

Further advice on the opinion of the Scientific Committee for Food expressed on the 19 September 1997 on a Maximum Residue Limit (MRL) of 0.01 mg/Kg for pesticides in foods intended for infants and young children (adopted by the SCF on 4 June 1998)

Terms of reference

In order to allow the Commission to fully understand the scientific implications of the Committee's advice in its opinion on a maximum residue limit (MRL) of 0.01 mg/kg for pesticides in manufactured foods intended for infants and young children, expressed on 19 September 1997 (Appendix I), the Committee is asked the following additional questions:

1. Should a distinction be made between "currently used data packages" and the earlier ones on which many of the current ADIs for pesticides are based? For example, would this difference be reflected in broad terms by the age of the evaluation?
2. Whether ADIs based on current data packages reflect the particular sensitivities of infants and young children to individual pesticides in foods.
3. Whether ADIs based on earlier data packages would in general reflect the particular sensitivities of infants and young children to individual pesticides in foods?
 - 3.1. If yes, what would be the criteria to identify those pesticides where there are reasons for concern that they may pose a risk to infants and young children.
 - 3.2. If the answer is negative or subject to doubt, how could those pesticides for which protection would not be ensured by a common limit covering the majority of substances, be identified in the absence of adequate ADIs?
4. What are the scientific criteria for determining limitations for the most toxic pesticides?
5. In the conclusions to its opinion expressed on 19 September 1997, the Committee stated that "The fact that infants and children have a relatively higher intake of some food items than adults should clearly be considered in the risk assessment. This is not always taken into consideration when setting MRLs". The Committee is asked to explain the safety implications of this statement for the setting of MRLs.

In view of the need to assess in general terms the adequacy of toxicological test regimes used to establish the current ADIs of pesticides in particular, the Commission requests the Committee to work in close collaboration with the Scientific Committee on Plants.

Background

In its opinion on an MRL of 0.01 mg/kg for pesticides in manufactured foods intended for infants and young children, expressed on 19 September 1997, the Scientific Committee for Food (SCF) concluded that the current Acceptable Daily Intakes (ADIs) would give a reasonable basis for evaluation of the health impact of pesticides in foods intended for infants and young children. It nevertheless indicated a number of limitations on the adequacy of toxicological testing regimes to identify risks to infants and young children. In this context, the Committee referred to the limitations of "standard toxicological tests" and "the currently used data packages". The Commission has requested that the Committee explain further the scientific thinking behind these references to limitations in standard toxicological tests and data packages. The Commission is seeking this further advice in order to decide what options are available to it for the management of pesticide residues in foods intended for infants and young children.

Committee response

The Committee re-affirms the conclusions of its earlier opinion expressed on 19 September 1997 and re-iterates its view that when an ADI for a pesticide is set, it should cover all age groups, from infants of 16 weeks of age up to and including adulthood. The Committee offers the following explanations of the comments in its earlier opinion, in response to the Commission's questions.

Question 1

Q. Should a distinction be made between "currently used data packages" and the earlier ones on which many of the current ADIs for pesticides are based? For example, would this difference be reflected in broad terms by the age of the evaluation?

Answer:

No, a distinction cannot be made between currently used data packages and earlier ones. It is not possible to determine the adequacy of data packages simply by their date of submission. In using the term "currently used data packages" in its earlier opinion, the Committee was acknowledging the steady improvement over recent years in both the range and quality of tests carried out in support of the safety of individual pesticides. In this respect, more recently generated data packages are likely to be more comprehensive and contain tests conducted to more modern protocols than is the case with earlier data packages. However, this is only a general statement and the adequacy of any particular data package with respect to risk assessment for infants and young children can only be judged on a case-by-case basis.

The Committee also considers that even currently generated data packages may lack information on certain endpoints that may be relevant to risk assessment in infants and young children. Knowledge of the importance of some of these endpoints has only emerged very recently. This aspect is discussed further in the section on "Additional studies" in the response to questions 2 and 3.

The Committee notes that the plant protection products Directive, 91/414/EEC, ¹ itself comments that the authorisation of any pesticide under the Directive may be reviewed at any time if there are indications that the criteria relating to the approval, for example the ADI, require re-assessment. In the view of the Committee, it is inevitable that some ADIs will need to be revised with progress in toxicological science, including new toxicological endpoints, and as new information emerges about possible risks to particular subgroups of the human population.

