AVAILABLE INFORMATION ON ASSESSING EXPOSURE FROM PESTICIDES IN FOOD

A USER'S GUIDE

U.S. Environmental Protection Agency
Office of Pesticide Programs

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DISCLAIMER

The following policy document is intended to provide guidance and information to EPA personnel and decision-makers, and to the public. As a guidance document and not a rule, the policy in this document is not binding on either EPA or any outside parties. Although this document provides a starting point for EPA risk assessments, EPA will depart from its policy where the facts or circumstances warrant. In such cases, EPA will explain why a different course was taken. Similarly, outside parties remain free to assert that a policy is not appropriate for a specific pesticide or that the circumstances surrounding a specific risk assessment demonstrate that a policy should be abandoned.

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INTRODUCTION

The Agency's Office of Pesticide Programs (OPP) regulates pesticides to ensure that their use does not pose unreasonable risks to human health or the environment and that exposure to pesticide residues in food is safe. These determinations rely on the process of risk assessment. In assessing risk, the Agency considers all sources of exposure (*e.g.,* food, drinking water, incidental exposure in and around the home, school, etc.) and the inherent toxicity of the pesticide.

The purpose of this *User's Guide* is to provide the reader with a comprehensive discussion and listing of U.S. Environmental Protection Agency (EPA or the Agency), U.S. Department of Agriculture (USDA), and U.S. Food and Drug Administration (FDA) guidance, policy documents, and databases that provide detailed, specific "how-to" information and/or data on assessing exposure to pesticides from the foods that we eat. To help the reader understand the context of this information, this guide first provides a basic overview of risk assessment for exposure resulting from pesticide residues in food.

This guide does not address aggregate exposure and risk assessment, which is the process of combining exposure to a single pesticide from all sources of exposure: food, drinking water, and through nonoccupational sources such as homes and recreational areas. And, this guide does not address cumulative risk assessment, which is the process of combining exposure and risk from all pesticides with a common mechanism of toxicity.

The first section, "A Primer on Pesticide Exposure and Risk from Food," provides a very simple overview of EPA's approach to estimating risk and exposure from pesticide residues in food. The following section, "Information Sources: Where-to-Find Data, Guidance, and Other Information on Assessing Exposure to Pesticides in Food," provides specifics on how to obtain or generate the data and/or information EPA uses in its assessments of exposure and risk from pesticides in food. The final section of this *User's Guide* provides a list of the “Where-to-Find’s,” arrayed by topic area. It is followed by the bibliography.

ACRONYMS

ADI	Acceptable Daily Intake
aPAD	Acute Population Adjusted Dose
CFR	Code of Federal Regulations
cPAD	Chronic Population Adjusted Dose
CSFII	USDA's Continuing Survey of Food Intake by Individuals
DEEM™	Dietary Exposure Evaluation Model
DPR	California Department of Pesticide Regulation
EPA	U.S. Environmental Protection Agency
FDA	U.S. Food and Drug Administration
FFDCA	Federal Food, Drug, and Cosmetic Act
FIFRA	The Federal Insecticide, Fungicide, and Rodenticide Act
FQPA	The Food Quality Protection Act of 1996
GLP	Good Laboratory Practices
HED	The Health Effects Division of the Office of Pesticide Programs
HHS	U.S. Department of Health and Human Services
LOAEL	Lowest Observed Adverse Effect Level
LOD	Limit of Detection
LOQ	Limit of Quantification
MOE	Margin of Exposure
MRM	Multiresidue Method
NAPIAP	USDA's National Agricultural Pesticide Impact Assessment Program
NARA	National Archives and Records Administration
NAS	National Academy of Sciences
NASS	USDA's National Agricultural Statistics Service
ND	Nondetects or nondetectable
NOAEL	No Observed Adverse Effect Level
NPRD	National Pesticide Residue Program
OPP	U.S. EPA's Office of Pesticide Programs
OPPTS	U.S. EPA's Office of Prevention, Pesticides, and Toxic Substances
PAD	Population Adjusted Dose
PAM	Pesticide Analytical Manual
PDP	U.S. Department of Agriculture's Pesticide Data Program
PHI	Preharvest Interval
PoD	Point of Departure
ppb	part per billion
ppm	part per million
QA/QC	Quality Assurance/Quality Control
q_1*	Q-Star or Q1-Star
RfD	Reference Dose
SAP	The FIFRA Scientific Advisory Panel
SOP	Standard Operating Procedure
SRM	Single Residue Method
USDA	U.S. Department of Agriculture
%CT	Percent of Crop Treated

A PRIMER ON PESTICIDE EXPOSURE AND RISK FROM FOOD

Risk = f (toxicity, exposure)

The risk that is posed by a pesticide in or on food depends on the toxicity of the pesticide and the amount of pesticide to which a person is exposed; this is expressed mathematically by the equation: risk = f (toxicity, exposure), which in words means risk is a function of toxicity and exposure. More simply stated, risk is equal to toxicity multiplied by exposure. A pesticide with low toxicity and high exposure could pose a similar risk as a pesticide with high toxicity and low exposure.

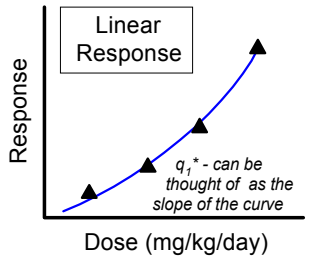
Exposure and Risk at a Glance

To determine whether there is any risk–which can result from either short- (*i.e.*, acute) or longer-term (*i.e.*, chronic) exposure–one considers both the toxicity of the pesticide (which is sometimes referred to as hazard) and the amount of pesticide to which an individual may be exposed.

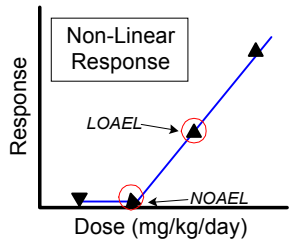
In the actual risk equations, which are discussed later on, toxicity is expressed as: an acute population adjusted dose (aPAD), a chronic population adjusted dose (cPAD), a potency factor (q_1*), or a Point of Departure. Which toxicity expression the risk assessor uses depends on the duration of exposure (*e.g.*, acute or chronic) and, in the case of a carcinogen, the method chosen for quantifying risk.

***Linear vs. Nonlinear Response**. One way toxic effects can be classified is whether they occur via a linear or nonlinear response.*

***A linear response** is one for which it is assumed that the toxic effect may occur, no matter how small the dose. The classic example of a linear response is certain types of cancer (note: some cancers have been shown to exhibit nonlinear responses).*



***A nonlinear response** is one in which the toxic effect is not seen until a certain dose is reached. An example of such an effect is cholinesterase inhibition.*



< The risk posed by carcinogens can be quantified using an equation that assumes the pesticide's toxic effect occurs via a **linear response** or, it can be calculated using an equation that assumes a **nonlinear response**.

The amount of pesticide to which an individual is exposed (*i.e.*, exposure) is determined by combining the amount of pesticide that is in or on the food (*i.e.*, residue levels) and the amount and type of foods that people eat (*i.e.*, food consumption).

Risk is estimated using a computer model that combines the toxicity, residue, and consumption information. This is further described under the “Risk” segment of this part.

The rest of this Primer is divided into three segments: Toxicity, Exposure, and Risk. Each elaborates on the principles introduced in this Glance. But first, a word on aggregate and cumulative assessments.

Aggregate and Cumulative Assessments

Under the Food Quality Protection Act of 1996 (FQPA), EPA is required to conduct aggregate exposure assessments, where all sources of exposure are considered in the dietary risk assessment. These include exposures from:

< Pesticide residues in food,

< Pesticide residues in drinking water, and

< Pesticide residues encountered through nonoccupational sources such as in the home, recreational areas, and schools.

This document only addresses exposure from pesticide residues found in food. Guidance and policy documents are under development for assessing exposure from drinking water and conducting aggregate and cumulative assessments.

