Safety Evaluation of Pesticide Residues in Food

The following are three short papers on current issues prepared by the IUPAC Commission on Agrochemicals and the Environment

The aim of the IUPAC Commission on Agrochemicals and the Environment is to critically examine important issues raised by the use of pesticides as related to the health of mankind and the safety of the environment. Topics examined include fundamental aspects of the chemistry of pesticides, their fate in food and the environment; methods of trace analysis; metabolism in animals, plants, water and soil. The Commission works through:

1 Projects which are developed to provide the consensus views of a panel of experts on particular aspects of pesticide chemistry. The reports from these projects are generally published in *Pure and Applied Chemistry*. Large reports are published as monographs. These reports include recommendations for future action either in research fields or in government regulations.

2 Acting as scientific sponsor for the IUPAC Congresses on Pesticide Chemistry which are held every four years.

3 Organizing workshops in developing nations (China, 1988; Thailand, 1992; Brazil, 1996).

4 Liaison with bodies such as WHO, FAO and UNEP to strengthen international collaboration.

The Commission membership comprises up to 18 elected prominent scientific experts. A balance in membership is sought to cover geographical interests, professional affiliations (academic, government research/regulation, commercial R&D) and particular skills in pesticide chemistry. The various nations affiliated to IUPAC can also nominate National Representatives.

The following three short papers summarize current approaches and issues on the safety evaluation of pesticides in relation to their use on human food. The areas of pesticide metabolism and toxicology are subject to stringent government regulation. The testing procedures now followed do give a high degree of assurance that undesirable effects will not occur under worst-case exposure situations. Dietary intake studies are an important means of evaluating the degree to which the population is exposed to pesticides. The more sophisticated current approaches to these studies recommended by IUPAC do provide a high degree of

assurance that the diet is generally very safe with respect to pesticides.

For further information on the Commission and copies of its reports contact: Secretary: Dr Patrick Holland, The Horticulture & Food Research Institute of New Zealand Ltd, Ruakura Research Centre, Private Bag 3213, Hamilton, New Zealand. Tel.: +64 (7) 856 2835; Fax: +64 (7) 838 5085.

I. Metabolism of pesticides in plants and livestock

The use of pesticides to control pests and disease is important for the production of sufficient quantities of safe and affordable food. However, the use of these agents sometimes leaves residues (the pesticide or its degradates) in/on plant parts used as human food or animal feed commodities. These residues may enter the human food chain either directly—through the consumption of treated foods, e.g. grain or fruit, or indirectly—through the transfer of residues to milk, eggs and meat products. To answer the question: 'What is the nature of the chemical residue in/on food or feed items resulting from the use of the pesticide?', plant and animal metabolism studies are carried out. This paper describes the aims and conduct of these studies.

Use of radiolabelled pesticides

The term metabolism generally refers to the chemical transformation of the pesticide which results from natural (metabolic) processes in the biological system under investigation. To measure the total residue, and to provide a means of selectively tracing products derived from the pesticide in the presence of biological material, the studies are carried out using radiolabelled pesticides. The radiolabel, usually carbon-14 or hydrogen-3, is incorporated into a metabolically stable portion of the compound. The use of the radiolabel requires that studies are carried out in controlled areas; for plants this can be either in small field plots or in pots housed in suitable growing environments. This restriction in scale implies that these studies are qualitative and, at best, a semi-quantitative estimate of the fate of pesticides under large scale field conditions.

Plant metabolism

In plant studies, the term 'metabolism' is used in a wider context, to include the formation of all products (degradates) of the pesticide in or on the plant, regardless of whether they result from internal plant metabolic processes, from chemical reactions (hydrolysis and photolysis) or biological processes which occur outside the plant (e.g. microbiological degradation in soil). A plant metabolism study is usually carried out on crops typical of those to which the pesticide will be applied. If the metabolism of the pesticide is the same in plants from three different crop groups, e.g. root, cereal, top fruit, then no further studies are conducted. If different metabolic routes are revealed then studies in a wider range of crops will be initiated. The radiolabelled chemical is formulated and applied to the crop in a similar manner to that used in actual agricultural practice. To define the amount and nature of residues that may be found in rotated crops grown in soil where a previous crop was treated with the pesticide, crop rotation studies are carried out. In these studies, the soil is treated with the radiolabelled pesticide and crops sown 30, 120 and 365 days after treatment. The crops are harvested at maturity and other intervals appropriate to normal agricultural practices, e.g. immature cereals which are fed to livestock as forage or silage.