Questions 2 and 3

Q2. Whether ADIs based on current data packages reflect the particular sensitivities of infants and young children to individual pesticides in foods?

Q3. Whether ADIs based on earlier data packages would in general reflect the particular sensitivities of infants and young children to individual pesticides in foods?

3.1. If yes, what would be the criteria to identify those pesticides where there are reasons for concern that they may pose a risk to infants and young children?

3.2. If the answer is negative or subject to doubt, how could those pesticides for which protection would not be ensured by a common limit covering the majority of substances, be identified in the absence of adequate ADIs?

Answer:

Since the Committee considers no clear chronological distinction can be made between current and earlier data packages with respect to adequacy for risk assessment for infants and young children, questions 2 and 3 are answered together.

It may be helpful to identify first the core studies that may trigger concerns relevant for risk assessment for infants and young children. These are usually present in earlier and current data packages, but there may be instances where they are not. Then, we will outline additional types of toxicological data that may be needed for risk assessment for this age group.

Core studies: The toxicological tests that may trigger concerns relevant for risk assessment for infants and young children are multigeneration studies, developmental toxicity (teratology) studies, short-term toxicity studies, long-term chronic toxicity/carcinogenicity studies and neurotoxicity studies.

These tests are all required to be included in core dossiers submitted for applications for EU authorisations under the plant protection products Directive, 91/414/EEC, ¹ unless scientific justification can be offered that the nature of the substance or its proposed uses indicate such data are unnecessary. In the years preceding the 1991 plant protection products Directive, the EU and the Member State authorities will have also required such studies to be submitted in connection with the establishment of harmonisation of MRLs and in support of national pesticide approvals respectively. Similarly, the Joint FAO/WHO Meeting on Pesticide Residues (JMPR), which has set many of the pesticide ADIs that are currently in use, stated in 1976 that all these studies should be available as part of the data package required for allocating an ADI. ² It is further noted that such studies have also been submitted in support of a number of compounds evaluated by the JMPR before 1976. ² However, the SCF is not in a position to know whether all the core tests relevant to risk assessment in infants and young children have been conducted for every individual pesticide currently in use in the EU, or which might occur as a pesticide residue in manufactured foods intended for infants and young children from countries outside the EU. A first step would be to check the content of the databases supporting any pesticides for which the JMPR allocated an ADI prior to 1977 or for which the JMPR has never set an ADI.

Additional studies: The Committee considers there are three relatively new areas of toxicity that deserve special consideration in relation to infants and young children.

The core tests mentioned above may indicate potential problems in these relatively new areas and trigger further special studies and such studies may be taken into account in setting the ADI.

However, some substances could have effects in the areas described below in the absence of any warning from the results of existing core studies. This applies not only to pesticides but is also the case for other types of chemicals.

i. Particular endocrine and reproductive effects

Most data packages for pesticides include a multigeneration study in one species and developmental toxicity (teratology) studies in two species. These are adequate to identify substances acting as reproductive toxicants in adults and substances causing malformations or affecting growth, postnatal survival and reproductive capacity in offspring.

Now however, there is recognition that there are some aspects of endocrine disruption that may not be adequately examined in multigeneration tests conducted according to currently used protocols. For example, while multigeneration studies conducted according to current EC or OECD guidelines should identify endocrine disrupters acting in developing animals in qualitative terms (e.g. by gross effects on fertility), unless they are conducted to an enhanced protocol which examines a wider range of parameters, they will not be adequate to identify any lower no effect levels for the more subtle expressions of endocrine disruption (e.g. reduced sperm production, underdevelopment of the epididymis and reduced ano-genital distance in male offspring). Similarly, the ability of developmental toxicity studies to pick up certain endocrine disrupters affecting male offspring requires extending the duration of treatment beyond the end of the conventional treatment period (day 6-16) to day 20-21 of pregnancy in the rat. This is because the vulnerable period for affecting male testis and accessory sex organs and characteristics occurs late in gestation through to the early postnatal period. At present, the OECD test guidelines for both the two-generation reproduction study and for the teratogenicity study (with a new title "Prenatal developmental toxicity") are in the process of being updated to cover these issues.