***Endpoint**. The type of toxic effect exhibited by a pesticide (e.g., if the pesticide affects the nervous system, the endpoint would be neurotoxicity). A pesticide may have more than one endpoint. Endpoints are determined for both acute and chronic exposures.*

Where-to-Find

Draft Guidance on conducting aggregate exposure can be found at:

"Guidance for Performing Aggregate Exposure and Risk Assessments;" draft document (EPA, 1999a)

http://www.epa.gov/pesticides/trac/science/#non-occupational

***Population Adjusted Dose (PAD)**. The reference dose divided by any additional safety factor retained due to concerns unique to FQPA.*

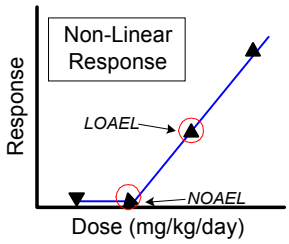
Toxicity

Risk = f (toxicity, exposure)

***Reference Dose (RfD).** A NOAEL divided by the appropriate uncertainty factors.*

Noncancer Endpoints

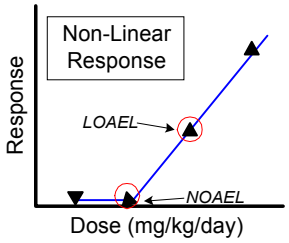
***FQPA Safety Factor**. A factor that is applied to pesticides that exhibit threshold effects to "take into account potential pre- and post-natal toxicity and completeness of the data with respect to exposure and toxicity to infants and children."*



EPA assumes that noncancer toxicity **endpoints** exhibit a nonlinear response. In assessing risk resulting from exposure to pesticide residues in food, the toxicity for such effects is expressed as a **Population Adjusted Dose** or PAD. A PAD is simply the **reference dose (RfD)** divided by any additional safety factor retained due to concerns unique to FQPA; it can be thought of as an amount of toxicant to which a person can be safely exposed. In practice, this additional safety factor is referred to as the **FQPA Safety Factor.**

The RfD is calculated by dividing the dose in laboratory animals at which no harmful effects are observed by uncertainty factors; these are discussed below. Separate PAD's and RfD's are calculated for both acute and chronic effects. These calculations are shown just after the "FQPA Safety Factor" segment.

***NOAEL**. The highest dose in a toxicity study at which no adverse health effect is seen. This dose is less than the lowest observed adverse effect level (LOAEL). It has units of mg per kg body weight per day (mg/kg/day).*



***LOAEL.** The lowest dose in a toxicity study at which an adverse health effect is seen. It has units of mg/kg/day.*

***Uncertainty Factors**. Factors applied to the NOAEL to account for things such as potential variation within the human population (e.g., age, gender) or a significant deficiency in the toxicity database. A separate factor is applied for each of these considerations.*

Where-to-Find...

A good discussion on the use of uncertainty factors and the FQPA Safety Factor can be found at:

"The Office of Pesticide Programs' Policy on Determination of the Appropriate FQPA Safety Factor(s) for Use in the Tolerance-Setting Process;" draft document (EPA, 1999b)

http://www.epa.gov/scipoly/sap/1999/may/10xpoli.pdf

Uncertainty Factors

In determining acute and chronic RfD's, the respective **NOAEL's** are divided by **uncertainty factors**. Listed in the following chart are the conditions under which a certain uncertainty factor may be applied, the magnitude of the factor, and when the factor is applied.

Condition for Uncertainty Factor	Magnitude of the Factor	When Factor Is Applied
Accounting for the potential variation within the human population (intraspecies)	10-fold	typically
Accounting for the potential differences between humans and animals as the animal data are translated to humans (interspecies)	10-fold	typically
Accounting for a gap in the toxicity database (*i.e.*, a key study is missing)	3-fold to 10-fold	when the nature of the toxicity database indicates its need
If a LOAEL is used instead of a NOAEL		

In total, the uncertainty factors applied to the NOAEL can range from the typical 100-fold inter-/intraspecies factor to over 3,000-fold for a pesticide where there are substantial concerns regarding the nature of toxicity database.

FQPA Safety Factor

FQPA directs OPP to include an additional 10-fold safety factor to assure the safety of infants and children. A different factor may be used if it provides adequate safety. In determining acute and chronic PAD's OPP conducts a case-by-case review of each chemical to determine whether the additional default 10-fold FQPA Safety Factor should be retained or whether another factor adequately protects infants and children. It should be noted that OPP considers all of the factors listed above (except the interspecies and intraspecies uncertainty factors) to be responsive to the FQPA mandate.

Equations for Acute Effects

For acute (noncancer) toxicological effects (*e.g.*, cholinesterase inhibition, which can occur following only one day of exposure), the toxicity portion of the risk equation is expressed as an acute PAD (aPAD). It is calculated as follows:

$$\text{aPAD} = \frac{\text{aRfD}}{\text{Safety Factor Unique to FQPA}}, \text{ where}$$

$$\text{aRfD} = \frac{\text{NOAEL}}{\text{Uncertainty Factors}}$$

An acute RfD (aRfD) is an estimate of the level of one-day exposure to a pesticide residue that is believed to have no significant deleterious effects. It is calculated by first determining the No Observed Adverse Effect Level (NOAEL) from acute animal toxicity studies and dividing it by the appropriate uncertainty factors.

Equations for Chronic Effects

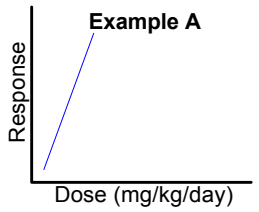
For chronic toxicological effects (*e.g.,* damage to the developing fetus; those effects that occur after exposure lasting a significant portion of the lifespan;), the toxicity portion of the risk equation is expressed as a chronic PAD (cPAD). It is calculated as follows:

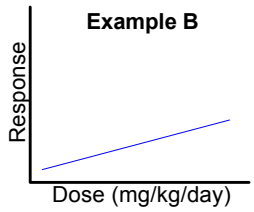
$$\text{cPAD} = \frac{\text{cRfD}}{\text{Safety Factor Unique to FQPA}}, \text{ where}$$

$$\text{cRfD} = \frac{\text{NOAEL}}{\text{Uncertainty Factors}}$$

A chronic RfD is an estimate of the level of daily exposure to a pesticide residue, which, over a 70-year life span, is believed to have no significant harmful effects. FDA refers to this level of exposure as an acceptable daily intake, or ADI. It is calculated the same way as the aRfD except the NOAEL is taken from chronic animal studies.

***Cancer Potency**. The potency of the pesticide in Example A is greater than the potency of the pesticide in Example B. Cancer potency is expressed as a q_1*.*

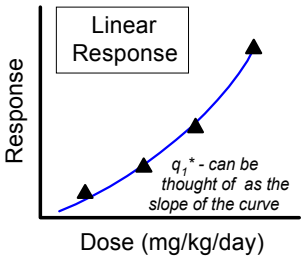




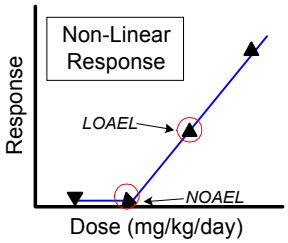
Cancer Endpoints

Linear

For carcinogenic effects that are thought to occur through a linear response, the toxicity portion of the risk equation is expressed as a **cancer potency** factor, more commonly known as a q_1*. A q_1* is the relative strength of a carcinogen. Mathematically, it can be thought of as the slope of the dose-response curve as shown in the examples to the left. In reality, a q_1* is a single number that is calculated from animal data using a sophisticated computer model that assumes linearity at low doses. The higher the q_1* value, the more potent the chemical is as a carcinogen.



Nonlinear



For carcinogenic effects that are shown to exhibit a nonlinear response, the toxicity portion of the risk equation is expressed as **Point of Departure or PoD**. A PoD is simply the toxic dose that serves as the "starting point" in extrapolating a risk to the human population. The PoD can be either an observed dose (*e.g.*, NOAEL) or it can be an interpolated value. Quite often, the PoD is equivalent to the NOAEL.

***Point of Departure (PoD)**. For cancer nonlinear risk assessment, the PoD marks the beginning of the extrapolation. For noncancer, it can serve as the basis for the RfD derivation. The PoD can be either a NOAEL, LOAEL, or a benchmark dose (ED_{10} for example).*

Exposure

***Tolerance**. The maximum, legal limit of a pesticide residue that is allowed to remain in or on a treated food commodity as it enters interstate commerce. Tolerances are enforceable.*

Risk = f (toxicity, exposure)

Under FQPA, EPA must consider risks from "aggregate" exposures to a pesticide when establishing a pesticide **tolerance** (*i.e.*, the legally permitted level of a pesticide in a food or feed). This means that in addition to considering the exposures from food, the Agency must also consider other exposures for which reliable data are available. These include exposure from drinking water and nonoccupational sources such as pesticides used in and around the home, recreational areas, etc. <u>This paper does not address aggregating exposures; it only discusses exposure from food</u>.

Estimates of exposure from food are derived from two distinct pieces of information: the amount of a pesticide residue that is present in and on food (*i.e.*, the residue level) and the types and amounts of foods that people eat (*i.e.*, food consumption).

