[CHAPTER 5]

Assessing Pesticide Risks to Human Health

Under California law (Statutes of 1969, Chapter 1169), the Department of Pesticide Regulation (DPR) must "eliminate from use" any pesticide that "endangers the agricultural or nonagricultural environment, is not beneficial for the purposes for which it is sold, or is misrepresented." To do this, the law requires the department to have "an orderly program for the continuous evaluation" of registered pesticides. DPR uses various tools to evaluate pesticide products to determine what risks they pose and whether changes to the use or proposed use are necessary.

A human health risk assessment is how DPR estimates the nature and likelihood of adverse health effects in humans who may be exposed to pesticides, now or in the future. Exposures may be in air, water or food, at homes or in the workplace. These scientific evaluations provide health-protective estimates of risk to defined populations exposed under defined exposure conditions. Risk assessments are often the driving force behind new regulations or other use restrictions. If satisfactory controls cannot be put into place to avoid harmful exposures, DPR will not register the pesticide or, if it is already registered, can cancel its use.

A pesticide risk assessment addresses questions such as:

- What type of health problems may be caused by exposure to pesticides?
- What is the chance that people will experience health problems from exposure?
- Is there an exposure level below which any risk to health is negligible?
- What pesticides are people exposed to, at what levels and for how long?
- Are some people more likely to be susceptible to harm because of age, genetics, pre-existing health conditions, ethnic practices, gender or other factors?
- Are some people more likely to be exposed because of where they work, where they play, what they like to eat or other factors?

The department has a formal process to prioritize pesticides for risk assessment, focusing on pesticides that pose the greatest potential risk. In addition, DPR may decide to begin a risk assessment for other reasons. For example, DPR scientists may identify possible adverse health effects when they review toxicology data, which can trigger a risk assessment before a decision is made to register a product. After registration, new toxicology studies or reports of adverse effects can also prompt a risk assessment. DPR may initiate a risk assessment when air monitoring by the department or other agencies finds concentrations of concern in community air. Another trigger might be anticipated changes in use patterns, such as when a product is intended as a replacement for another widely used pesticide.

RISK ASSESSMENT PROCESS

The department's capability to conduct formal risk assessments came after the 1984 passage of the Birth Defect Prevention Act (BDPA; see *Page 43)*. This law

Toxic effects in a biological system are not produced by a chemical agent unless that agent or its metabolic breakdown products reach appropriate sites in the body at a concentration and for a length of time sufficient to produce a toxic manifestation ….Thus, whether a toxic response occurs is dependent on the chemical and physical properties of the agent, the exposure situation, how the agent is metabolized by the system, and the overall susceptibility of the biological system or subject.

— Casarett & Doull's Toxicology: The Basic Science of Poisons

Proposition 65

In 1986, California voters passed a ballot initiative called The Safe Drinking Water and Toxic Enforcement Act, more familiarly known by its ballot position, "Proposition 65." It is based on the premise that the public and workers have a right to be informed about exposures to chemicals that can cause cancer, birth defects or other reproductive harm. Among other mandates, it requires the state to publish a list of chemicals known to the state to cause cancer or reproductive harm and to update this list at least once a year.

Chemicals can be added to the Proposition 65 list in one of four ways:

- State experts conclude that scientifically valid testing shows the chemical clearly may cause cancer, birth defects or other reproductive harm.
- An authoritative body has formally identified it as causing cancer, birth defects or other reproductive harm. Authoritative bodies include the U.S. Environmental Protection Agency, U.S. Food and Drug Administration, National Institute for Occupational Safety and Health, National Toxicology Program and International Agency for Research on Cancer.
- If an agency of the state or federal government has formally required it to be identified or labeled as causing cancer or reproductive harm.
- If chemicals meet certain scientific criteria and are identified in the California Labor Code as causing cancer or birth defects or other reproductive harm.

Proposition 65 requires businesses to notify Californians about significant amounts of chemicals in the products they buy, use in their homes or workplaces, or that are released into the environment. Proposition 65 also prohibits California businesses from knowingly discharging significant amounts of listed chemicals into sources of drinking water.

CalEPA's Office of Environmental Health Hazard Assessment (OEHHA) administers the Proposition 65 program. OEHHA also evaluates available scientific information on substances being considered for placement on the Proposition 65 list. The Department of Pesticide Regulation (DPR) works with OEHHA in evaluating pesticides.