Livestock metabolism

Studies are carried out in agricultural livestock whenever a pesticide is applied directly to animals or when treated plant commodities are used for animal feed. Typically, the most important species in agriculture are ruminants and poultry, however if the use pattern of the pesticide targets other species then studies would be carried out accordingly. Metabolism studies are carried out in representative species from these groups; usually lactating goats or cows and laying hens are the species of choice. Treatment is carried out to closely approximate expected exposure.

(a) For ingested residues—oral dosing is usually carried out over a period of several days to allow the residues in tissues, milk, and eggs to reach a steady state. The dosing (test) material should reflect the major component of the terminal residue in treated crops. This is frequently the parent compound, however where the parent is not the major component of the residue the test material may consist of a single metabolite, a synthetic mixture of metabolites or plant material resulting from the metabolism studies.
(b) For dermal applications, the radiolabelled chemical is applied, formulated, in a way that reflects the proposed use pattern.

The size of the dose given to the animals is often more than that expected from normal agricultural practice to facilitate the detection, isolation and characterization of metabolites. Samples of milk, eggs and excreta are taken throughout the dosing period. The animals are usually sacrificed within 24 h after the final dose and tissues are taken *post mortem*.

Animal studies must be carried out according to Good Laboratory Practice (GLP) principles (*cf.* the accompanying paper 'The Role of Toxicology in the Evaluation of New Agrochemicals').

Measurement and characterization of the residue

In the case of compounds with a complex structure it may be necessary to conduct two or more metabolism studies with the radiolabel located in different parts of the compound. The use of radiolabelled materials facilitates monitoring of the distribution of the residue throughout the system and provides an estimate of the total residue. By linking radioactive detection with chromatographic separation systems and spectral analysis the individual components of the residue can be isolated, characterized and identified. From this information, the fate of the compound in the test system, i.e. the biotransformation pathway, can be defined.

How the data are used

Once the amount of the total radioactive residues has been determined and the structures of the major metabolites are known, the toxicological significance of the residues can be assessed. If the plant metabolism data indicate that the metabolites formed are both qualitatively and quantitatively similar to those formed in mammals the plant metabolites may be considered to have been tested in animals in the same studies as those performed on the parent compound. If significant qualitative or quantitative differences are found between plant and animal metabolites, additional toxicological data concerning the plant metabolites in animals may be required. The nature and extent of the additional toxicity studies will depend on the nature of the metabolite involved. Using the information from the radiolabelled studies, analytical methods are developed to determine as much of the terminal residue as possible and particularly for those components which are considered of toxicological interest. The development of analytical methods is facilitated using samples from the metabolism studies to optimize the efficiency of the extraction and clean-up procedures.

Conclusions

It is essential that metabolism studies provide an accurate description of the composition of the terminal residues in food and feed items. The nature of the individual components of the terminal residue must be defined before analytical methods, residue levels and toxicity data can be generated. An adequate metabolism study fulfils at least three main purposes;

(i) to identify the composition of the terminal residue in all plant commodities and livestock tissues, milk and eggs.

(ii) to indicate the distribution of the residues, i.e.
(a) in plants, whether the residues are absorbed through roots and foliage or are entirely surface residues and whether the residues are translocated,
(b) in livestock, to indicate the distribution of residues in tissues, eggs and milk and to provide evidence of storage or accumulation in tissues.

(iii) to provide a basis for determining the efficiency of extraction and clean up procedures used in the development of analytical methodologies.

Michael W. Skidmore

Zeneca Agrochemicals, Jealotts Hill, Bracknell, Berkshire, UK. E-mail: mike.m.s.skidmore@gbjha.zeneca.com

Further reading:

Pesticide Metabolism: extrapolation from animals to man. Monograph: Blackwell Scientific Publications, Oxford, 1988 (120 pp).

Use of isolated cells to study the metabolism of agrochemicals in animals. *Pure Appl. Chem*. 1993, **65**, 2299–2312.

Detection and significance of active metabolites of agrochemicals and related xenobiotics in animals. *Pure Appl. Chem*. 1995, **67**, 1487–1532.

II. The role of toxicology in the evaluation of new agrochemicals

The widespread use of agrochemicals as crop protection agents, wood preservatives, vector control agents or industrial/medicinal disinfectants, may result in exposure of man, animals and the environment to these chemicals. Humans may be exposed during production or application and to a lesser extent as consumers of food products which may contain trace levels of residues.