Crop Field Trials. *Testing that is conducted, using crops in the field, where the pesticide is applied at the label's maximum rate using the maximum number of applications (frequency) and the minimum preharvest interval (PHI).*

PHI*. The interval between the last application of pesticide and harvest of the crop.*

% Crop-Treated (%CT). *An estimate of the acreage under cultivation that is actually treated with the pesticide at least once. It is expressed as a percentage of the total acreage for that crop.*

The residue level is primarily developed from:

< The numerous **crop field trials** and monitoring programs (*e.g.*, PDP, FDA) where the amount of pesticide residues on a given commodity is measured;

< Use information such as the percent of crop that is treated (**% crop treated or %CT**); and

< Commercial and consumer practice information such as washing, cooking, processing, and peeling practices.

Consumption information comes from the USDA's Continuing Survey of Food Intake by Individuals (CSFII), which provides survey data of what people eat.

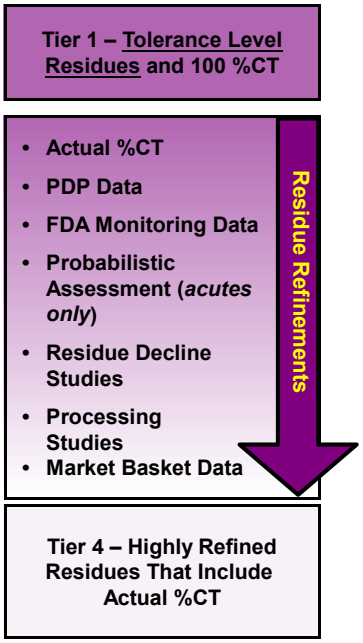
Calculating the Residue Levels

Residue levels for use in acute exposure assessment are estimated a bit differently from residues levels that are to be used in chronic exposure assessments. In an acute exposure assessment, the risk assessor is attempting to estimate how much of a particular pesticide residue might be consumed in a single day. Acute exposure calculations tend to employ a full range of data including high-end residue values, high-end consumption, and high-end %CT estimates. For a chronic exposure assessment, the risk assessor is attempting to estimate how much of a given pesticide residue might be consumed on a daily basis over the course of a lifetime. Consequently, the risk assessor tends to use average residue values, average consumption values, and average %CT estimates.

The Tiered Approach to Acute and Chronic Exposure Assessment

***Tolerance Level Residues**. These are based on crop field trial data and are used in setting tolerances. They are the highest residues that could possibly be found on food resulting from maximum use according to the label. Tolerance level residues represent levels not likely to be found on foods in interstate commerce.*

In assessing acute and chronic risks from pesticides in food, EPA uses a "tiered approach" where it performs an initial risk assessment using "worst-case" assumptions. For example, at the first tier (Tier 1), EPA would assume that for both acute and chronic risk assessments, the residues are at tolerance levels and that 100% of the crop was treated. Generally speaking, the level of resources and data needed to refine exposure estimates increase with each tier.



Lower tier (Tiers 1 and 2) exposure assessments use residue levels derived from guideline crop field trial data (tolerance levels) and can (for certain crops) use readily available usage information such as the percent of the crop that has been treated (%CT) with a particular pesticide. These estimates tend to overestimate actual pesticide residue levels in food. Generally, if risks from pesticide residues in food are not of concern using lower tier exposure estimates, no further refinements are made. With the aggregate and cumulative assessments now required by FQPA, it is likely that higher tier (Tiers 3 and 4) exposure estimates will be needed.

***Bridging, Residue Decline, and Residue Degradation Studies**. Bridging studies look at the relationship between residue levels that result from maximum applications vs. those that would result from typical applications.*

Both residue decline and residue degradation studies look at the degradation of pesticide residues over time; the difference between the two is the time frame. Residue decline studies look at the degradation that occurs between application and harvest while degradation studies look at the degradation between harvest and consumption.

Data that may be used in these higher tier refinements include:

< Percent of crop treated;

< FDA Monitoring Data;

< USDA Pesticide Data Program (PDP) Monitoring Data;

< Other market basket (monitoring) studies;

< **Bridging studies**;

< **Residue decline studies**;

< **Residue degradation studies**; and

< Commercial and consumer practices such as washing, cooking, and peeling.

Each of these data types is described in the "Where- to-Find" section of this paper. That section also provides information on obtaining guidance for generating data and how specifically the Agency applies the tiering system.

Consumption

Food consumption data are provided by USDA from its Continuing Survey of Food Intake by Individuals or CSFII. USDA has been conducting such food surveys since the 1930's by means of personal interviews in which interviewers ask individuals, who are selected statistically, to recall everything they ate and drank over the previous 24 hours.

In the late 1970's, USDA conducted the National Food Consumption Survey, which was a large and comprehensive survey that sampled thousands of households to learn about what, and how much, people ate.

Over the course of the last 20+ years, people's dietary habits have changed and the public health community has become more concerned with the unique patterns of children's exposure to pesticides through their diets. In 1993, the National Academy of Sciences raised the concern that current food consumption data do not provide sufficient sample sizes to adequately estimate exposure to pesticide residues in the diets of children (NAS, 1993). In 1996 FQPA directed USDA to "conduct surveys to document dietary exposure to pesticides among infants and children."

As a result of these concerns and changes in dietary habits, EPA and USDA have been working to update the food consumption information by periodically conducting the CSFII. In the next several months, EPA will start using the latest CSFII information–that of a 1994-1996 survey–and 1998 data collected through a Children's Supplemental Survey, which was conducted to collect more information on what infants and young children eat. Where-to-Find food consumption information is in "Information Sources..."

Risk

Risk = f (toxicity, exposure)

The basic algorithm or equation used to calculate risk resulting from exposure to pesticide residues in food depends on the duration of exposure (*i.e.*, acute, chronic) and the type of response -- linear or nonlinear. EPA assumes that all noncancer endpoints exhibit a nonlinear response. The basic equations used to calculate dietary risks are provided below. The actual risk estimates are calculated using a sophisticated computer model that uses these algorithms. It is described below.

Tool for Calculating Risk

Risk resulting from exposure to pesticide residues in food, be it from acute exposure or chronic exposure, is calculated using a sophisticated computer software tool that combines food exposure data (both residue levels and %CT, and consumption) with toxicity to produce a risk value. The backbone of this model is USDA's food consumption survey information.

The model yields risk values for the general U.S. population and 26 population subgroups, including infants, children, and nursing women. It has the ability to determine which crop/pesticide combinations contribute the highest exposures and in turn, risks. Also, it can run **probabilistic analyses** for acute risk assessments.

Probabilistic Analysis. *The use of a statistical technique (e.g., Monte Carlo) to quantify both the range of exposures to pesticide residues and the probability or chance of exposure to any particular level.*

EPA is currently using a model that was developed by Novigen Sciences, Inc.; it is called the Dietary Exposure Evaluation Model or DEEM™.

Where-to-Find...

A full description of the DEEM™ model and how it operates may be found in:

"Background Document for the Sessions: Dietary Exposure Evaluation Model (DEEM™) and DEEM™ Decompositing Procedure and Software;" (Novigen, 2000)

NOTE: Novigen Inc. prepared this document for a March 2000 FIFRA Scientific Advisory Panel (SAP) meeting.

http://www.epa.gov/scipoly/sap/index.htm

Basic Risk Equations for Noncancer Endpoints

Provided below are the basic equations that are used to estimate risk resulting from exposure to pesticide residues in food for noncancer endpoints. EPA assumes that noncancer toxicity endpoints exhibit a nonlinear response.

Acute Risk

Acute food risk is expressed as a percentage of the aPAD. If the calculated % aPAD is less than 100, the risk is generally considered to be acceptable.

$$\% \text{ aPAD} = \frac{\text{Food Exposure(mg/kg/day)}}{\text{aPAD (mg/kg/day)}} \text{ X } 100$$

Chronic Risk

Chronic food risk is expressed as a percentage of the cPAD. If the calculated % cPAD is less than 100, the risk is generally considered to be acceptable.

$$\% \text{ cPAD} = \frac{\text{Average Food Exposure(mg/kg/day)}}{\text{cPAD (mg/kg/day)}} \text{ X } 100$$

Basic Risk Equations for Cancer Endpoints

Linear

Linear cancer risk is expressed as a probability. For example, a calculated risk of 1×10^{-6} means that a person receiving a lifetime exposure to the pesticide increases his or her chance of developing cancer by one in a million. That is, for every one million exposed persons, one would expect, at the most (upper-boundary) one more cancer than would otherwise occur, and it may be less. This probability is calculated using the relationship:

$$\text{Cancer Risk} = \text{Average Food Exposure (mg/kg/day) X } q_1^* \text{ (mg/kg/day)}^{-1}$$

Nonlinear

***Margin of Exposure (MOE)**. A ratio of the toxicity PoD (e.g., NOAEL) and the exposure level. For example,*

$$\text{MOE} = \frac{\text{PoD}}{\text{Exposure}}$$

Nonlinear cancer risk is calculated using the MOE approach where a **margin of exposure (MOE)** would be calculated. For nonlinear cancer risk assessment, EPA has not yet determined an appropriate target MOE. It is currently developing criteria by which to make that judgment.