DPR's hazard communication regulations (which govern pesticide and worker safety requirements) also provide a foundation for employers to meet the Proposition 65 warning requirements for employees in the pesticide workplace. Proposition 65 regulations also allow warnings to be provided in the same manner stated in the federal hazard communication program regulations for workplace exposures.

California's hazard communication program requires that whenever employees are working in treated fields or handling pesticides, the employer must display certain leaflets in the Pesticide Safety Information Series produced by DPR's Worker Health and Safety Branch. The leaflets are available in English, Spanish and Punjabi and must be read on request to any employee. In addition, specific information about each pesticide application must be displayed at a central location when the operator of the property receives notice of the completion of an application and before any employees are allowed to enter the treated field. The specific information must remain displayed for 30 days or until employees are no longer present, whichever occurs earlier.

For exposures to the public, the warning may be given by various means, such as labeling a consumer product, posting signs in affected areas, sending notices to affected residents or publishing notices in a newspaper. For instance, signs can be found on most gas pumps and some utility companies include warning notices in their billings. In some instances, the companies comply with Proposition 65 by removing listed chemicals from their products.

Birth Defect Prevention Act

In 1984, the Legislature passed the Birth Defect Prevention Act (BDPA, Chapter 669 , SB 950). The law mandated that registrants of pesticides registered before 1984 bring health effects data on their chemicals up to current scientific standards. It also required that the Department of Pesticide Regulation (DPR) not register new active ingredients without a full complement of health effects studies. The required studies (primarily done on experimental animals) were chronic toxicity, mutagenicity, neurotoxicity, oncogenicity, reproductive effects and teratology. The BDPA required DPR to use these and other data to determine if a pesticide would cause human health problems. If continued use of a pesticide presents a significant health hazard that cannot be adequately mitigated, DPR is required to cancel the registration of products containing that active ingredient.

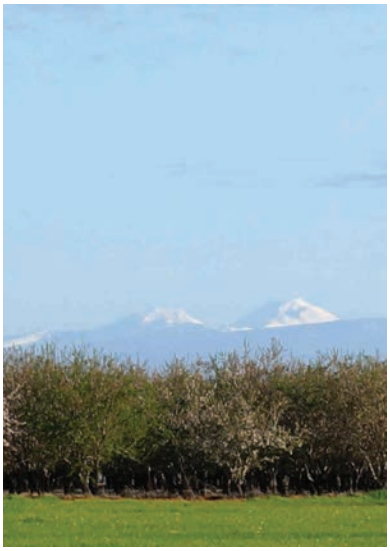
The BDPA mandated that DPR begin by developing a list of 200 active ingredients that would be the first focus of enforcement. These were chemicals with the most significant data gaps, widespread use, and which were suspected of being of greater health concern. (A data gap means that DPR lacks adequate health effects studies in any one of the required categories noted above.)

In January 1986, DPR notified registrants of data gaps for pesticide products containing any of the 200 priority active ingredients. DPR found that much of the data submitted in response to the data call-in notice did not meet U.S. Environmental Protection Agency guidelines. Because these studies had been performed years earlier, many registrants were unable to get the data necessary to upgrade the studies from the laboratories that did the original work. Although registrants contracted with laboratories for new studies, most failed to complete and submit new chronic health effects studies within the time frames set by law. The BDPA required submission of data on priority-list pesticides by March 1991, a deadline the Legislature later extended to March 1996 (Chapter 1228, Statutes of 1991, SB 550). Later legislation (Chapter 1, Statutes of 1995-1996, SB 1XXX) extended until December 1997 the deadline for submission of final studies on two pesticides, methyl bromide and pentachlorophenol.

In 2001, DPR presented its final report to the Legislature on the status of the chronic health effects studies required by the BDPA. The department reported that of the priority 200 active ingredients, 143 remained subject to the data call-in and no data gaps existed for any of these compounds, including methyl bromide and pentachlorophenol. DPR had granted exemptions for products containing two active ingredients. (Under the BDPA, a pesticide may be exempted from the data requirements if it is determined the chemical has only limited use and there is insignificant exposure to workers or the public.) Of the remaining priority pesticides, 47 had been withdrawn from the market by their manufacturers and DPR had suspended 8 for failure to submit required data. Product registrations are suspended if data for any active ingredient cannot be upgraded with additional information or if data were not submitted. Once a pesticide registration is suspended, registrants must halt all sales. Retail dealers may continue selling affected products for two years and consumers may continue to use products on hand.

