Pesticide Regulation

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Process for Human Health Risk Assessment Prioritization and Initiation

Risk assessment plays a critical role in the California Department of Pesticide Regulation's (DPR) evaluation of the potential hazards to human health associated with pesticide exposure. Risk assessment is a process designed to answer questions about how toxic a chemical is, what exposure results from its various uses, what the likelihood that use will cause harm, and how to characterize that risk. DPR takes a California-specific, comprehensive approach to risk assessment and assesses potential dietary, workplace, residential and ambient air exposures as appropriate. Risk assessments are often the basis for new regulations and other use restrictions.

Assessing pesticide risks is a dynamic process, evolving with advancements in science and with changes in pesticide use patterns. DPR strives to protect human health and make the best use of resources by prioritizing risk assessments to address the greatest potential risks. Risk assessments may be initiated for a number of reasons. For example, the identification of possible adverse health effects during review of toxicology data submitted under the Birth Defect Prevention Act may trigger a risk assessment. A risk assessment may also be initiated when use of a pesticide results in exposures of concern from ambient air, or from programs to eradicate exotic pest infestations. It can also be initiated when DPR receives an application for registration of a new fumigant pesticide.

DPR sets priorities for risk assessments through a single process, regardless of the impetus. Setting priorities is critical to making the best use of staffing and other resources. It also allows DPR to focus on the chemicals of greatest interest. DPR has modified its priority-setting process over the years to make it more consistent, understandable and as transparent as possible. This document describes the priority-setting process as it is today and the way in which priority-setting will be documented.

Overview of Prioritization/Selection Process:

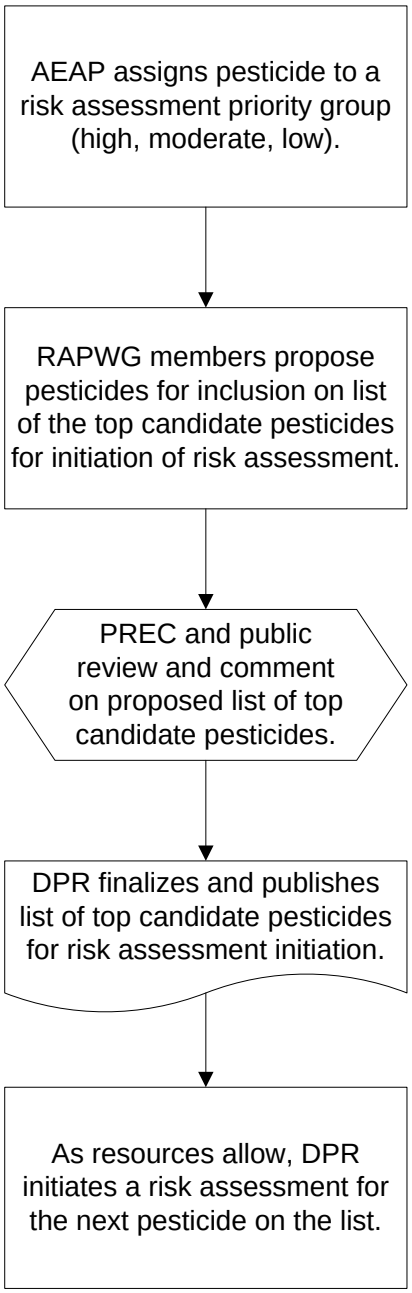
I. Adverse Effects Advisory Panel Ranking
II. Candidate Pool Selection for Initiation of Risk Assessment
III. Criteria to Prioritize Active Ingredients
IV. Initiation of Risk Assessments
V. Selection of Active Ingredients for the Toxic Air Contaminant Process

Schematic Diagram of DPR's Candidate Selection and Priority-Setting Process for Health Risk Assessment of Pesticide Active Ingredients
(This process is activated on an as-needed basis)

AEAP: Adverse Effects Advisory Panel consists of staff from DPR-Human Health Assessment, DPR-Environmental Monitoring, OEHHA, EPA-Region 9

RAPWG: Risk Assessment Prioritization Work Group consists of staff from DPR-Human Health Assessment, DPR-Environmental Monitoring, OEHHA, ARB

PREC: Pesticide Registration and Evaluation Committee consists of staff from Cal/EPA boards, departments, offices; Dept of Food and Agriculture; Dept of Fish and Wildlife; Dept of Industrial Relations; Dept of Public Health; Structural Pest Control Board; EPA-Region 9; ag commissioners; University of CA



I. Adverse Effects Advisory Panel Ranking

Active ingredients entering the prioritization process have a complete toxicology database required for federal registration under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA). While this FIFRA database serves as the primary source of toxicity information, scientific staff will consider other reliable data during both the prioritization and risk assessment processes. Because a comprehensive exposure database is generally not available at the time of prioritization, estimates of exposure potential are based on the best available information. This process also serves to identify potential need for additional exposure or toxicity data.