INFORMATION SOURCES: Where-to-Find Data, Guidance, and Other Information on Assessing Exposure to Pesticides in Food

Registrant. *A person or company who has registered any pesticide pursuant to FIFRA.*

Estimating exposure from pesticide residues found in or on food is a complex process. First, data must be obtained. EPA requires **registrants** to generate a large body of scientific data. The risk assessor gathers other information such as percent of the crop treated and how the pesticide is used from existing sources. Then, the data must be evaluated by Agency scientists and transformed into exposure estimates.

The following segments of this section provide a comprehensive discussion regarding the sources of these data and other information. The first part primarily discusses sources of actual pesticide residue data while the second part presents sources of information on calculating acute and chronic exposure estimates using the gathered data.

Residue Data and Collection

Assessing the level of pesticide residue that is in or on the foods that we eat–for both fresh raw foods such as lettuce and apples and processed foods such as frozen french fries and canned beans–is a complex process that requires data from numerous sources. The registrants are required under FIFRA to generate the basic residue data (*i.e.*, the crop field trial data, which are discussed later). EPA obtains other data, which are often used to refine the basic residue data, from: state and federal monitoring programs, other government sources, and voluntary submissions from registrants or other entities such as grower groups. The sources of these data are listed below.

The 40 CFR 158.240 Residue Chemistry Requirements

Under the authority of the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), EPA requires registrants (under the regulations at 40 CFR 158.240) to submit a full battery of residue chemistry data that reflect pesticide residue concentrations in food and feeds. These data are used to estimate the U.S. population's level of exposure to pesticide residues in food and to set and enforce tolerances for pesticide residues in food or animal feed.

Results of these studies provide EPA with, among other things, the information it needs to determine:

< The nature of the residue (*i.e.*, what are the metabolites; how is the pesticide broken down by the plant or in livestock that is used for food), and

< The amount of the residues in food or feed.

Crop Field Trials. *Testing that is conducted, using crops in the field, where the pesticide is applied at the label's maximum rate using the maximum number of applications (frequency) and the minimum preharvest interval (PHI).*

These **crop field trial** residue data may be considered "worst-case" because the testing guidelines require that the pesticide under investigation be applied at the maximum application rate using the maximum number of applications and the minimum PHI. These worst-case residues reflect the most extreme use pattern allowed on the label. Because actual use (in practice) can be significantly less than label maximums, and for other reasons, the residue levels encountered by the consuming public are likely to be much lower.

Where-to-Find...

The residue chemistry data requirements are at:

40 CFR 158.240 (NARA, 1999)

http://www.epa.gov/epacfr40/chapt-I.info/subch-E/40P0158.pdf

The guidance for fulfilling the data requirements is:

Series 860 of the OPPTS Harmonized Test Guidelines (EPA, 1996a)

http://www.epa.gov/docs/OPPTS_Harmonized/870_Health_Effects_Test_Guidelines/

Supplemental guidance on crop field trials, which is one of the 40 CFR 158.240 data requirements, is available:

"HED SOP 98.2: Supplementary Guidance on use of OPPTS Residue Chemistry Test Guidelines 860.1500, Crop Field Trials (residue zone maps - Canadian extension);" [4/8/98] (EPA, 1998a)

USDA Pesticide Data Program Data

USDA started the Pesticide Data Program in May 1991 to collect data on pesticide residues in food; to date it has published its findings for calendar years 1991 through 1998. PDP's sampling procedures were designed to capture residues in the food supply reasonably close to the time of consumption. PDP has tested about 40 different commodities including fresh/frozen/canned fruit & vegetables, fruit juices, whole milk, grain, and corn syrup for more than 160 different pesticides.

Note: Even though the PDP samples are collected at a point in the channels-of-trade where residues are close to those at consumption, these are not "grocery store" or "dinner plate" levels, where residues may be reduced even further.

PDP continues to focus on the National Academy of Sciences' conclusions as indicated in the 1993 report Pesticides in the Diets of Infants and Children (NAS, 1993). In that report, the Academy recommended that pesticide residue monitoring programs target foods highly consumed by children, and that analytical testing methods used be standardized, validated, and subject to strict quality control and quality assurance programs (QA/QC). Consequently, since 1994, PDP has modified its commodity testing profile to include not only fresh fruits and vegetables, but also canned and frozen fruits/vegetables, fruit juices, whole milk, wheat, soybeans, oats, corn syrup, peanut butter, and poultry.

PDP pesticide monitoring activities are a federal-state partnership, whereby 10 participating states, which represent about 50 percent of the nation's population and all regions of the country, collect samples of fruit, vegetables, and other commodities. These samples are collected close to the point of consumption–at terminal markets and large chain store distribution centers immediately prior to distribution to supermarkets and grocery stores. This allows the capture of sample identity data, takes into account pesticide degradation during transit and storage, and provides data on residues resulting from postharvest applications of fungicides and growth regulators.

The number of samples to be collected is apportioned according to state population or commodity production figures. Samples are randomly chosen without regard for commodity origin or variety. They reflect what is typically available to the consumer throughout the year. PDP's statistically-reliable sampling protocol is designed to select random samples that best represent pesticide residues in the food supply to allow for a realistic estimate of exposure to these chemicals. In addition, PDP also conducts special surveys on single-serving sized food items to support acute exposure studies.

The PDP data are EPA's preferred monitoring data for use in assessing risk for exposure resulting from pesticide residues in food. The sampling protocol was developed in cooperation with the Agency; the sampling frame is statistically-designed to be representative; and the data generated are specifically designed to be used for risk assessment. Also, the **Limits of Detection (LOD)** are low and a significant number of samples are collected over multiple years.

***The Limit of Detection (LOD)**. The minimum concentration that an analytical method, which includes the laboratory instrumentation (equipment), can detect or "see." A typical LOD might be 0.01 part per million (ppm).*

***Translating**. A process of using one crop's residue data to estimate the residue level for other similar crops.*

Where-to-Find...

To obtain more information on the PDP program or to access summaries of the data contact USDA at:

http://www.ams.usda.gov/science/pdp/index.htm

For more information on how the Agency uses the data, contact EPA:

U.S. EPA
Health Effects Division (7509C)
Reregistration Branch 4
1200 Pennsylvania Ave., NW
Washington, DC 20460

703-305-7351

Using the PDP Data: Translating to Other Crops

PDP data have been collected for about 40 different food crops. There are hundreds of food crops for which EPA conducts assessments for exposure resulting from pesticide residues in what we eat. To expand the utility of the PDP data beyond the 40 or so crops that are sampled, EPA has established a policy on **translating** PDP data to other similar crops when certain conditions are met.

These conditions and details on the translation policy can be found in:

Where-to-Find... "Translation of Monitoring Data. HED Standard Operating Procedure 99.3 (3/26/99);" (EPA, 1999f)

Using the PDP Data: Decompositing

***Composite**. A method of sampling and analysis where a number of individual items (e.g., apples) is combined and/or blended into a single sample or analysis.*

***Probabilistic Technique**. For pesticide exposure assessment, a statistical method where the range of exposures to pesticide residues and the probability of exposure to any particular level is quantified. A common probabilistic technique in Monte Carlo.*

***Decompositing**. The process of statistically converting composite residue information into "individual item" residue information.*

When a chemist in the laboratory is trying to determine the level of a pesticide residue in a particular commodity (*e.g.*, apples) he or she often does this through a **composite** sample. In assessing acute exposure using a **probabilistic technique**, the pesticide concentration is needed in terms of an individual item such as an apple, not in terms of an average value for a large number of apples. The reason for this has to do with the nature of probabilistic analysis and what people actually eat.

To get such individual item residue data, the chemist could perform a residue analysis for each single apple. Alternatively, this individual item data could be ascertained through statistical adjustment of the composite data. EPA is now in the process of developing statistical procedures for **decompositing** composite residue data into individual item data (*i.e.*, residues for one apple *vs.* residues for a five pound sample of apples).