In 1992, DPR began calling in data for the 703 registered active ingredients that were not on the priority list, as required by 1991 legislation (Chapter 1227, AB 1742).

As of late 2016, there remain only 57 active ingredients for which DPR is making determinations if more studies are needed to close data gaps.



Risk assessments have many uses, but a major one is to assist decision makers with the complex choices regarding the options in managing or reducing the potential human health risks associated with a substance or product. … Using experience and judgment, the (risk) manager must determine a level of risk that is acceptable.

— Risk assessment, risk evaluation, and risk management, C.J. Henry (in *Food Safety and Toxicity*)

required the state to bring the toxicological database on pesticides up to current scientific standards and collect the data needed to find out if adverse health effects were possible. Department scientists were then to assess the risks to decide if those health effects were significant. These mandates prompted the creation of the Medical Toxicology Branch in 1985 to evaluate toxicological data and manage human health risk assessments. Exposure assessments were conducted by scientists in the Worker Health and Safety branch at that time. In 2014, the department created the Human Health Assessment Branch where scientists conduct both the risk and exposure assessments and continue to evaluate toxicological studies for pesticide registration.

To fulfill the BDPA mandate, in the late 1980s DPR set up a procedure to classify pesticides as high, moderate or low priority for risk assessment. Chemicals registered before the passage of the BDPA were on a different risk assessment track than new active ingredients not yet registered. Policy dictated that the latter, if assigned high-priority status, could not be registered without a complete risk assessment. Requiring risk assessments for new compounds postponed their entry into the marketplace. Moreover, staff resources devoted to risk assessments on newer compounds (which often posed lower risks) meant delays in evaluating older pesticides registered decades before, when little or no scientific evaluation was done.

In 1996, DPR changed this policy to make more efficient use of resources and to concentrate on the greatest risks. Provided all required toxicology and other data had been submitted, new active ingredients classified as high-priority for risk assessment could be registered after a review of data and a screening evaluation, but without a full risk assessment. DPR retains the option of conducting a full risk assessment before registration. (The U.S. Environmental Protection Agency typically conducts a comprehensive review of new pesticide active ingredients before federal registration.)

At the same time, DPR integrated its risk assessment tracks into a single priority list. The priority status of active ingredients was determined by a panel made up of scientists from DPR and CalEPA's Office of Environmental Health Hazard Assessment (OEHHA). In 2005, DPR changed its priority-setting to make it more consistent and transparent. DPR formed the Risk Assessment Prioritization Work Group of senior scientists from DPR's Medical Toxicology Branch (now Human Health Assessment), Worker Health and Safety, and Environmental Monitoring branches, as well as a senior scientist from both the Air Resources Board (ARB) and OEHHA. From a larger priority list, the work group develops a ranked list of 10 high-priority compounds for risk assessment initiation. Prioritization is based on the nature and number of the potential adverse health effects identified in toxicity studies, number of species affected, potential for human exposure and information from DPR's Pesticide Illness Surveillance Program. Other considerations include physical-chemical characteristics (such as volatility), use patterns, amount of pesticide used and U.S. EPA evaluations.

The work group's list and detailed findings are posted online for public comment. They are also presented to DPR's Pesticide Registration and Evaluation Committee for further discussion before being finalized by DPR. The work group reviews the list periodically, in part to add new chemicals to replace those deleted after risk assessment completion. Based on new information—such as new toxicology or exposure data, or recent regulatory actions by DPR or other state or federal agencies—they may also revise the rankings. The department also publishes a public notice each time it begins a risk assessment.

In 2013 DPR asked the National Academy of Sciences (NAS) to conduct an independent peer review of DPR's risk assessment practices to ensure that DPR's risk assessment process uses the best scientific information and current methods. The National Research Council (NRC), of the NAS, completed its review and issued its report, including recommendations to improve DPR's risk assessment

process and reports in April 2015. The chart and text on Page 50 describe the revised DPR risk assessment process based on the NRC recommendations.