ii. Developmental neurotoxicity

Neurotoxicity testing on adult animals has not been mandatory for all pesticides, though certain tests will have been conducted on those pesticides belonging to a class of known neurotoxicants. For example, pesticides such as the organophosphates and carbamates inhibit acetyl cholinesterase and this effect is often the critical endpoint which sets their ADIs. Some of these pesticides are known to inhibit brain cholinesterase to a greater extent in neonatal and young animals than in adults, while others have similar or lesser effects in neonates and young animals compared with adults.³⁻⁹ This effect could be critical to setting an ADI but it is not clear to this Committee whether this aspect has routinely been investigated and, where necessary, taken into account in setting the ADI. The Committee notes that a joint FAO/WHO expert group has recommended this be done routinely for pesticides with anticholinesterase activity.¹⁶ Infants may be particularly vulnerable to reductions in brain acetyl cholinesterase given that acetyl choline plays an important role in normal brain development and resting levels of plasma and erythrocyte (and therefore probably brain) cholinesterase do not reach adult values until 6-12 months of age.¹⁰⁻¹³

Some developmental neurotoxicants, acting by other mechanisms, and perhaps causing only transient or no obvious neurotoxicity in adults, may also cause irreversible effects if exposure occurs during the lengthy period of brain development which extends both pre- and postnatally.

This raises the question of whether and when developmental neurotoxicity tests should be required for risk assessment for infants and young children. Currently, developmental neurotoxicity tests are rarely conducted on chemicals in general, including pesticides. The US Environmental Protection Agency (EPA) has developed criteria for triggering a requirement to conduct developmental neurotoxicity tests as a second tier study, after consideration of the results of core studies.¹⁴ The EPA finalised a guideline for such testing in 1991. An OECD guideline is also under development.

The SCF is not aware of any wide discussion having taken place in the EU on whether and when developmental neurotoxicity studies might be needed for pesticides. The Committee recommends that this issue be addressed by appropriate experts, with a view to setting criteria which can be applied in the future to decide when developmental neurotoxicity studies are needed.

iii. Immunotoxicity

Pesticides as a group are not thought to have any greater immunotoxic potential than any other types of chemical and this aspect of toxicity is, as yet, poorly researched. However, in the context of risk assessment for infants and young children, it needs to be addressed since some chemicals may interfere with the developing immune system and give rise to persistent adverse effects, such as reduced ability to respond to immune challenge. As was discussed for developmental neurotoxicity, there may be a case for consideration of criteria that might trigger a requirement for immunotoxicity studies in developing animals, though it is recognised that this field is less advanced than that of neurotoxicity. The Committee notes that the OECD test guideline for 90-day oral toxicity study in rodents is being updated to place additional emphasis on immunological endpoints.

The Committee also considered the question of whether carcinogenicity bioassay protocols adequately cover the potential sensitivity of young organisms to carcinogens has been debated for some time. In the most commonly employed protocols for rodent bioassays, exposure does not commence until 6-8 weeks of age. The SCF is aware that the US Food and Drug Administration employ certain criteria when considering whether food additives are candidates for carcinogenicity testing in which exposure commences *in utero*. However, the animal studies available to date show that exposure regimes commencing *in utero* rarely identify new carcinogens, though they may show earlier and more extensive development of tumours compared with juvenile/adult only exposure.¹⁵ Unless more compelling evidence should emerge of an independent effect following *in utero*/perinatal exposures, the Committee considers that conventional carcinogenicity bioassay procedures are adequate for risk assessment for infants and young children.

In summary, the Committee considers there is some doubt as to whether all existing pesticide ADIs have been set using databases which include all the core tests now considered necessary for risk assessment for infants and young children. The majority will have, but a few may not. The first step in a suggested strategy to manage this situation is to check the content of the databases supporting any pesticides for which the JMPR allocated an ADI prior to 1977 or for which the JMPR has never set an ADI. Should this reveal that some ADIs have been set in the absence of some core tests, then

risk assessment/risk management decisions will need to be taken on a case-by-case basis.

The question of which additional tests might be needed is more difficult to resolve in the short-term. It should be remembered that the toxicological data package required for pesticides has, for some time, been more comprehensive than those for most other classes of chemical to which humans are exposed and that where results from these data packages have triggered concerns, they will have been followed up with further studies. However, there remains the possibility that for some areas of toxicity (discussed above), data from existing studies may not have revealed all potential effects. This is particularly the case for developmental neurotoxicity and immunotoxicity. The Committee has recommended that the Commission seek further advice on a strategy for dealing with these aspects of toxicity from appropriate experts. Such advice would be relevant not only for pesticides but also for other types of chemicals.