The initial ranking for risk assessment purposes involves evaluation by the Adverse Effects Advisory Panel (AEAP). This panel consists of senior scientists from two DPR branches (Environmental Monitoring and Human Health Assessment) and from Cal/EPA's Office of Environmental Health Hazard Assessment (OEHHA). This panel groups the active ingredients into high, moderate or low categories based on the criteria described below.

This process is qualitative, employing a weight-of-evidence approach to identify active ingredients most likely to present significant health risks. The criteria used include the results of the review of the required FIFRA database (e.g. chronic toxicity, oncogenicity, reproductive toxicity, teratogenicity, genotoxicity, etc.) and the exposure potentials indicated by label-uses. All criteria are considered equally. No greater weight is given to any single or group of criteria in establishing an active ingredient's rank for risk assessment.

The Adverse Effects Advisory Panel meets periodically to update the groupings as active ingredients become available to be added or new data becomes available that may affect the ranking of a currently listed ranked-active ingredient. An active ingredient is deleted from the ranking list when its risk assessment is completed or registration is cancelled.

II. Candidate Pool Selection for Initiation of Risk Assessment

Senior scientists from DPR's Human Health Assessment and Environmental Monitoring branches along with invited senior scientists from OEHHA and the California Air Resources Board (ARB) comprise the Risk Assessment Prioritization Work Group (RAPWG) for this step of the prioritization process. Drawing on their expertise in and detailed knowledge of pesticides, this panel of senior scientists recommends ten active ingredients (drawn mainly from the AEAP's high-priority category) for further examination. The panel members -review the exposure potential, physical-chemical properties, and toxicity of each of the ten active ingredients to determine the level of concern for each of the three criteria. Based on this evaluation, the ten active ingredients are ranked in a proposed priority from one to ten. An active ingredient is removed from the candidate pool when a risk assessment has been initiated. The DPR, OEHHA and ARB senior scientists review the candidate list as needed, in part to make recommendations for additional active ingredients to replace those deleted. They also review any new information (e.g. toxicology or exposure data, or regulatory activity by DPR or other state or federal agencies) and make recommendations to modify the candidate list.

Beginning in 2014, DPR is expected to complete at least five risk assessments a year. Therefore, DPR has to analyze staffing and other resources every one to two years to determine what pesticide risk assessments will be initiated next. Branch chiefs and senior scientists from Human Health Assessment, Worker Health and Safety, and Environmental Monitoring branches also recommend specific active ingredients to initiate risk assessments on. All recommendations in the notice are forwarded through the programmatic assistant directors to the DPR Chief Deputy Director for approval.

Upon approval by the DPR Chief Deputy Director, DPR proposes the list of active ingredients for initiation of the risk assessment process, and begins a 45-day comment period. The announcement includes a brief description for each of the ten active ingredients, as well as their ranking in the candidate pool. This announcement is posted on DPR's website and sent to interested parties including the Cal/EPA Scientific Review Panel. This information is also presented at a meeting of DPR's PREC for the members' advice and comments. DPR decides which pesticide active ingredients will enter the risk assessment process after reviewing all comments. DPR publishes a formal "Notice to Registrants" with this information.

III. Criteria to Prioritize Active Ingredients

The criteria used to prioritize all active ingredients for risk assessment and to identify those that could pose the greatest risks can be divided into three categories: **physical-chemical properties**, **toxicity**, and **exposure**. Other considerations that may impact prioritization include eradication programs for invasive pests and regulatory actions by other state or federal agencies.

The **physical-chemical properties** of an active ingredient may affect the manner and degree to which it will be released into and persist in the environment. A higher vapor pressure may increase the risk for air exposures. A longer half-life under various environmental conditions may enhance the persistence of the chemical, thus increasing potential exposure. A chemical more soluble in water may be more likely to move into drinking water by leaching through soil into ground water, or by runoff into surface water. Conversely, greater soil binding capabilities of a chemical could increase environmental persistence and the potential for exposure via soil particles. While not necessarily a physical-chemical property, a chemical's propensity to bioaccumulate or bioconcentrate is also an important consideration.

Greater **toxicity** of a chemical results in greater risk if all other factors are equal. The prioritization process considers a number of factors that may raise or lower the toxicological concern. Two chemicals may cause different effects at the same dose. The magnitude or severity of these effects may differ greatly. The chemicals may differ in the number of species responding in toxicological studies. They may differ in the seriousness of the response. For example, skin irritation may not present the same level of concern as convulsions or cancer. Consideration may be given to whether the effects are systemic (e.g. neurotoxicity) or local (e.g. skin irritation).

Two chemicals may cause the same effects, but one may cause the effects at a significantly lower dosage. In determining priorities panel scientists compare severity of effects among chemicals and the timeframe to onset. Another consideration is the shape of the dose-response curve, that is, the relationship between the dose and the response. A steep curve, where a small change in dose can greatly increase toxicity, may have significantly different consequences than one where large changes in the dose are required for an effect. The mechanism of action, if known, will also be considered. In some cases, the mechanism of action may impact the level of concern for an effect seen in animal studies as being relevant to people. Toxic effects seen in people, such as those identified through epidemiology studies or illness reports, may be considered in conjunction with animal data to determine the level of toxicological concern.