HAZARD AND RISK

Hazard and risk are two distinct but interrelated concepts—the first a reflection of potential effect and the second of likelihood it will occur.

Toxicity is an inherent property of all substances. That is, all chemical substances can produce harmful health effects at some level of exposure. A hazardous substance has the potential to harm health if it is present in the environment and if people are exposed to it. Fortunately, many hazards can be either contained or avoided, so not every potential hazard poses a health risk. A risk, in turn, is defined as the likelihood of the hazard occurring in a given situation.

Scientists determine the potential risk in two ways. Some risks can be measured directly by exposing humans to a toxin or by observing past and present disease incidence patterns in the human population. Risks can also be calculated indirectly by estimating the theoretical level of human exposure and the potential severity of health effects as predicted by experimental studies. The health risks from low-level exposure to environmental hazards such as pesticides are commonly determined by the indirect method. This is because there is not enough consistent and reliable evidence of measurable health effects in human populations exposed to low levels of hazardous environmental agents. As a result, the expressed risks from low-level environmental exposure are the product of scientific evaluation and analysis, not observed facts.

ASSESSING PESTICIDE RISK

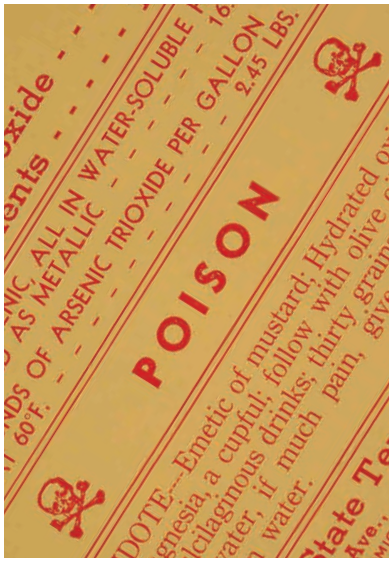
Before registration, DPR conducts a premarket evaluation of pesticide products based on standards used by U.S. EPA and studies required by California statutes to decide if the product can be used safely. These evaluations may prompt DPR to deny registration, propose registration conditional on receipt of additional data, or propose registration with additional oversight provided by making the pesticide a restricted material. Restricted materials require a permit and are subject to site-specific restrictions. The department may refuse to register the product under the U.S. EPA-approved label, giving the registrant the option of obtaining approval from U.S. EPA of a revised label that incorporates additional protections satisfactory to DPR. (Label changes must be approved by U.S. EPA, which has sole authority over label language.)

Premarket evaluations also help point out if a more comprehensive risk assessment is needed before the pesticide is registered. Pesticides already in use are also subject to periodic review to assess risks associated with use that may not have been predicted, or risks that may no longer be acceptable in light of current scientific standards. Evidence of significant hazard to health or the environment can trigger reevaluation and possible regulatory action. (*See Chapter 4 for a discussion of reevaluation.*)

Both premarket evaluations and full risk assessments are based on a prescribed set of scientific data provided by registrants as well as information from available scientific literature and other sources. These include exposure monitoring studies conducted by DPR's Worker Health and Safety Branch and air and water monitoring studies conducted by the Environmental Monitoring Branch. The application for product registration must provide all information needed to support the different uses proposed. (*See Chapter 3 for more information on the registration process.*) Only products with a database that includes all required studies are allowed to progress through evaluation. In limited instances, some chronic health effects data may be waived in consultation with OEHHA.

Conservation of human wellbeing is of utmost importance. The commercialization of an insecticide poison often is attempted as soon as the new toxicant has emerged from the laboratory, frequently with little or no pharmacological information. Before there is commercial exploitation and introduction into homes for intimate contact with unsuspecting users, more data as to acute or chronic intoxication should be available. The determination of toxicities of pesticides is imperative.

— 1943 California Department of Agriculture annual report



The concept of a poison is considered by many people to be an all-or-none phenomenon; a chemical is either a poison or it is not, with no shades of gray in between. Nothing could be further from the truth. Such simplistic reasoning is counterproductive to an understanding of how and why chemicals cause harm.