Question 4

Q. What are the scientific criteria for determining limitations for the most toxic pesticides?

Answer:

Scientific criteria for determining limitations for safe use do not differ between pesticides, irrespective of whether they are slightly toxic, toxic or very toxic. The parameters determining the limitations are exposure data and the ADI derived from the toxicological database.

Question 5

Q. In the conclusions to its opinion expressed on 19 September 1997, the Committee stated that "The fact that infants and children have a relatively higher intake of some food items than adults should clearly be considered in the risk assessment. This is not always taken into consideration when setting MRLs". The Committee is asked to explain the safety implications of this statement for the setting of MRLs.

Answer:

The Committee would like to take the opportunity to point out that the wording in a sentence of its earlier opinion was not very precise. It should have said "This may not always have been taken into consideration when deciding whether proposed MRLs were acceptable." Acceptance of MRLs for pesticides on individual commodities on the basis that adult intakes do not exceed the ADI implies that the infant and young child may not necessarily be protected to same extent as adults. This is because the worst case approach used in the SCF opinion to estimate intake of foods for infants, namely 48 g/kg b.w./day and assuming all food consumed is manufactured, implies that use of adult intakes may underestimate exposure in the infant and young child. The adult average energy requirement per kg body weight is about 1/3 that of an average 1 year old child. The Committee has been in doubt as to what extent the infant and young child has been protected and wishes to be reassured that the intakes of infants and young children are considered in the EU when deciding whether proposed MRLs for foods in general or any limits for manufactured foods intended for infants and young children are acceptable.

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Appendix I

Opinion on a maximum residue limit (MRL) of 0.01 mg/kg for pesticides in foods intended for infants and young children (expressed on the 19th September 1997)

Terms of reference

The Committee is asked to advise the Commission as to whether a maximum residue limit (MRL) of 0.01 mg/kg for pesticides in manufactured foods intended for infants and young children (dietetic foods) would be adequate to protect the health of this section of the population or whether there are instances where there are reasons to be concerned that the presence of even lower levels might constitute a risk. In the latter case, the Committee is invited to provide criteria for the identification of the pesticide residues concerned and for the establishment of appropriate residue limits for them.

Background

In its opinion on the essential requirements for weaning foods (European Commission 1990), the Committee defined "Infants" as children aged less than 1 year and "Young children" as children aged between 1 and 3 years. For the purposes of the present opinion, "older infants" are those aged between 4-12 months and "childhood" is understood as the period from 1 year to 12 years (young child 1-3, older child 3-12 years).

Foods for particular nutritional uses (dietetic foods) intended for infants and young children are covered by two directives: Directive 91/321/EEC (EEC, 1991a) as amended by directive 96/4/EC (EEC, 1996a) on infant formulae and follow-on formulae and Directive 96/5/EC (EEC, 1996b) on processed cereal-based foods and baby foods. Article 6 of each of these directives specifies that the products covered "shall not contain any substance in such a quantity as to

endanger the health of infants and young children. Necessary maximum levels shall be established without delay".

The terms used in these Directives are consistent with those defined by the Committee.

Pesticide residues are regulated by Directives 76/895/EEC (EEC 1976), 86/362/EEC (EEC 1986a), 86/363/EEC (EEC 1986b) and 90/642/EEC (EEC 1990) and their amendments. These directives do not harmonise the situation for foods intended for infants and young children, however, the Commission declared to the Council during the adoption of these Directives its intention to present proposals for maximum levels of pesticides in foods intended for infants and young children by 1 January 1999.

Taking account of the various scientific, practical and socio-economic factors, the Commission has asked the Committee to advise it on the health implications of a limit of 0.01 mg/kg for pesticides in manufactured foods intended for infants and young children in the light of current scientific knowledge.

Current procedures for establishing maximum residue levels (MRLs) for pesticides

The use of pesticides is regulated on the basis of the MRLs established for residues on various crops. The establishment of a MRL should, among other things, take into account that the Acceptable Daily Intake (ADI) for humans for that particular pesticide is not exceeded when the foods are ingested by the consumer. The ADI is defined as "an estimate of the amount of a residue, expressed on a body weight basis, that can be ingested daily over a lifetime without appreciable health risk" (WHO, 1987). The ADI is intended to cover all vulnerable groups (including different age groups) within the human population. It has been stated that the ADI is applicable to children older than 12 weeks of age. (FAO/WHO, 1978). JMPR (Joint FAO/WHO Meeting on Pesticide Residues) has been establishing ADIs since the early 1960s.