The purpose of this paper is to demonstrate that currently used toxicological test methods and safety assessment procedures safeguard humans against potential adverse effects of agrochemicals. Particular emphasis will be on the assessment of exposure of humans to pesticide residues in foods.

The World Health Organization (WHO) and the Food and Agricultural Organization (FAO) have conducted programmes designed to protect the health of the consumer for more than 35 years. Since 1961 experts from governments and academia have evaluated approximately 230 pesticides (Joint Meetings on Pesticide Residues, JMPR). Monographs are annually issued containing detailed reviews of studies relevant to the establishment of maximum permitted levels of pesticide residues in foods. It should be noted that foods containing residues at the maximum permitted levels are safe for consumption, but the permitted levels are not safety limits.

Strategies of toxicity testing

General principles

All substances exert some degree of toxicity to various forms of life, depending on the exposure level of the

substance. Toxicity studies are focused on the characterization of the precise nature and extent of toxic effects and on the determination of dose levels which do not exert adverse effects (No Observed Adverse Effect Level, NOAEL). Data are generally obtained from experiments with laboratory animals and cultured cells. Occasionally data from occupational or accidental exposure of animals and man to agrochemicals may be used to supplement laboratory animal data. Based on these data and using extrapolation or uncertainty factors, an Acceptable Daily Intake for humans (ADI) may be calculated, i.e. the amount of a substance which may be consumed by humans on a daily basis during the entire life span, without appreciable risk for the occurrence of adverse effects. Comparison of these values with potential exposure of humans to a compound in the environment, including dietary exposure or intake from all foods, will indicate whether the use of an agrochemical may be permitted. Approaches to estimate the dietary intake of pesticide residues in food are described in an accompanying paper 'Dietary Intake of Pesticide Residues'.

Animal studies

The purpose of toxicity studies primarily carried out in laboratory animal species, is to characterize the toxicological profile of a test compound. Choice of the appropriate animal test species is important and ideally species are chosen which respond to a toxic stimulus in a way similar to that expected for humans. Usually rodents (rats, mice, guinea-pigs), dogs and non-human primates are used. The choice of the test animal species depends also on practical considerations such as availability, ease of handling and housing, and availability of background data.

Animal studies must be carried out according to Good Laboratory Practice (GLP) principles. This internationally accepted set of guidelines describes requirements for test facilities, the design of a study protocol and the conditions for performance of experiments, procedures for data recording and reporting, responsibilities for management of a study, and quality assurance procedures. These guidelines are continuously updated according to the latest developments in toxicology and chemistry.

Prior to animal experimentation, test compounds must be characterized with respect to chemical identity, purity and stability. Different types of toxicological studies have been designed in order to characterize a compound:

Pharmacokinetic and metabolism studies—These studies are performed to determine the 'fate' of a compound upon entering the animal body, i.e. absorption, distribution and elimination. In many cases foreign compounds may be converted into substances (metabolites) which are more readily eliminated from the body than the original compound, and therefore information must be obtained concerning the nature of these metabolites. Furthermore, information must be obtained whether a test compound or metabolite accumulates in the body at specific sites and whether the compound interferes with biochemical pathways. Studies of the metabolism of pesticides in plants and livestock are described in the companion paper 'Metabolism of Pesticides in Plants and Livestock'.

(Sub)acute toxicity studies—(Sub)acute studies are performed to screen for potential toxic effects resulting from (unexpectedly) high exposure to a compound. Animals treated with a single or multiple dose of the test compound via the oral, dermal or inhalation route are examined for signs of acute toxicity, skin or eye irritation or sensitization. These studies are of particular relevance for humans involved in the production or application of agrochemicals. These data are used for classification and labeling of compounds.

Long term toxicity studies—These studies are designed to investigate the effects induced by a chemical in animals exposed during a substantial part of their normal life span. Extensive analyses are carried out during and upon termination of the experiment. Blood and urine are analyzed, food and water intake and changes in body and organ weights are recorded, organ functions evaluated, and histopathological analysis of tissues and organs is performed. Insight in the mechanisms of observed toxicity may be obtained from these studies. These studies when properly conducted should provide information on toxic responses caused by increasing dose levels of the test compound and may demonstrate a dose level which does not produce observable adverse effects (NOAEL).