— *The Dose Makes the Poison: A Plain Language Guide to Toxicology,* by M. Alice Ottoboni

If toxicologists decide more data are needed and the pesticide is not yet registered in California, the department can require applicants to submit more data. If the pesticide is already registered and concerns of either environmental or public health issues are received from reports, DPR may conduct its own studies to validate those concerns or request the data from registrants through a formal reevaluation process.

CONDUCTING A HEALTH RISK ASSESSMENT

If scientists launch a full risk assessment, they begin with a planning and scoping stage to decide the purpose and scope. The next phases can be divided conceptually into four elements:

- Hazard identification. What toxic effects are caused by the pesticide?
- Dose-response assessment. At what dose levels do these effects occur?
- Exposure assessment. How much of the pesticide are people exposed to during a specific period (long-term, short-term) and in what situations (work, home, play)? Also, who is most vulnerable (for example, farmworkers, children, women of childbearing age)?
- Risk characterization. What are the significant uncertainties inherent in the nature (animal studies) and quality of the data on which the analysis relied? At what exposure levels are harmful effects not likely to occur?

Hazard identification

Hazard identification determines the various toxic effects associated with the chemical. Adverse effects may be acute (arising from short-term exposure), subchronic (exposures longer than a few days but less than a year), or chronic (the result of exposure of a year or more, including lifetime). Risk assessments commonly examine certain critical effects, including:

- Carcinogenic (cancer).
- Genotoxic (heritable traits or impacts).
- Developmental (birth defects and miscarriages).
- Reproductive (male and female fertility).
- Endocrine (hormonal function).
- Neurological (brain and nervous system disorders).
- Immunological (resistance to infectious diseases; occurrence of hypersensitivity disorders and autoimmune diseases).

Controlled clinical studies on humans can provide the best evidence linking a chemical to a resulting effect. However, data from poorly conducted human studies can be inferior to other available data. Moreover, human studies are usually not available since there are significant ethical concerns associated with human testing of environmental hazards.

Epidemiological studies involve a statistical evaluation of human populations to examine whether there is an association between exposure to a chemical and a human health effect. The advantage of these studies is that they involve humans. However, these studies typically do not have accurate exposure information. It is also difficult to tease out the effects of exposure to one pesticide from the effects of exposures to the many chemicals of daily life.

The main source of information for identifying pesticide hazards and the relationship between dose and response are animal toxicity studies, which are considered well-understood predictors of toxicity in humans. Scientists rely on data from

laboratory animals (for example, rats, mice or rabbits) to draw conclusions about the potential hazard to humans.

Although effects seen in animals can also occur in humans, there may be subtle or even significant differences in the ways humans and experimental animals react to a chemical. When relying on animal studies, scientists decide whether a chemical's health effects in humans are likely to be similar to those in the animals tested. Evaluation may also involve characterizing behavior of a chemical within the human body and chemical interactions within organs, cells or even parts of cells.

Dose-response assessment

The dose-response assessment (often combined with hazard identification in a single step) documents the quantitative relationship between dose and toxic effect. Scientists consider the toxic properties of a chemical and determine the lowest dose of the chemical that results in a harmful effect. The dose-response relationship can be defined in toxicity studies by administering increasing doses to groups of animals and measuring the percentage of animals exhibiting pathological changes or disease symptoms at each dose level, and the severity of the effects. State and federal guidelines require that laboratory animals receive high enough doses to produce toxic effects, including doses that may be much higher than those to which people might be exposed. The results of such studies defines the dose-response relationship across a wide range of dose levels, from high doses where pathological changes are frequent to low doses where changes are infrequent or absent.

Dose-response relationships seen in animal studies must be adjusted to account for differences in dose from typical human exposures, and to predict how the responses seen in animals relate to what humans might experience. These extrapolations, among others, introduce uncertainty into the dose-response analysis. Scientists apply several uncertainty factors to compensate for the variation of responses within animal species and between humans and animals.

Uncertainty factors are mathematical adjustments used when scientists have incomplete information. The uncertainty factors differ depending on the chemical, on the quality of the studies evaluated, and on the severity of the effects seen in those studies. As they review data for a risk assessment, scientists continually make judgment calls on the completeness of the information and its applicability to human beings. These uncertainty factors consider:

- Known differences between laboratory animals and humans, and the uncertainty introduced by extrapolating from animal data to humans. Humans are much more diverse than the inbred strains of laboratory animals used in studies, so varied susceptibility among humans must be considered.
- The strength of the evidence that the chemical presents a hazard to human health.
- The kind of potential health effects seen in the studies, and their severity.
- The potency of the toxic agent.
- Quality of the experimental data, and known differences between experimental conditions and realistic exposures.