MRLs are subsequently derived based on GAP (Good Agricultural Practice in the use of pesticide includes the nationally authorized safe uses of pesticides under actual conditions necessary for effective and reliable pest control. It encompasses a range of levels of pesticide applications up to the highest authorized use, applied in a manner which leaves a residue which is the smallest amount practicable. (Codex Alimentarius Commission, CL 1996/33 - PR, p.17) supervised trials and compared with the ADI. In the EC there is a tiered approach in the setting of the MRLs (Directives 86/362, 86/363, 90/642 and 91/414 (EEC 1991b)). Firstly, the TMDI (theoretical maximum daily intake) is calculated from the MRL proposals based on the results of the GAP supervised trials and the estimated food consumption per person. If the ADI is exceeded according to this calculation, more refined methods are used to calculate a more realistic intake using e.g. the actual median residue levels determined after GAP supervised trials, and reduction factors from the processing of food. If the ADI is still exceeded after use of the refined calculation methods, then the proposed MRLs cannot be endorsed.

Differences in susceptibility between infants, children, and adults

In contrast to adults, children, and in particular infants are in a progressive stage of development and growth. Potential differences in susceptibility to pesticides are dependent on toxicokinetic and toxicodynamic parameters (such as organ sensitivities), including genetic, physiological, and metabolic factors, mechanism of action of the chemical and dose-effect and dose-response relationships. Special concerns for infants and children relate to the early developmental state of their biochemical and physiological processes. Therefore it needs to be considered whether exposure of these age groups to pesticides may lead to more serious toxicological effects or even effects not induced in the adult.

The susceptibility of the developing foetus, neonate, infant and child to delayed functional toxicity becoming manifest in adult life, as a result of exposure to apparently subtoxic doses of pesticides during a developmental period of high susceptibility (critical window) is of particular concern. Developmental functional toxicity may be particularly relevant for the developing central nervous system, but also applies to other systems, such as the endocrine, reproductive (e.g. reduced semen quality due to impairment of Sertoli cell development), and immune systems. Although delayed neurotoxicity has been observed in experimental animals after exposure to some pesticides, the current databases do not allow any unified conclusions about the potential for delayed toxicity in humans from exposure to pesticides.

The overall experience gained from toxicological studies in experimental animals strongly suggest that it is not possible to make general statements about age-related differences in toxico-dynamic parameters, such as organ sensitivity. For some chemicals, immature animals are more sensitive than adults while in other cases they are less sensitive, depending on the compound and its effects. In humans, the same picture emerges from experimental and clinical data on pharmaceuticals, while knowledge about age-related differences in susceptibility to pesticides is virtually absent. Therefore, the issue of age-related differences in susceptibility to pesticides should be addressed on a case by case basis.

Adequacy of current animal testing protocols for the risk assessment of pesticide residues in the diet of infants and young children

The reproduction studies cover different developmental periods up to weaning, and in the case of multi-generation studies from conception to adulthood, while the usual chronic two-year toxicity/carcinogenicity tests, starting at 6-8 weeks of age in the rat, cover only the late period of juvenile growth. The ADI derived from these studies is thus intended to cover exposure of older infants and children as well as exposure of the foetus during pregnancy and the neonate and young infant during the nursing period.

An examination of age-related differences in toxico-kinetics has shown that there are no major systematic differences between neonatal and young animals and their human counterparts for several toxico-kinetic parameters, and that an increased uncertainty factor is not required for inter-species differences provided that the toxico-dynamic endpoints have been adequately studied and considered carefully.

In several respects, the human neonate is more developed at birth than the neonatal rat. For instance, the major growth of the brain takes place before birth in humans while this occurs after birth in the rat. During lactation, the human infant will therefore probably not be as vulnerable as the neonatal rat toward effects on the development of the central nervous system. Therefore, the new born rat is not developmentally parallel to the new-born human, and studies using new born pigs or monkeys may provide better models for the exposure situation for young human infants.

Carcinogens will generally be detected in regular carcinogenicity studies. The U.S. EPA has made a comparison of carcinogenicity studies with perinatal and adult exposure, and adult exposure only (EPA, 1997). They found that the incidence of tumours may increase, and the latency period may be reduced in studies with combined perinatal and adult exposure compared to adult exposure only. Perinatal exposure though, rarely identifies carcinogens that are not found in standard carcinogenicity studies.