As with toxicity, greater **exposure** results in greater risk if all other factors are equal. Potential exposure is characterized based on available information at the time of the prioritization process. The types of potential exposures are important considerations (i.e., occupational, residential, ambient air, food residues, drinking water, etc.). Use patterns (i.e., agricultural, residential, manufacturing, etc.) and projected changes in use can have a major impact on exposure. If a pesticide is applied infrequently and only on a single ornamental crop, it will generally be prioritized lower than one with uses on a large number of crops. Prioritization also takes into account anticipated changes in use patterns, such as when a pesticide is intended as a replacement for another widely used pesticide.

Typical locations where pesticides may be used will also be considered. If a pesticide is often used in or near residential communities, the higher the population density means more people could be affected by exposure via ambient air or offsite movement compared to rural areas with lower population density.

Method of application also potentially impacts exposure. Air-blast or aerial applications may generate aerosols that can increase inhalation and dermal exposures. These modes of application also increase the possibility of offsite and ambient exposures. Application rate obviously has a direct impact on exposure potential since application rates can range from fractions of an ounce per acre to hundreds of pounds in the case of some fumigants.

The type of formulation may have an impact on exposure potential. Generally, there is less exposure using granular formulations, enclosed baits, or tree injections than exposure associated with wettable powders mixed in solution or dust formulations directly applied to crops. Illness surveillance data are also valuable indicators of exposure potential, demonstrating that the potential is real and not theoretical.

IV. Initiation of Risk Assessments

Risk assessments prepared by DPR are intended to be California-specific, comprehensive documents and consider all appropriate exposure routes and scenarios (e.g. oral, inhalation, dermal, occupational, residential, industrial, institutional, bystander, dietary, ambient air, water, etc.). When a risk assessment is initiated for an active ingredient, DPR scientists determine if additional data are needed and, if so, DPR will request it from the appropriate source. DPR may

also conduct surface and/or ground water monitoring data. DPR may also do conduct exposure monitoring to generate data. If adequate air monitoring data are not available, the ARB may also be requested to conduct such monitoring.

The risk assessment is prepared in the form of a risk characterization document (RCD). The RCD assembles, critiques and interprets all pertinent scientific data on an active ingredient's toxicology and exposure.

V. Selection of Active Ingredients for the Toxic Air Contaminants (TAC) Process

The prioritization and risk assessment process takes into account DPR's mandate to evaluate the ambient air risks from pesticides. Active ingredients that meet established criteria are designated as TAC after a specific review and evaluation process. To complement DPR's comprehensive risk assessment process and the TAC mandate, every active ingredient is evaluated through the risk assessment process as a potential TAC candidate. DPR scientists make specific evaluations as the risk assessment proceeds through the hazard identification stage to determine screening reference doses (RfDs) and screening air references concentrations (RfCs). If adequate ambient air data are available, the screening RfCs are compared with the monitored air levels. Projected changes in use patterns are also evaluated for their potential impact on ambient air.

If monitoring and projected ambient air levels are well below concentrations that would meet the regulatory criteria for identification as a TAC (California Code of Regulations, Title 3, Section 6864)[1], it is unlikely the active ingredient would be listed as a TAC. In these instances, DPR would not submit the active ingredient to the TAC Scientific Review Panel (SRP) for consideration.

If monitored or projected ambient air concentrations are near or above those concentrations that meet the criteria for identification as a TAC, DPR will initiate the TAC process. The RCD will be prepared with an extensive section on ambient air and will be submitted to the SRP for review and evaluation.

If the RCD is ready for completion without adequate ambient air data, the RCD will be finalized with a section on ambient air describing the current status and anticipated concerns. An addendum covering ambient air may be generated at a later date and a decision could be made to pursue TAC listing should the data support that action.

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[1] As specified in Section 6864, a pesticide shall be identified as a toxic air contaminant if its concentrations in ambient air are greater than the following levels (for the purposes of this Section, a threshold is defined as the dose of a chemical below which no adverse effect occurs):

(a) For pesticides which have thresholds for adverse health effects, this level shall be ten-fold below the air concentration which has been determined by the director to be adequately protective of human health.

(b) For pesticides which do not have thresholds for adverse health effects, this level shall be equivalent to the air concentration which would result in a ten-fold lower risk than that which has been determined by the director to be a negligible risk.

In certain instances, ambient air monitoring data may not be necessary to recognize that an active ingredient (e.g. some fumigants) has the potential to be a TAC. In these cases, it may be inappropriate to delay the TAC process and it would be initiated concurrently with the risk assessment. Ambient air monitoring may still be requested from ARB and /or the registrants in these instances, to be used in the control phase for determining appropriate control measures.