Usually the dose-response relationship used for risk assessments will be based on data collected from the most sensitive species of test animal available, an example of the health-protective approach taken in regulatory risk assessment.

Exposure assessment

Exposure is a critical connection between potentially harmful substances like pesticides and human health effects. Exposure assessment examines what is known about the duration, frequency (continuous or intermittent), and level of contact

Risk assessment entails the evaluation of information on the hazardous properties of substances, on the extent of human exposure to them, and on the characterization of the resulting risk. Risk assessment is not a single, fixed method of analysis. Rather, it is a systematic approach to organizing and analyzing scientific knowledge and information for potentially hazardous activities or for substances that might pose risks under specified conditions.

***— Science and Judgement in Risk Assessment,* National Academy of Sciences**

Dietary Risk Assessment

Dietary exposure is a function of the type and amount of food consumed and the pesticide residues in or on that food.

There are three elements to calculating dietary risk from pesticide exposure:

- Estimating the toxicity of a pesticide (*see discussion of hazard identification, Chapter 5*).
- Estimating the amount of pesticide residues that might be in or on food, and in drinking water.
- Finding out how much food might be eaten by various subpopulation groups (considers cultural dietary practices).

Scientists in the DPR's Human Health Assessment Branch use available data, standard analytical methods and predictive models, together with assumptions designed to be protective of public health, to produce separate exposure estimates for each exposed subgroup of the general population.

Estimating how much residue might be in or on food and in drinking water involves several things. If the pesticide is used on food crops, field trials are always done to determine the maximum legal residue (tolerance) that could result from maximum permissible use of the pesticide, that is, the maximum application rate as close as possible to harvest. Because this data may overestimate typical residues, the U.S. Food and Drug Administration (FDA), U.S. Department of Agriculture (USDA) and DPR all have programs in which they test random samples of fresh produce for residues. The FDA and USDA also test for residues in cooked and processed foods. Because these samples are analyzed closer to the point of consumption, the resulting data can characterize pesticide residues in food to more closely approximate real-world exposures. Nonetheless, DPR may rely on field trial data when scientists believe the information will provide more accurate exposure estimates.

USDA conducts nationwide surveys every several years to estimate the kinds and amount of food that people eat. Food consumption is reported for people of different racial and ethnic groups, age groups, genders, geographical regions and seasons. The consumption rate is expressed in terms of body weight and accounts for a potentially higher intake by children, as compared to adults, per pound of body weight.

Dietary exposure to a pesticide is based on the estimated food consumption coupled with the estimated pesticide residue levels on the food. These dietary exposure estimates are combined with the toxicity data to assess the risk to various population subgroups, including infants and children, from the exposure to pesticide residues in food. Both chronic and acute dietary exposures are generally considered. Chronic exposure occurs over a long period; therefore, it is calculated using average consumption and residue values. In contrast, acute exposure considers the highest single (acute) exposure. It is calculated using individual consumption data. The resulting information on dietary risk is then included in an overall assessment of the risk posed by the pesticide for all uses.

with a pesticide. In this phase of risk assessment, scientists examine potential exposure to a pesticide at work, at home, in air, and from dietary food and water. Scientists then calculate a numerical estimate of exposure or dose.

Toxicologists determine who might be exposed and then evaluate subpopulations by occupation, age, gender, ethnicity and other factors. Subpopulation groups might include pesticide handlers, farmworkers, other pesticide users (for example, people using home-and-garden products), bystanders (people near treated areas), and others who may be exposed (for example, by entering treated areas or eating treated food). The intent is to characterize exposure to the most vulnerable or highly exposed populations. For example, for some (but not all) substances, children may be more at risk than adults. This can be because they eat, drink and breathe more in proportion to their body size. Their bodies are still developing and may process the pesticide differently. They also behave differently—for example, crawling and hand-to-mouth activity can expose them more to chemicals. DPR, like other regulatory agencies, makes it a high priority to identify and assess environmental health risks that may disproportionately affect children.