Reproduction studies—Reproduction studies are performed in order to verify that agrochemicals do not affect the reproductive capacity of male and female animals nor affect new borns or young animals. To this end, one or multi-generation studies may be performed with specific attention to potential adverse effects on male and female fertility, incidence of resorptions and abortions, litter size, sex ratio, birth weight and growth of new borns.

Carcinogenicity studies—Of great concern is the potential of certain chemicals to interfere with replication processes of cells, which may lead to the formation of tumours. Specific animal studies are designed to screen for the potency of a test compound to induce tumours. These studies are usually carried out in two rodent spe-

cies orally exposed to various dose levels of the test compound during most of the entire lifespan. Besides evaluation of physiological, clinical and histopathological parameters, tumours are identified on the basis of their histogenic origin. Carcinogenicity studies are performed when:

(i) relevant amounts of residues of a pesticide may be expected in foods,
(ii) structural similarity of the test compound or its metabolites with other known carcinogens has been noted,
(iii) experimental evidence suggests that the test compound may induce early signs of carcinogenicity,
(iv) the test compound has been shown to interact with cellular DNA or chromosomes (mutagenic effects) or
(v) the test compound exhibits new structural characteristics.

Mutagenicity studies—Specific tests have been designed to screen for the genotoxic potency of compounds, i.e. the capacity of a substance to react with the genetic material of living cells (DNA, chromosomes), which may lead to tumour formation or heritable defects. Usually a combination (battery) of different tests is used with bacteria, animals and cells from animal and human origin to detect these types of adverse effects. Results from these studies are used as supplementary information for the establishment of the carcinogenic potential of a compound.

Specialized toxicity studies—Special studies have been designed to assess the potential adverse effects of a chemical on the immune and neural system, and to test for skeletal malformations and other alterations induced by chemicals in foetuses during the period of organogenesis (teratogenic effects). These studies are carried out when the structural properties of a compound or data from toxicity studies indicate potential adverse effects, or in case of compounds with completely new structures.

In-vitro studies—The use of isolated cells, subcellular fractions, or perfused organs and tissues derived from different animal species has become common practice when the toxic properties of agrochemicals are studied. In particular the use of isolated liver epithelial cells (hepatocytes) has been successful in identifying the biotransformation profiles of compounds, and for rapid screening of their toxic potency. Proper use of these systems may complement and reduce whole animal experimentation.

Evaluation of data

The available data provide the basis for the safety assessment of compounds and should include NOAELs for the most sensitive animal species. Knowledge on the comparative metabolism of compounds in animals and man, and on differences in responses to toxic effects of substances, is taken into account when the NOAEL is established. From the NOAEL, normally expressed as mg/kg body weight per day, the Acceptable Daily Intake (ADI) for humans may be calculated, i.e. the amount of a pesticide residue in food and drinking water which can be ingested daily over a lifetime by humans without appreciable health risk:

$$\frac{\text{NOAEL animal studies (mg/kg body weight)}}{\text{SF (safety factor)}} = \text{ADI for humans (mg/kg body weight/day)}$$

In order to extrapolate results from animal studies to humans, safety factors (SF) are applied to allow for potential differences in toxic responses between animal species and man, and to account for possible differences in sensitivity within the human population. Normally a safety factor of 100 is used: 10 (extrapolation between animal species) $\times$ 10 (differences in sensitivity within the human population). However, depending on the available data and their quality, lower or higher factors may be chosen.

The US EPA approach to assess the risks of chemicals is similar to the one described above. Instead of an ADI, a Reference Dose (RfD) is defined derived from the NOAEL by consistent application of uncertainty factors (UF) and of modifying factors (MF). The RfD is a reference point from which potential effects of a chemical at other doses may be estimated. Tenfold UFs are used for extrapolation of experimental results and a MF less than or equal to 10, to reflect scientific uncertainties with respect to completeness of the data base.

Short-term exposure to acutely toxic pesticides such as the organophosphorus or methyl carbamate insecticides, whose toxic action is based on acetylcholinesterase inhibition may not be covered appropriately with the traditional ADI-approach, which assumes a daily exposure to a chemical throughout life. In these cases WHO proposes 'short-term ADIs' or acute Reference Doses (acute RfD), using the same basic principles and methods as for traditional ADIs or RfDs. A NOAEL would be identified on the basis of single or short-term dosing of a chemical.