In May 1999 the Agency solicited advice from the FIFRA Scientific Advisory Panel (SAP) on a proposed method for decompositing residues (see box on the next page). This methodology, when applied, would permit the use of monitoring data from PDP and FDA (which are collected and analyzed as composite samples) to be "statistically adjusted" such that they could be used in acute probabilistic exposure assessment. In May 2000, EPA returned to the SAP with a review of other methods that might be appropriate for decomposition, invited the Panel to compare these methods to the earlier proposed method, and sought a recommendation as to which method might be most suitable.

Provided below are the sites for the original draft paper and the paper that EPA presented to the SAP in May 2000 that describes the principle of decompositing in general and compares the earlier proposal with the additional methods. EPA expects to issue final guidance on decomposition in the winter of 2001.

Where-to-Find...

The draft original proposal:

"Statistical Methods for Use of Composite Data in Acute Dietary Exposure Assessment;" (EPA, 1999e)

http://www.epa.gov/scipoly/sap/1999/may/hanssap.pdf

SAP paper describing decomposition and comparing the decomposition methods:

"Office of Pesticide Programs' Comparison of Allender, RDFgen, and MaxLIP Decomposition Procedures;" (EPA, 2000a)

http://www.epa.gov/scipoly/sap/index.htm

FDA Monitoring Data

FDA operates an ongoing program of monitoring for pesticide residues in foods; the results of the program are published annually. The program consists of three components:

- Regulatory monitoring, which includes both surveillance and compliance;
- Incidence/level monitoring; and
- The Total Diet Study.

Regulatory Monitoring

FDA's regulatory monitoring program is directed toward enforcing tolerances in imported foods and in domestically produced foods shipped in interstate commerce. Under regulatory monitoring, FDA samples individual lots of domestically produced and imported foods and analyzes them for pesticide residues. Domestic shipments are collected as closely as possible to the point of production in the distribution system; import samples are collected at the point of entry into U.S. commerce. Emphasis is on the raw agricultural product, which is analyzed as the unwashed, whole (unpeeled), raw commodity. Processed foods are also included.

Domestic and import food samples collected for analysis are classified as either "surveillance" or "compliance." Most samples collected by FDA are the surveillance type; that is, there is no prior knowledge or evidence that a specific food shipment contains illegal pesticide residues. Compliance samples are collected as follow-up to the finding of an illegal residue or when there is other evidence of a pesticide problem.

***Composite**. A method of sampling and analysis where a number of individual items (e.g., apples) is combined and/or blended into a single sample.*

To analyze the large numbers of samples (which are collected and prepared as **composites**) for which the pesticide treatment history is usually unknown, analytical methods capable of simultaneously determining a number of pesticides are used. These **multiresidue methods (MRM's)** can detect and quantify about half of the approximately 400 pesticides with EPA tolerances, as well as many others that have no tolerances. The most commonly used MRM's can also detect many metabolites, impurities, and alteration products of pesticides. **Single residue methods (SRM's)** or selective MRM's are used to determine pesticides not covered by an MRM. An SRM usually measures one pesticide; a selective MRM measures a relatively small number of chemically-related pesticides.

***Multiresidue Method (MRM)**. An analytical method that is capable of detecting more than one compound.*

***Single Residue Method (SRM).** An analytical method that is capable of detecting just a single compound.*

Incidence/Level Monitoring

A complementary approach to regulatory monitoring, known as incidence/level monitoring, has been used to increase FDA's knowledge about particular pesticide/commodity combinations by analyzing certain foods to determine the presence and levels of selected pesticides. From 1995 to 1997, a survey of triazines was done.

Total Diet Study

The Total Diet Study is FDA's annual market basket program that provides data on pesticide residue levels that are present in table-ready foods. Because the study has been under way for more than 30 years, trends can be discerned, such as the decrease in dietary levels of DDT (chemical name: dichlorodiphenyltrichloroethane) and related residues.

As part of the Total Diet Study, FDA staffers shop in supermarket or grocery stores four times a year, once in each of four geographical regions of the country. Shopping in three cities from each region, they buy the same 259 foods, including meat, selected from nationwide dietary survey data to typify the American diet. The purchased foods are called "market baskets."

Foods from the market baskets are then prepared as a consumer would prepare them. For example, a “beef and vegetable stew” is made from the collected ingredients, using a standard recipe. The prepared foods are analyzed for pesticide residues, and the results, together with USDA consumption studies, are used to estimate the dietary intakes of pesticide residues for fourteen age-sex groups ranging from six-month-old infants to 70+ year-old men and women.

The analytical methods used in the Total Diet Study are modified to permit measurement at levels five to ten times lower than those normally used in regulatory monitoring. In general, residues present at or above one part per billion (ppb) can be measured.

Where-to-Find...

For further information on the FDA monitoring program, including data summaries from the monitoring programs, contact:

U. S. Food and Drug Administration
Center for Food Safety and Applied Nutrition
200 C Street SW
Washington, DC 20204

http://vm.cfsan.fda.gov/~dms/pesrpts.html

Using the FDA Data: Decompositing

As discussed under the segment "Using the PDP Data: Decompositing," the decomposition technique also applies to FDA data, as appropriate. Please refer to that segment for further information.

State Monitoring

A few states (*e.g.*, California and Florida) collect their own pesticide monitoring data. When these are available, they may be used by EPA in food exposure assessments.

The National Pesticide Residue Database

The National Pesticide Residue Database (NPRD) is being developed as a comprehensive, electronically-accessible database of quality pesticide residue food monitoring data collected in the U.S. It includes data from:

- The FDA pesticide residue monitoring program; FDA Total Diet Study;
- USDA's PDP data and meat, poultry, and egg monitoring data;
- U.S. Department of the Interior Fish and Wildlife Service fish monitoring data; and
- State pesticide enforcement programs.

It will also include monitoring data from private monitoring sources such as the National Food Processors Association, as well as data collected by the pesticide chemical and food industries.

EPA is creating this database in response to the National Academy of Sciences' recommendation that all pesticide monitoring data are maintained in a standardized computer database (NAS, 1993).

Where-to-Find...

For further information on the NPRD, contact:

U.S. EPA Office of Pesticide Programs
Health Effects Division (7509C)
Reregistration Branch 4
1200 Pennsylvania Ave., NW
Washington, DC 20460

703-305-7351

Market Basket Survey

A market basket survey is a study in which the level of pesticide residues in foods as purchased is measured. Market basket data are intended to characterize the difference between the level of the residue that is found on commodities in the field and the residues that remain on foods at the time of purchase by the consumer. Market basket surveys make use of statistically-defined sampling procedures. Generally, samples are collected at the point of sale to the consumer (*e.g.*, supermarkets or convenience stores). Samples may be prepared as if for consumption (*e.g.,* peeled or washed).

FDA, in its annual Total Diet Study, conducts a market basket survey where more than 200 different foods are sampled nationwide.

Where-to-Find...

Information on conducting market basket studies can be found in:

"Guidance for Refining Anticipated Residue Estimates For Use in Acute Dietary Probabilistic Risk Assessment;" (EPA, 2000b)

http://www.epa.gov/fedrgstr/EPA-PEST/2000/June/Day-23/o-p15917.htm

Quality Assurance: Good Laboratory Practices

It is critically important to the functioning of EPA's pesticide regulatory system that the Agency and the public are able to trust the data on which decisions are based. Therefore, EPA has programs to assure that data submitted to the Agency in support of product registrations are reliable. For example, EPA establishes detailed guidelines describing how studies must be performed. In addition, the laboratories conducting the studies must follow the Good Laboratory Practices (GLP) regulations under 40 CFR 160 (NARA, 1999).

The GLP Standards is a management tool to ensure that studies are conducted according to certain scientific standards. Each laboratory conforms with GLP requirements by implementing Standard Operating Procedures (SOP's) and maintaining quality assurance (QA) oversight through a Quality Assurance/Quality Control Unit that conducts internal audits of raw data and laboratory practices.

The mission of EPA's GLP program is to assure the quality and integrity of studies submitted to the Agency in support of pesticide product registration. EPA accomplishes this mission by conducting data audits to assure compliance with the GLP regulations; more than 300 study audits are conducted every year. These studies that are being audited vary from chemical analyses of pesticides to long-term toxicity and carcinogenicity studies in mammals. Other audited studies may look at the effects of pesticides on the environment, residues of pesticides on commodities, and the efficacy of public health antimicrobial products.

Once the Agency receives data supporting registration (*e.g.*, residue chemistry, product chemistry, and, if applicable, toxicology and environmental fate/effects), scientists from appropriate scientific disciplines thoroughly review the data. These reviews look not only at the substantive results, but also look for signs that the data may not be trustworthy, *e.g.*, internal inconsistencies, discrepancies with tests run on similar products, or missing information on GLP compliance. If EPA has concerns regarding the submitted data, additional data may be requested, or the Agency may require that a laboratory audit be conducted.