Exposure assessments begin with an evaluation of the physical and chemical characteristics of a pesticide. Scientists evaluate whether pesticide breakdown products occur, the half-lives of the chemical in various media (for example, air or water), and other properties. To better understand exposure, scientists review human exposure studies, pesticide product labeling, worker activity information and pesticide use data to identify every situation where a pesticide is used. Scientists also review pesticide illness and injury data to identify potential health problems caused by exposure to the pesticide. To evaluate dietary exposure, scientists review data to find out potential residues on and in food and drinking water. (*See Page 48 for more information on dietary risk assessment.*)

Scientists prefer to use chemical-specific and activity-specific exposure data to derive exposure estimates for the risk assessment. However, when such data are unavailable (which is often the case), they may use a surrogate approach. Surrogate data are substitute data or measurements on one substance (or population) used to estimate analogous or corresponding values for another substance (or population). Scientists can use data from surrogate studies or from generic databases such as the Pesticide Handlers Exposure Database (PHED) developed by Health Canada, U.S. EPA and the pesticide industry. PHED is a generic (multiple products and studies as opposed to activity- and product-specific) pesticide worker exposure database containing measured values of dermal and inhalation exposures from dozens of field studies.

To improve the accuracy of exposure information, DPR scientists conduct field studies to monitor human exposure, using surveys, measurements of residues in soil, in air, in water, in food, and on plants, skin and clothing, as well as blood and urine analyses. (*See Chapter 8 for more information on exposure monitoring studies.*)

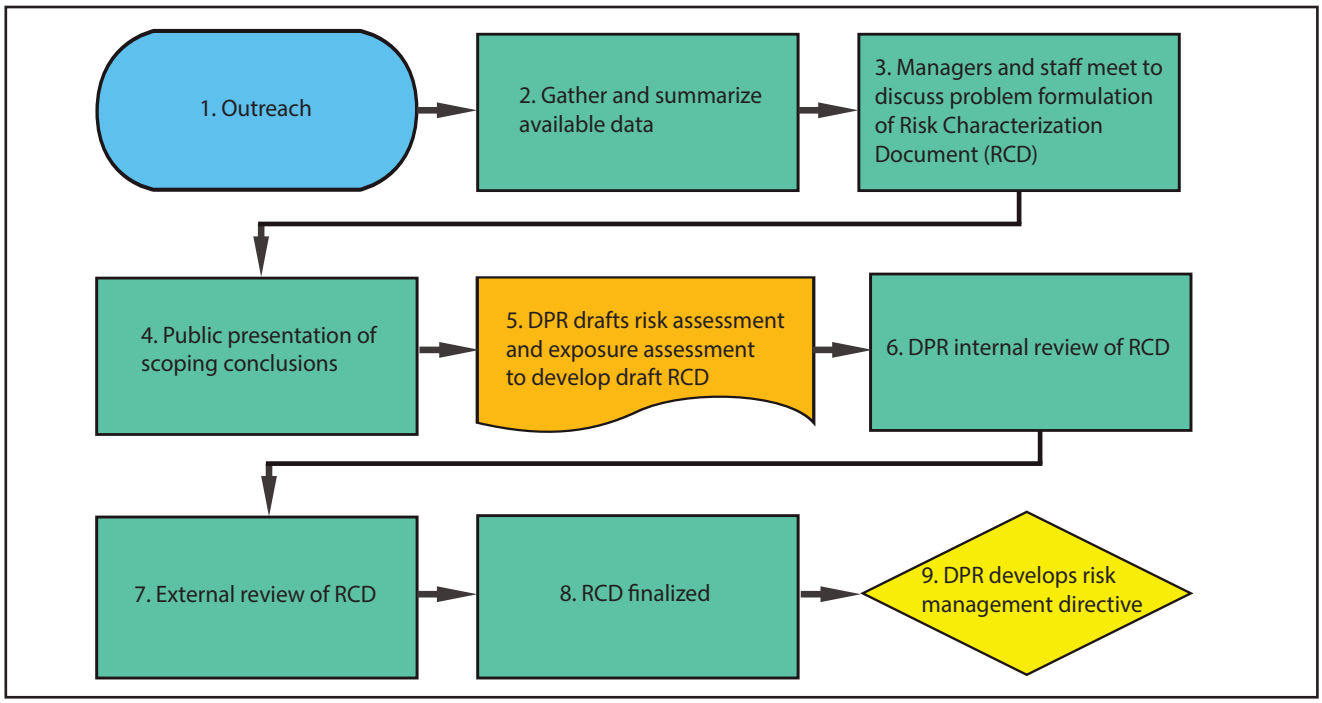
Exposure assessment considers both the exposure pathway (the course a pesticide takes from its source to the person) as well as the exposure route (how the pesticide enters the body). DPR's risk assessors consider all likely exposure routes: inhalation (breathing), dermal (skin or eyes), and oral (dietary food and water). They also look at all exposure scenarios, including occupational, residential, industrial, institutional, environmental and bystander (exposure to off-target drift).