The ADI concept is not applicable to every type of compound. For instance ADIs cannot be established for those compounds which are slowly eliminated from the body and thus may accumulate. For certain biological effects, such as irreversible bone marrow damage, or genotoxicity a NOAEL may not be identified. In these cases a quantitative risk analysis is made in order to estimate an acceptable risk for the human population.

Since the mechanisms of carcinogenicity are not fully understood, a prudent approach is chosen for the as-

sessment of an ADI. The biological activities of a specific compound are taken into account, and in particular knowledge on the comparative metabolism of the compound in test animal species and humans may facilitate extrapolation of animal carcinogenicity data to humans.

In some cases data on exposure of humans to agrochemicals during production or application or through accidents may be of additional value for the safety evaluation. However in many cases exact exposure levels of chemicals and duration of the exposure are not known.

Conclusions

Principles for the toxicological assessment of pesticide residues in food are based on animal experimentation and other relevant data and are accepted world-wide as the basis for safety evaluation. The ADI concept can be considered as a 'safety-first' approach. Usually large safety factors are applied in establishing the ADI-value, which provides additional assurance that exposure exceeding the ADI-value for short time periods will probably not result in adverse effects. Application of large safety margins is recommended, since humans in practice are exposed to low levels of mixtures of foreign chemicals present in the environment. The experience gained to date indicates that human safety upon exposure to agrochemicals is sufficiently protected. Dietary exposure of humans to residues of pesticides in food resulting from uses according to label instructions is too low to induce adverse health effects in humans. It is important to note that since 1982 established ADIs are being re-evaluated and where necessary revised based on new toxicity data developments in methods of detection, and in improvement of models to evaluate the toxicity of chemicals.

Harry A. Kuiper

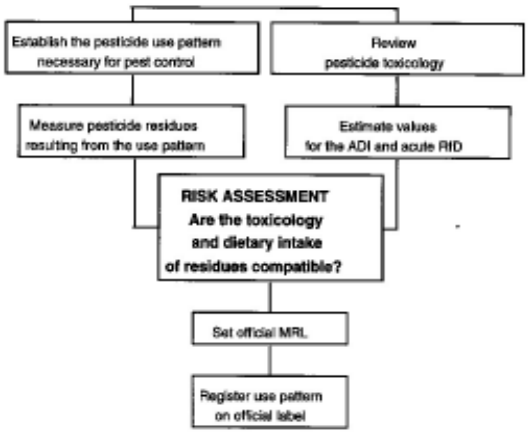
State Institute for Quality Control of Agricultural Products (RIKILT-DLO), PO Box 230 NL-6700 AE Wageningen, the Netherlands. E-mail: h.a.kuiper@rikilt.dlo.nl

Further reading

Principles for the Toxicological Assessment of Pesticide Residues in Food. Environmental Health Criteria 104, WHO-IPCS (1990)

III. Dietary intake of pesticide residues

Decisions on the levels of pesticide residues in foods and the amount of residues likely to be consumed are part of the pesticide evaluation and approval process. The results of two important sets of studies, toxicology studies and studies on likely residues in foods arising from the use of the pesticide, must be reconciled before pesticide uses are approved. Reconciling dietary intakes of residues likely to occur in practice and acceptable intakes derived from toxicology studies is known as the risk assessment process. The place of risk assessment in the pesticide approval process is shown in the simplified diagram (other aspects such as environmental and occupational health aspects are not included here). The conclusions from the toxicological studies and the residue studies must be based on sound science and valid data obtained using convincing experimental methods and should satisfy critical scientific review. An ADI (acceptable daily intake) can be established if the toxicological data are sufficient and valid. The place of toxicology is described in a companion paper 'The Role of Toxicology in the Evaluation of New Agrochemicals'. Estimates of dietary intake of a pesticide residue on a food are obtained by multiplying the level of residue in that food prepared for eating by the weight of that food consumed. The dietary intake of a pesticide residue is then the sum of intakes for those foods where residues of that pesticide occur. Dietary intake assessment of pesticide residues is a difficult task, but is best approached in a scientific manner. We should aim to provide the most realistic estimates possible making the best use of available data. This approach will assist the recognition of genuine problems.