Where-to-Find...

The "Good Laboratory Practice Standards" are at:

40 CFR 160 (NARA, 1999)

http://www.epa.gov/epacfr40/chapt-I.info/subch-E/40P0160.pdf

Analytical Methods: Pesticide Analytical Manual

For each new pesticide tolerance, the registrant must provide an analytical method that can be used for enforcement purposes. For an existing pesticide, the analytical method can be found in FDA's Pesticide Analytical Manual (PAM).

FDA is responsible under the Federal Food, Drug, and Cosmetic Act (FFDCA) for enforcing tolerances established by EPA. In meeting this responsibility, FDA collects and analyzes food from commercial channels-of-trade. PAM is published by FDA as a repository of the analytical methods used in FDA laboratories to examine food for pesticide residues for regulatory purposes. The manual is organized according to the scope of the analytical methods:

< PAM Volume 1. This contains multiresidue methods that are used by FDA on a routine basis because of their efficiency and broad applicability, especially for analyzing foods of unknown pesticide treatment history.

< PAM Volume 2. This contains methods designed for analyzing commodities for residues of only a single compound (although some methods are capable of determining several related compounds). These methods are most often used when the likely residue is known and/or when the residue of interest cannot be determined by common MRM's.

Where-to-Find...

The Pesticide Analytical Methods can be found at:

PAM, Volumes 1 and 2 (HHS, 1994 and HHS, 1997)

http://vm.cfsan.fda.gov/~frf/pami1.html

Acute and Chronic Exposure Estimates

FQPA requires EPA to reassess all existing tolerances, based on available information, according to new, more stringent standards. Among these new standards are specific determinations regarding the potential for increased sensitivity of infants, children, and other subpopulations to the pesticide; assessment of the potential for aggregate exposures from various sources (such as food, drinking water, and pesticide uses in and around the home); and cumulative assessments of pesticides with a common mechanism of toxicity. EPA anticipates that refinements will be key to developing more realistic estimates of the actual residue levels on food as EPA proceeds through the aggregate, and particularly the cumulative, assessment of pesticides. More realistic residue estimates ultimately improve the Agency's ability to make informed regulatory decisions that fully protect public health and sensitive subpopulations, including infants and children.

As mentioned earlier, EPA develops these estimates of pesticide residue levels through a “tiered approach,” where estimates of acute pesticide exposure are calculated slightly differently from those for chronic estimates. Where-to-Find information on the tiered approach, along with sources on how acute and chronic exposure estimates are calculated, is presented below.

The Basic Framework: The Tiered Approach

EPA uses a "tiered approach" in assessing acute and chronic risks from pesticides in food. Under this approach, acute exposure estimates are calculated differently from chronic exposure because in an acute assessment, the risk assessor is trying to estimate how much of a pesticide residue might be consumed in a single day while in a chronic assessment, the risk assessor is trying to estimate how much of a pesticide residue might be consumed on a daily basis over the course of a lifetime. Acute exposure calculations tend to employ high-end residue values, high-end consumption, and high-end percent of crop treated (%CT) estimates. Chronic exposure calculations tend to use average residue values, average consumption values, and average %CT estimates.

In summary, the types of data that can be used in the tiering process include:

- Percent of crop treated;
- FDA Monitoring Data;
- USDA PDP Monitoring Data;
- Other market basket (monitoring) studies;
- **Bridging studies**;
- **Residue decline studies**;
- **Residue degradation studies**; and
- Commercial and consumer practices such as washing, cooking, and peeling.

Bridging, Residue Decline, and Residue Degradation Studies. *Bridging studies look at the relationship between residue levels that result from maximum applications vs. those that would result from typical applications.*

Both residue decline and residue degradation studies look at the degradation of pesticide residues over time; the difference between the two is the time frame. Residue decline studies look at the degradation that occurs between application and harvest while degradation studies look at the degradation between harvest and consumption.

A good overall description of the tiering process can be found at:

Where-to-Find... "Classification of Food Forms With Respect to Level of Blending. HED Standard Operating Procedure 99.6;" (EPA, 1999c).

Acute Exposure Estimates

In assessing acute exposure estimates, the risk assessor is estimating how much of a particular pesticide residue might be consumed in a single day. General information on the acute exposure assessment policy and specific information on the types of data that can be used to estimate acute exposure can be found in:

OPP's policy on how to estimate acute exposure resulting from exposure to pesticide residues in food:

Where-to-Find... "Classification of Food Forms With Respect to Level of Blending. HED Standard Operating Procedure 99.6;" (EPA, 1999c)

Descriptions of the types of data that EPA can use to refine acute residue estimates:

"Guidance for Refining Anticipated Residue Estimates For Use in Acute Dietary Probabilistic Risk Assessment;" (EPA, 2000b)

http://www.epa.gov/fedrgstr/EPA-PEST/2000/June/Day-23/o-p15917.htm

Chronic Exposure Estimates

In assessing chronic exposure estimates, the risk assessor is calculating how much of a particular pesticide residue might be consumed on a daily basis over the course of a lifetime. Guidance on estimating chronic exposure resulting from exposure to pesticide residues in food can be found in:

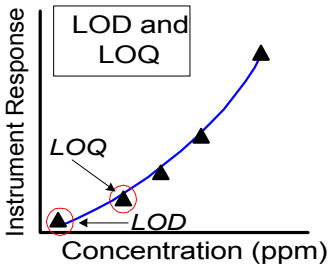
Where-to-Find...

Guidance on calculating chronic food exposure under the tiering system can be found in:

"Guidelines for the Use of Anticipated Residues in Dietary Exposure Assessment;" (EPA, 1991a).

The Limit of Detection (LOD)*. The minimum concentration that an analytical method, which includes the laboratory instrumentation (equipment), can detect or "see." A typical LOD might be 0.01 part per million (ppm).*

Limit of Quantification



(LOQ). *The minimum concentration that an analytical method, which includes the laboratory instrumentation (equipment), can reliably and consistently quantify.*

Limit of Detection and Limit of Quantification

The **limit of detection (LOD)** is the minimum concentration that an analytical method can detect and the **limit of quantification (LOQ)** is the minimum concentration that an analytical method can detect <u>and</u> reliably and consistently quantify.

Quite frequently, in analyzing food or other substances for pesticide residues, residues are not detected at concentrations above the LOD. Even though the laboratory equipment cannot detect a residue, a residue may be present, at some level below the LOD, and such residues may contribute to exposure resulting from pesticide residues in food.

In general, OPP utilizes a default value of one-half the LOD or one-half the LOQ for commodities that have been treated with a pesticide but for which no detectable residues are measured. The policy for assigning values to nondeductible residues is intended to avoid underestimating exposure to potentially sensitive or highly exposed groups such as infants and children while attempting to approximate actual residue concentrations as closely as possible. Both biological information and empirical residue measurements support EPA's belief that these science policies are consistent with these goals.

The Agency has developed statistical methods for handling data sets that contain both detected and nondetected (ND) residues; these are provided in the document listed below. The document also describes OPP's policy of performing a sensitivity analysis to determine the impact of using different assumptions (*e.g.,* assuming ND's equal to LOD instead of one-half LOD) in evaluating nondetectable residues.

Where-to-Find...

The statistical methods for handling nondetects can be found in:

"Assigning Values to Non-detected/ non-quantified Pesticide Residues in Human Health Food Exposure Assessments;" March 23, 2000 (EPA, 2000c)

http://www.epa.gov/pesticides/trac/science/trac3

Percent of Crop Treated

The Agency frequently uses information on how much of a crop is actually treated with a given pesticide to make as accurate an estimate of exposures as possible. EPA obtains this information from a variety of agricultural and nonagricultural data sources, including:

- The USDA National Agricultural Statistics Service (NASS);
- USDA National Agricultural Pesticide Impact Assessment Program (NAPIAP);
- Various state surveys/census, including California Department of Pesticide Regulation (DPR) census; as well as
- A variety of proprietary data sources.

These data sources contain pesticide information from all major crop producing states. EPA economists analyze all available information and provide it for risk assessment, as appropriate.

Where-to-Find...