An area of particular concern is the possibility that interactions of chemicals with specific endocrine receptors during foetal life and infancy may have profound effects on morphological and functional properties of these systems after maturation. This raises the question whether the current toxicological database for pesticides is sufficient to fully assess potential developmental adverse effects. This may not always be the case, as for instance impairment of the central nervous system, leading to behavioural, memory and learning deficits are rarely examined in conventional studies, and delayed toxicity resulting from exposure to low levels of a toxicant during a particularly sensitive developmental period may not always be adequately addressed by current testing procedures.

At present, no single test approach for developmental behavioural toxicity has been identified as the most appropriate.

Although the clinical examinations performed in the currently used toxicity tests, including multi-generation studies, may reveal obvious signs of functional deficits, this aspect deserves more attention in the future. It would be expected, that many, but not all substances having a toxic effect in the nervous system of the new born, would show some effect in the adult at least at higher doses. In the light of the present knowledge, the standard test package ought to be refined in both design of studies and the choice of parameters examined. More attention should be given to parameters that adequately address the function of the nervous, reproductive, endocrine, and immune systems. A new guideline regarding developmental neuro-toxicity is being prepared within the OECD test guideline programme in order to obtain more information about these effects.

None of the present standard toxicological tests mimic the situation where a human infant is exposed to chemicals via infant formulae. Therefore special considerations are needed for pesticides likely to be found in infant formulas for infants below the age of 16 weeks.

Exposure of infants and young children to pesticides from commercial infant formulae, cereals and other weaning foods

Infants and young children have a higher food intake than adults when expressed on a per kg body weight basis. The dietary exposure of infants in their first few months of life to pesticides arise primarily from breast-feeding (human milk), infant formulae, and water. From the age of about 4 months, infants are exposed to pesticides through consumption of manufactured foods including infant formulae, follow on formulae and weaning foods and also from 'family food' and drinking water used to reconstitute dry products.

Infant formulae can be divided into "ready to feed" products and those consisting of dry powder for mixing with water immediately before use. Water is the major ingredient in infant formula and the water used for the "ready to feed" formulations during manufacturing is understood to be purified by for example active carbon filtration and is thus anticipated not to contain pesticide residues of concern. Tap water is most commonly used to reconstitute infant formula in the home although bottled and natural mineral water may also be used. In this risk assessment, the Committee has taken note of the current and proposed EU limits for pesticides in drinking water (EEC 1990, European Commission 1994) which are 0.1 µg/l for individual substances and 0.5 µg/l for the total pesticide content. The Committee estimated that the contribution to the overall pesticide content arising from the use of drinking water containing pesticides at these maximum permissible levels to reconstitute dry products would be one or two orders of magnitude lower than that which could result from the products themselves if they contained pesticides at the MRL of 0.01 mg/kg.

The solid fraction of liquid infant formula typically constitutes about 13 % of the finished product. The main part is processed cows milk or soy products and corn syrup. All raw materials used have been processed which should reduce the pesticide content. It has been stated that, in general, none or very small amounts of pesticides are found in infant formulas (NRS, 1993).

The estimation of the potential exposure from manufactured food was made by adopting a worst case approach i.e. assuming that these foods constitute the total diet of a reference child. The calculation uses the physiological requirements of infants at various ages for energy and macronutrients to determine the amount of "solid matter" being consumed daily in formulas and weaning foods. As they mature, infants consume smaller volumes of formulas as their intake of weaning foods increases. i.e. the energy density of their diet increases and the hydration factor for the solids consumes falls. On this basis a worst case scenario for exposure to solids can be hypothesised for 12 month old infants. For such infants, using a hydration factor of 33 % and an energy requirement of 1000 kcal/d, an energy density of 3 kcal/g can be derived which in turn gives an intake of 30g/kg body weight per day for a 10 kg infant. By applying two standard deviations (the standard deviation from the literature for these data is 30 %) to this mean, the value of 48 g/kg/d is obtained.

The Committee had the opportunity to test this approach by comparing this calculated value with an estimate made from the the results of the DONALD study (Forschungsinstitut für Kindernahrung, Dortmund) which employs consecutive three-day weighed diet records to study the food consumption patterns of infants and young persons in families from favourable social backgrounds in the Dortmund area of Germany. The study provided data for the consumption of manufactured infant formulae (dry), cereals and milk cereals (dry), and other weaning foods (ready-to-eat) as sold.