The evaluation process.
***ADI (acceptable daily intake):* estimate of the amount of a pesticide in food and drinking water which can be ingested daily over a lifetime by humans without appreciable health risk.**
***MRL (maximum residue limit):* maximum concentration of a residue that is legally permitted or recognized as acceptable in, or on, a food, agricultural commodity or animal feedstuff as set by Codex or a national regulatory authority.**

Pesticide residues in food

A pesticide residue in food is any substance or mixture of substances in the food resulting from the use of a pesticide, and includes products of biological and chemical breakdown and impurities.

Supervised residue trials are designed to produce reliable data on residues occurring in food and feed commodities under normal commercial practice. The trial conditions are chosen from the efficacy studies, which demonstrate the use pattern (application rate, method, timing, etc) necessary for pest control, but using no more pesticide than necessary.

Because the supervised trials are intended to generate residue data to support the establishment of MRLs (maximum residue limits) we choose the conditions from the efficacy studies which will be the maximum allowable conditions on the registered label. The supervised trials also provide the basic residue data for dietary intake estimation. For dietary intake purposes we are most interested in the residues likely to be present in the edible portion of the food prepared for eating. For enforcement purposes pesticide residue standards (MRLs) are established on the commodity of trade, which may not be the same as the portion which is eaten. A very simple example is fruit with inedible peel such as bananas. The standards of trade are set on the whole fruit, but dietary intake estimates must be made on the residue in the banana pulp. For many pesticides discarding the banana peel also discards most of the residues which might be on the banana. Common household processes such as rinsing and wiping fruit and vegetables remove considerable amounts of surface residues and some pesticides are present mainly as surface residues. However, it is difficult to take this information into account in dietary intake estimations because the degree of cleaning, if any, will be very uneven between households. Vigorous cleaning is often an early step in commercial food processing, e.g. in the milling of wheat and the juicing of apples or tomatoes. If residues are depleted or removed during commercial cleaning or during other parts of the process intake estimations should allow for the reduced residue levels in processed commodities. Some pesticides are destroyed by cooking. Intake estimations make use of this information for commodities such as potatoes, which are always cooked, and for processed food such as canned fruit, vegetables or juices, which are also cooked.

Experience has shown that many pesticide residues concentrate in wheat bran and deplete in flour when wheat is milled. In this example we need to know the consumption of bran and flour (as bread, noodles, etc) separately to make use of such information in the estimation of dietary intake of residues. Metabolism and toxicology studies suggest which of the parent pesticide and its metabolites comprise the residue of concern for dietary intake purposes. This residue is not necessarily identical to the residue used for enforcement purposes on food commodities of trade, but usually the two are identical. The residue for enforcement purposes should be kept as simple as possible because of the difficulties and costs of complex chemical analysis. If the parent pesticide or a metabolite is the main component of the residue it is the best choice for enforcing regulations such as ensuring that a pesticide has been used according to the label. Metabolites of toxicological concern should be included in analyses for total diet studies and for supervised trials being used for intake assessment, even when inclusion is not necessary for enforcement.

Cases occur where cooking produces an undesirable degradation product from the parent pesticide. An example is the production of ethylene thiourea (ETU) from the ethylenebisdithiocarbamate fungicides during heating and boiling phases of food processing. Dietary intake estimations should take into account ETU levels in the processed food even though ETU is not present in the raw commodity. Vigorous washing and cleaning at an early stage of the process substantially reduces the levels of the parent fungicide and the opportunity for ETU production during subsequent cooking.

Chronic and acute intake

Estimates of chronic dietary intake of a pesticide residue on a food are obtained by multiplying the expected or typical level of residue in that food prepared for eating by the average weight of that food consumed daily. The chronic dietary intake of a pesticide residue is then the sum of residue intakes of those foods where residues of that pesticide occur. For chronic intake the long term average or most likely residue in the edible portion is the preferred starting point. In practice the median residue (in the edible portion) from a set of supervised residue trials at the approved use pattern is taken as the starting point estimate of the likely residue for chronic intake. The chronic intake of pesticide residues on minor food commodities is usually insignificant for the reason that, on average, the weight of a minor food consumed is small. It is legitimate to raise the question about large consumption of a food item, particularly a minor food item, on a single occasion, or at least, over a few hours. The question is better answered with the methodology of short term intakes and acute reference doses.

Estimated chronic intake should be compared with the ADI. Estimated short term consumption should be compared with an acute reference dose (acute RfD). The acute RfD should be derived from the toxicology database relating to acute exposure and effects. For acute intake estimates the highest residue in the edible portion from the supervised trials is the best starting point. Residues in individual pieces of fruit or vegetables may need to be considered in some situations because for acute intake the consumer is eating a specific piece, not the average in the consignment.