For further information on how percent of crop treated is determined and used in risk assessment, see:

"The Role of the Use-Related Information in Pesticide Risk Assessment and Risk Management;" DRAFT Document (EPA, 1999d).

http://www.epa.gov/oppbead1/use-related.pdf

Probabilistic Analysis

Probabilistic Analysis. *The use of a statistical technique (e.g., Monte Carlo) to quantify both the range of exposures to pesticide residues and the probability or chance of exposure to any particular level.*

Deterministic Analysis*. The use of a single value to quantify a point in the range of exposures. An example of a deterministic analysis is calculating the average value.*

One technique used to calculate acute exposure and risk in the more refined tiers–Tiers 3 and 4–is **probabilistic analysis,** where the entire range of residue data from the numerous crop field trial studies (or other sources) together with the range of consumption values is used to estimate the distribution of exposure for the population of concern and the probability of exposure to any particular level. This technique allows for a more realistic estimate of exposure. At this time, the probabilistic technique can be used only for acute assessment because of limitations in the consumption database.

Probabilistic analysis is in contrast to **deterministic analysis,** where only a single, high-end residue value (*e.g.*, tolerance levels on foods) or a statistical tendency (for example, average values from appropriate field trial data) is used with the range of consumption estimates. Such single-value risk estimates do not provide information on the variability and uncertainty that may be associated with a risk estimate. The Agency has traditionally used deterministic analyses involving point estimates of specific parameters to generate a single estimate of exposure and risk based on various assumptions about the concentration of pesticide in any given medium (*e.g.*, food, water, air, etc.) and the amount of that medium consumed, breathed, or otherwise contacted.

Where - to-Find...

Guidance on the submission and review of probabilistic human health exposure assessments can be found in:

"Guidance for Submission of Probabilistic Human Health Exposure Assessments to the Office of Pesticide Programs;" draft document (EPA, 1998b).

http://www.epa.gov/pesticides/trac/science/#monte

NOTE: *This guidance document also provides a good overall discussion of the probabilistic methods.*

Bridging Study

Bridging Study. *A study in which the investigator examines the relationship between residues that occur as a result of maximum pesticide application versus those expected to occur at the range of more typical rates.*

A **bridging study** is one in which the study investigator examines the relationship between residue levels that occur as a result of maximum pesticide application (*e.g.,* maximum rate, highest application frequency, and shortest PHI) versus those expected to occur at the range of more typical rates. This relationship is then used to adjust the maximum residue levels originally obtained from the crop field trials.

EPA uses the residue data obtained from these field studies in conjunction with information on what fraction of the crop is treated at each rate to refine its exposure estimates. Specific guidance on conducting bridging studies can be found in the document listed below.

Where-to-Find...

Detailed guidance on conducting bridging studies may be found at:

"Guidance for Refining Anticipated Residue Estimates for Use in Acute Dietary Probabilistic Risk Assessment;" (EPA, 2000b)

http://www.epa.gov/fedrgstr/EPA-PEST/2000/June/Day-23/o-p15917.htm

Residue Decline Study

Residue Decline Study. *A study in which the investigator examines the relationship between residue levels at the time of application versus residue levels at the range of typical harvest times.*

A **residue decline study** is one in which the study investigator examines the relationship between residue levels at the time of application versus residue levels at the range of typical harvest times. That is, the investigator is looking at how quickly the pesticide being studied degrades between application and harvest. Because pesticides degrade and dissipate at different rates over time, it cannot be assumed that this relationship is linear (*e.g.*, that doubling the preharvest interval would result in half the residue). In a residue decline study, samples from a single field trial are collected at multiple PHI's and analyzed to determine rates of residue disappearance/dissipation.

EPA uses the residue data obtained from these decline studies in conjunction with information on what fraction of the crop is harvested at each interval to refine its exposure estimates. Information from residue decline studies may be particularly useful when the pesticide of interest decays quickly and/or a large period of time elapses between the pesticide application date and the harvest date. Specific guidance on conducting residue decline studies can be found in the document listed below.

The following provides detailed guidance on conducting residue decline studies:

Where-to-Find... "Guidance for Refining Anticipated Residue Estimates for Use in Acute Dietary Probabilistic Risk Assessment;" (EPA, 2000b)

http://www.epa.gov/fedrgstr/EPA-PEST/2000/June/Day-23/o-p15917.htm

Residue Degradation Study

Residue Degradation Study. *A study in which the investigator examines the relationship between residue levels at harvest versus the residue levels at consumer purchase.*

A **residue degradation** study is one in which the study investigator examines the relationship between residue levels at harvest versus the residue levels at consumer purchase. A residue degradation study is similar to a residue decline study; however, the time interval being studied is later. Residue degradation studies are designed to characterize the decreasing amounts of pesticide residues over time on commodities during storage or transportation. In a residue degradation study, samples are collected before storage or transportation begins and at different points in the "process" that correspond to times that consumers may purchase the food.

Information from a residue degradation study may be particularly useful when a substantial period of time elapses as during extended transportation or storage. OPP recognizes, for example, that some crops such as apples and potatoes can be typically stored for relatively long periods of time after harvest and before purchase by the consumer. Other items (*e.g.*, tomatoes and bananas) may be typically picked green for ease of transport; of necessity, many days can, therefore, pass between harvest and consumption.

Information on residue degradation studies can be found in:

Where-to-Find...

"Guidance for Refining Anticipated Residue Estimates for Usein Acute Dietary Probabilistic Risk Assessment;" (EPA, 2000b)

http://www.epa.gov/fedrgstr/EPA-PEST/2000/June/Day-23/o-p15917.htm

Consumer and Commercial Practices

Cooking and processing data permit better estimates of pesticide exposure by incorporating information on actual consumer and industry food preparation practices. Home processing such as cooking, washing, peeling, etc. can significantly reduce exposure to pesticide residues. For example, potatoes would likely be cooked prior to consumption, and oranges and bananas would typically be peeled. Commercial preparation practices such as canning, washing, peeling, various cooking methods, etc. can also reduce exposure to pesticide residues.

In commercial processing studies, samples are collected from at least two points in the processing procedures (*e.g.,* before processing/cooking, after washing, after peeling, at the end of processing, etc.) and a processing factor is calculated. The processing practices used in the study should reflect typical commercial practices (whether the raw agricultural commodity is typically washed, peeled, cooked or otherwise treated before canning, freezing, drying or other types of processing).

Information on commercial and consumer practices can be found in:

Where-to-Find...

"Guidance for Refining Anticipated Residue Estimates for Use in Acute Dietary Probabilistic Risk Assessment;" (EPA, 2000b)

http://www.epa.gov/fedrgstr/EPA-PEST/2000/June/Day-23/o-p15917.htm

Consumption Information

The food consumption data that EPA uses in its risk assessment for exposure resulting from pesticide residues in food are provided by USDA from their periodic food consumption surveys.

For further information on USDA's food consumption surveys, contact:

Where-to-Find...

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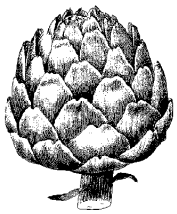

LIST OF Where-to-Find Information On...

Topic and Description	Name of Document (as applicable)	Page
Acute Exposure Estimates. OPP's policy on how to estimate acute exposure resulting from exposure to pesticide residues in food.	"Classification of Food Forms With Respect to Level of Blending. HED Standard Operating Procedure 99.6;" (EPA, 1999c).	34
Acute Exposure Estimates. Descriptions of the types of data EPA can use to refine acute residue estimates.	"Guidance for Refining Anticipated Residue Estimates for Use in Acute Dietary Probabilistic Risk Assessment;" (EPA, 2000b)	34
Aggregate Exposure. Draft guidance on conducting aggregate exposure assessment.	"Guidance for Performing Aggregate Exposure and Risk Assessments;" draft (EPA, 1999a)	5
Analytical Methods. Analytical methods (single residue and multiresidue methods) for determining the concentration of pesticide residues in food.	PAM, Volumes 1 and 2 (HHS, 1994 and HHS, 1997)	31
Bridging Data. Detailed guidance on conducting bridging studies.	"Guidance for Refining Anticipated Residue Estimates for Use in Acute Dietary Probabilistic Risk Assessment;" (EPA, 2000b)	40
Chronic Exposure Estimates. Guidance on calculating chronic food exposure under the tiering system.	"Guidelines for the Use of Anticipated Residues in Dietary Exposure Assessment;" (EPA, 1991a)	35
Commercial and Consumer Practices. Information on how commercial and consumer practices can be factored into assessments for exposure resulting from pesticide residues from food.	"Guidance for Refining Anticipated Residue Estimates for Use in Acute Dietary Probabilistic Risk Assessment;" (EPA, 2000b)	43
Data Requirements. OPP's data requirements for residue data on food.	40 CFR 158.240 (NARA, 1999)	19
Decompositing. A paper discussing the "Allender" method for "decompositing," which is the process of statistically translating composite residue information into "individual item" residue information.	"Statistical Methods for Use of Composite Data in Acute Dietary Exposure Assessment;" (EPA, 1999e)	23
Decompositing. A paper comparing EPA's method for decomposition to two others: RDFgen, and MaxLIP.	"Office of Pesticide Programs' Comparison of Allender, RDFgen, and MaxLIP Decomposition Procedures;" (EPA, 2000a)	23