The data from the DONALD study were used to generate a frequency distribution for the total daily consumption of manufactured infant formulae (dry), cereals and milk cereals (dry), and other weaning foods (ready-to-eat) as sold based on the individual dietary records of children in each age category.

The 95 % iles of consumption estimated from the DONALD study were judged to be consistent with the value of 48g/kg body weight as calculated above on the basis of energy requirements. A worst case intake estimate was made by assuming this level of daily consumption for all infants and young children and that all the commercial products

consumed were appropriately hydrated and contained a pesticide residue at 0.01 mg/kg. This would lead to a maximum estimated intake of a pesticide of about 0.0005 mg/kg b.w./day. On the other hand, if the infant's intake were derived from a commercial/manufactured dry product which was reconstituted as recommended (customarily 2 parts dry food product to 1 part water), the resultant exposure from a residue of 0.01 mg/kg would be 0.0003 mg/kg.b.w./day.

Conclusions

The Committee is asked to advise the Commission as to whether a maximum residue limit (MRL) of 0.01 mg/kg for pesticides in manufactured foods intended for infants and young children (dietetic foods) would be adequate to protect the health of this section of the population or whether there are instances where there are reasons to be concerned that the presence of even lower levels might constitute a risk. It concludes as follows:

The ADI covers all groups of the population. The Committee does not recommend the use of special uncertainty factors for infants and children or the establishment of special ADIs for this age group. The toxicological database should adequately cover the most sensitive effects and the most sensitive age groups and the ADI should cover all sensitive segments of the population, irrespective of age. If there is scientific evidence that infants and children are the most sensitive populations to a particular pesticide, that evidence must drive the derivation of the ADI.

The Committee recognised that the currently used data package for the establishment of the ADI was not in all respects optimal to reflect a particular sensitivity of infants towards the potential toxicity of a given pesticide. However, it was the opinion that in most cases the toxicological studies would have provided indications if such special sensitivities were to exist. The Committee concluded that the current ADIs would provide a reasonable basis for evaluating the health impact of pesticides in foods intended for infants and young children.

The fact that infants and children have a relatively higher intake of some food items than adults should clearly be considered in the risk assessment. This is not always taken into consideration when setting MRLs.

The Committee considered 0.0005 mg/kg b.w to be a realistic worst case estimate for the upper limit for the daily intake of a pesticide arising from the consumption of manufactured infant formulae (dry), cereals and milk cereals (dry), and other ready-to-eat weaning foods . The estimate assumes that all infants and young children consume commercial products at the highest recorded 95 percentile every day and that all commercial products contain the pesticide at a level of 0.01 mg/kg in the products as sold.

The Committee concluded that if the maximum residue limit were to be set at 0.01 mg/kg in foods intended for infants and young children, there is a possibility that an infant could exceed the ADI for pesticides having an ADI at 0.0005 mg/kg b.w. or lower

This would imply that the Commission and the Member States should carefully reconsider pesticides that have been allocated ADIs at 0.0005 mg/kg b.w. or lower as to the health impact of their presence in baby food. This consideration should include an examination of their actual use and the basis on which the ADIs was set, i.e. whether the toxicological data package gives any reason for special concerns for infants and children.

The Committee was also aware that some pesticides share a common mechanism for their critical toxic effect which determined the ADI, but do not necessarily share a group ADI. The Committee recommends that further consideration be given by the appropriate bodies to the potential for additive effects and whether the risk management of residues in foods specially manufactured for infants and young children needs to take these into account.

In giving its opinion, the Committee wishes to note that the limit of 0.01 mg/kg has not been proposed on the basis of toxicological evaluation. Therefore, for those pesticides having an ADI greater than 0.0005 mg/kg b.w., their presence in foods intended for infants and young children at levels exceeding 0.01 mg/kg does not necessarily imply a risk to their health.

When setting MRLs for pesticides in foods intended for infants and young children, the Committee draws attention to limitations of current routine analytical methods for determination of some pesticides particularly at levels around 0.01

mg/kg.

The Committee notes that pesticides are subject to continuous re-evaluation within the EC and elsewhere, and recommends that special attention is paid to the potential higher susceptibility of infants and children to certain compounds during this process. This will require further research which may lead to improved test strategies.

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