Likely routes of exposure are chiefly inhalation of air containing dusts and vapors, skin contact either with the pesticide spilled on skin or by contact with treated foliage, soil or other surfaces (for example, carpets), and eating foods and drinking water with pesticide residues. Depending on the chemical and physical properties of the substance, a particular exposure might not be considered significant. For example, a given chemical might not be absorbed by the body when spilled on the skin (because of a low dermal absorption rate) but may be absorbed

Risk assessment is a set of tools, not an end in itself.

***— Science and Judgment in Risk Assessment,* National Academy of Sciences**

Developing a Risk Characterization Document



when present in drinking water. On the other hand, with some chemicals, such as those that cause significant irritating effects (for example, eye or breathing irritation), and those with rapid entry into the body, exposure may be the driving factor in an exposure assessment. Exposure to a chemical, therefore, is not necessarily synonymous with how much chemical is absorbed by body fluids and tissues.

In all health risk assessments, scientists must make assumptions to estimate human exposure to a chemical. To avoid underestimating human exposure to a chemical, scientists typically look at the range of possible exposures. Some individuals may have a high degree of contact for an extended time (for example, agricultural applicators). Other individuals may have a lower degree of contact for a shorter time (for example, people using home-and-garden products).

RISK CHARACTERIZATION

A risk characterization presents qualitative or quantitative estimates of the likelihood that any of the hazards associated with the pesticide will occur in exposed people. It examines how well the data support conclusions about the nature and presence or absence of risks, and describes how the risk was assessed and where assumptions and uncertainties exist.

In practice, each part of the risk assessment—hazard identification, dose-response assessment and exposure assessment—has an individual risk appraisal describing key findings, assumptions, limitations and uncertainties. These risk appraisals provide the basis for an integrative risk characterization document (RCD). The RCD informs risk managers and others about the rationale behind the scientists' approach to the risk assessment—why the assessors did what they did to assess the risk.

Although scientists can estimate risks caused by toxins in animals exposed experimentally or in humans who have unusual exposures, extrapolating these estimates to those expected in people under a wide range of conditions is difficult and complex. By their nature, risk estimates rely on the underlying data and assumptions and may not be completely accurate. Scientists seldom have enough

information on actual exposure and on how toxins harm human cells. The exposure assessment often draws its conclusions from multiple sources that include physical chemical properties, monitoring data and computer models. To convert results of animal experiments at high doses to human exposures at low doses, dose-response relationships often rely on assumptions about the effects of toxins on cells.

When data are lacking or uncertain, risk assessors must use a combination of scientific information and their best judgment to characterize risks. Risk analysts generally make health-protective assumptions that tend to prevent them from underestimating the potential risk—that is, they err on the side of safety to better prevent harmful effects.

After review by DPR scientists, draft RCDs undergo external peer review by scientists at OEHHA. DPR also sends each RCD to U.S. EPA for review and may call on other scientific experts for external review. In addition, state law requires draft RCDs for pesticides that are potential toxic air contaminants to be evaluated by a scientific review panel. Peer review is intended to uncover any technical problems or unresolved issues in a draft work product through the use of independent experts. DPR scientists use the information provided by reviewers to revise the draft as necessary so the final work product reflects sound scientific information and analyses. Peer review is designed to strengthen a scientific work product so that the decision or position taken by DPR, based on that product, has a sound, credible basis.

OEHHA scientists perform external peer reviews on DPR's risk characterization documents.