Chronic intake

= sum of (average consumption of food item x typical residue in food ready to eat)

Compare estimated chronic intake with ADI.

Acute intake

= large portion weight × maximum expected residue in food ready to eat

Compare estimated acute intake with acute RfD

Diets

WHO has information on five cultural diets which may be used in dietary intake estimates at the very broadest level. The five cultural diets are the Middle Eastern, Far Eastern, African, Latin American and European type diets. These cultural diets are based on FAO Food Balance Sheets, which are compiled from a country's food production, imports and exports. Individual countries have much more detailed information derived from specific food consumption surveys on a large number of households or individuals. Food consumption data are then classified according to age, sex, geographic distribution and ethnic background and are available to be used in more accurate dietary intake estimates of pesticide residues for these groups of people.

Individual consumers may eat large portions of specific food items and the food consumption surveys should also capture this information which is needed for the acute or short-term intake estimates.

Total diet studies

The IUPAC Commission on Agrochemicals and the Environment defines a total diet study as pesticide residue monitoring to establish the pattern of residue intake by a person consuming a defined diet. Primary sampling is as for a market basket survey but the samples are further processed as for domestic consumption ie. further trimming and cooking as appropriate to local practice.

Properly conducted total diet studies give the most accurate estimate of pesticide residue intake in the diet. In the total diet study residues in food prepared for eating are measured by chemical analysis. Intakes are calculated from the chemical analysis data and the various relevant diets.

Total diet studies have consistently shown that dietary intakes of residues are well below ADIs. However, total diet studies are limited in their scope because of their cost and complexity. Obviously, they also do not apply to pesticides only recently introduced to the market, or about to be marketed.

Conclusions

The risk assessment of pesticide residue dietary intake is a complex and developing discipline at the centre of the pesticide approval process. It is the link between the toxicology and residue studies. It has become more formalized and has attracted increasing attention in recent years.

Copious quantities of data are available on modern pesticides and we should use the data to make the most realistic estimates for residue dietary intake. We should also recognize that problems as they arise are best solved according to open scientific examination.

Denis Hamilton

Chemical Services, Animal and Plant Health Service, Department of Primary Industries, GPO Box 46, Brisbane QLD 4001, Australia. E-mail: hamiltdj@dpi.qld.gov.au

Further reading

Effects of storage and processing on pesticide residues in plant products. *Pure Appl. Chem.* 1994, **66**, 335–356.

Optimum use of available residue data in the estimation of dietary intake of pesticide residues. *Pure Appl. Chem.* 1997, in press (June issue).

Names and Addresses

Full details (names, addresses, telephone/telex/Fax numbers and E-mail) of the officers of IUPAC bodies were published in The *IUPAC Handbook 1996–1997*. The IUPAC Secretariat has been notified of the following changes:

Prof. Arnošt Kotyk (Chairman, JCBN) Institute of Physiology, Akademie véd Ceske Republiky, Vldenská 1083, CZ-142 20 Prague 4, Czech Republic. Tel.: 42 0 (2) 475 25 56; Fax: 42 0 (2) 471 22 53; E-mail: kotyk@sun1.biomed.cas.cz.

Dr Anders Kallner (President, Clinical Chemistry Section, VII.C), Tel.: +46 (8) 5177 4943; Fax: +46 (8) 5177 28 99; E-mail: Kallner_A/cc@cc.ks.se

Prof. Irina P. Beletskaya (Chairperson, EAB-21st Monograph), E-mail: beletska@elorg1.chem.msu.su

Prof. Rolf D. Schmid (Chairman, COB), Institut für Technische Biochemie, Universität Stuttgart, Allmandring 31, D-70569 Stuttgart, Federal Republic of Germany. Tel.: +49 (711) 685 3193/3192; Fax: +49 (711) 685 3196/4569. E-mail: rolf.d.schmid@rus.uni-stuttgart.de.

Dr Robert D. Vocke (Secretary Commission II.1) A-23 Physics Building, Analytical Chemistry Division, National Institute of Standards and Technology, US Department of Commerce, Gaithersburg, Maryland 20899, USA. Fax: +1 (301) 869 0413; E-mail: vocke@nist.gov.

Dr Margaretha Sluyters-Rehbach (Secretary, Commission I.3), Fax: +31 (30) 253 7483.