Topic and Description	Name of Document (as applicable)	Page
DEEM™. A full description of the DEEM™ model and how it operates.	"Background Document for the Sessions: Dietary Exposure Evaluation Model (DEEM™) and DEEM™ Decompositing Procedure and Software;" (Novigen, 2000)	15
FDA Monitoring Data. Where-to-Find information, including data summaries from the monitoring programs, on FDA's pesticide monitoring programs.	Not applicable	26
Food Consumption Information. Where-to-Find information on the USDA food consumption surveys.	Not applicable	43
FQPA Safety Factor. OPP's policy for determining the appropriate FQPA Safety Factor and a good general discussion on the use of uncertainty factors, modifying factors, and the FQPA Safety Factor.	"The Office of Pesticide Programs' Policy on Determination of the Appropriate FQPA Safety Factor(s) for Use in the Tolerance-Setting Process;" draft document (EPA, 1999b)	6
Good Laboratory Practices. The standards that are to be used by laboratories in conducting studies to be used in setting tolerances, etc.	40 CFR 160 (NARA, 1999)	30
Guidelines. Guidelines for the 40 CFR 158.240 data requirements.	Series 860 of the OPPTS Harmonized Test Guidelines (EPA, 1996a)	19
Guidelines. Supplemental guidance on crop field trials.	HED SOP 98.2: Supplementary Guidance on use of OPPTS Residue Chemistry Test Guidelines 860.1500, Crop Field Trials (residue zone maps - Canadian extension) [4/8/98] (EPA, 1998a)	19
LOD and LOQ. The statistical methods for handling nondetectable pesticide residues in food.	"Assigning Values to Non-detected/ non-quantified Pesticide Residues in Human Health Food Exposure Assessments;" March 23, 2000 (EPA, 2000c)	36
Market Basket Studies. Information on how to conduct a market basket study for purposes of refining residues for use in acute exposure assessments.	"Guidance for Refining Anticipated Residue Estimates for Use in Acute Dietary Probabilistic Risk Assessment;" (EPA, 2000b)	28
Nondectable Residues. The statistical methods for handling nondetectable pesticide residues in food.	"Assigning Values to Non-detected/ non-quantified Pesticide Residues in Human Health Food Exposure Assessments;" March 23, 2000 (EPA, 2000c)	36
NPRD. Where-to-Find information on the NPRD.	Not applicable	27

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Percent of Crop Treated. Information on how percent of crop treated is determined and used in risk assessment.	"The Role of the Use-Related Information in Pesticide Risk Assessment and Risk Management;" draft document (EPA, 1999d)	37
PDP. Obtaining information on USDA's PDP program or how to access data summaries.	Not applicable	21
PDP. Who to contact for information on how the Agency uses PDP data.	Not applicable	21
Probabilistic Assessment. Guidance on the submission and review of probabilistic human health exposure assessments.	"Guidance for Submission of Probabilistic Human Health Exposure Assessments to the Office of Pesticide Programs;" draft document (EPA, 1998b)	39
Residue Decline Studies. Detailed guidance on conducting residue decline studies.	"Guidance for Refining Anticipated Residue Estimates for Use in Acute Dietary Probabilistic Risk Assessment;" (EPA, 2000b)	41
Residue Degradation Studies. Information on conducting residue degradation studies.	"Guidance for Refining Anticipated Residue Estimates for Use in Acute Dietary Probabilistic Risk Assessment;" (EPA, 2000b)	42
Tiering Process. How OPP assesses exposure to pesticide residues in food through the four-tier process.	"Classification of Food Forms With Respect to Level of Blending. HED Standard Operating Procedure 99.6;" (EPA, 1999c)	34
Translating PDP Data to Other Crops. The conditions under which translating is appropriate and details on the translation policy.	"Translation of Monitoring Data. HED Standard Operating Procedure 99.3 (3/26/99)" (EPA, 1999f)	22
Uncertainty Factors. A good general discussion on the use of uncertainty factors, modifying factors, and the FQPA Safety Factor.	"The Office of Pesticide Programs' Policy on Determination of the Appropriate FQPA Safety Factor(s) for Use in the Tolerance-Setting Process;" draft document (EPA, 1999b)	6

BIBLIOGRAPHY

National Academy of Sciences (NAS), 1993. "Pesticides in the Diets of Infants and Children." National Academy Press, Washington, DC.

National Archives and Records Administration (NARA), 1999. “Code of Federal Regulations Protection of Environment Parts 150 to 189.” U.S. Government Printing Office, Washington D.C. July 1, 1999.

Novigen Sciences Inc., 2000. Background Material for the March 2000 FIFRA Scientific Advisory Panel Meeting. “Background Document for the Sessions: Dietary Exposure Evaluation Model (DEEM™) and DEEM™ Decompositing Procedure and Software.” February 29 to March 3, 2000.

U.S. Environmental Protection Agency (EPA), 1991a. “Guidelines for the Use of Anticipated Residues in Dietary Exposure Assessment;" March 25, 1991.

U.S. Environmental Protection Agency (EPA), 1996a. “Residue Chemistry Test Guidelines OPPTS 860;” August 1996. (EPA 712-C-96-169)

U.S. Environmental Protection Agency (EPA),1998a. Memorandum from Margaret Stasikowski to Jim Jones, Anne Lindsay, and Lois Rossi. "Supplementary Guidance on use of OPPTS Residue Chemistry Test Guidelines 860.1500, Crop Field Trials (residue zone maps - Canadian extension).” April 8, 1998.

U.S. Environmental Protection Agency (EPA), 1998b. "Guidance for Submission of Probabilistic Human Health Exposure Assessments to the Office of Pesticide Programs;" draft document. November 4, 1998. (63 FR 59780)

U.S. Environmental Protection Agency (EPA), 1999a. “Guidance for Performing Aggregate Exposure and Risk Assessments;" draft document. October 29, 1999. (65 FR 459)

U.S. Environmental Protection Agency (EPA), 1999b. “The Office of Pesticide Programs‘ Policy on Determination of the Appropriate FQPA Safety Factor(s) for Use in the Tolerance-Setting Process;" draft document. May 10, 1999. (64 FR 48617)

U.S. Environmental Protection Agency (EPA), 1999c. “Memorandum from Margaret Stasikowski, Director Health Effects Division to Health Effects Division Staff. “Classification of Food Forms With Respect to Level of Blending. HED Standard Operating Procedure 99.6 (8/20/99);” August 20, 1999.

U.S. Environmental Protection Agency (EPA), 1999d. “The Role of the Use-Related Information in Pesticide Risk Assessment and Risk Management;" draft document. June 29, 1999. (64 FR 37977)

U.S. Environmental Protection Agency (EPA), 1999e. Background Document for the May 26, 1999 Meeting of the FIFRA Scientific Advisory Panel. “Statistical Methods for Use of Composite Data in Acute Dietary Exposure Assessment;” May 26, 1999.

U.S. Environmental Protection Agency (EPA), 1999f. Memorandum from Margaret Stasikowski, Director Health Effects Division to Health Effects Division Staff. “Translation of Monitoring Data. HED Standard Operating Procedure 99.3 (3/26/99);” March 26, 1999.

U.S. Environmental Protection Agency (EPA), 2000a. Background Document for the March 1, 2000 Meeting of the FIFRA Scientific Advisory Panel. “Office of Pesticide Programs' Comparison of Allender, RDFgen, and MaxLIP Decomposition Procedures;” February 1, 2000.

U.S. Environmental Protection Agency (EPA), 2000b. "Guidance for Refining Anticipated Residue Estimates for Use in Acute Dietary Probabilistic Risk Assessment;" June 15, 2000. (65 FR 39147).

U.S. Environmental Protection Agency (EPA), 2000c. "Assigning Values to Non-detected/non-quantified Pesticide Residues in Human Health Food Exposure Assessments;" March 23, 2000. (65 FR 17266)

U.S. Department of Health and Human Services (HHS), 1994. “Pesticide Analytical Manual Volume I: Multiresidue Methods;” 3rd Edition (Revised, September, 1996; October 1997; and October 1999). January 1994.

U.S. Department of Health and Human Services (HHS), 1997. “Pesticide Analytical Manual, Volume 2.” February 1997.