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RISK ASSESSMENT AND MANAGEMENT IN SETTING FOOD STANDARDS FOR ADDITIVES AND CONTAMINANTS IN AUSTRALIA

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Introduction

1. The primary task of the National Food Authority (NFA) is to assess and develop food standards and variations to food standards, for the protection of public health and safety (*National Food Authority Act 1994*).

2. This paper summarises how the Authority defines, assesses and manages risk in relation to the setting and varying of food standards in Australia. Risk assessment and management underlie the existing regulatory structure and procedures in general applying in Australia and these are described more fully in an Authority paper that can be made available to interested parties.

3. A more informed debate about acceptable levels of risk in relation to food can only be achieved through a greater awareness of risk assessment and management practices.

4. Risk assessment and risk management are regarded as two distinct processes and the various aspects of each are discussed in this document.

5. For the purposes of this paper, the following definitions are used:

- *Hazard* is the intrinsic property of a substance to cause harm;

- *Risk assessment* is the process of using available information to evaluate the hazard of a substance and its potential to cause adverse health effects at different levels of exposure;

- *Risk management* is the process of integrating risk assessment results with social, economic and political concerns and, after consideration of alternative strategies, of identifying a strategy to minimize or eliminate the identified risk.

Concept of risk

6. Risk can be defined as the potential for the occurrence of unwanted negative consequences of an event. In relation to food, this is usually interpreted as the potential to cause either immediate or long-term adverse health effects. The broad concept of "risk", however, has many dimensions, and the probability of adverse health effects, as determined from a scientific viewpoint, is just one. Other dimensions include psychological factors, social and ethical factors, and political and economic

factors. Risk assessment, as performed at the National Food Authority, is defined as the scientific assessment of risk and is performed independently of these other dimensions of risk, although they may contribute to the subsequent risk management decisions.

7. Fundamental to an estimation of risk is the acceptance of a degree of uncertainty. The basis of this uncertainty is two-fold. Firstly, there is uncertainty with regard to the quantity and quality of the information upon which a decision is made. Secondly, there is uncertainty with regard to the validity of the assumptions upon which the prediction of risk is made, such as species extrapolation, dietary modelling or the degree of heterogeneity in the population. Together, these determine the degree of uncertainty in the risk estimation in a particular circumstance.

Food-related risks

8. The protection of public health and safety is the most important of the factors taken into consideration when setting and maintaining food standards. Public health and safety in relation to food refers to all those aspects of the diet which could adversely affect human health either in the short (safety) or long term (public health). The two terms, "public health" and "safety" are sometimes used interchangeably because of their close relationship but each have characteristics which differentiate them.

9. For agricultural and veterinary chemicals regulation in Australia, maximum residue limits (MRLs) are enforced by State and Territory authorities according to the Australian Food Standards Code. MRLs are established largely by other agencies, namely, the National Registration Authority for Agricultural and Veterinary Chemicals (NRA) and the Department of Human Services and Health.

Steps in risk assessment

10. The process of risk assessment can be divided into four distinct steps, namely, hazard identification, hazard characterization, exposure assessment, and risk characterization. The various steps in the scientific assessment of risk are considered below. Because chemicals in food constitute a much larger and diverse group of potentially hazardous substances than the microbiological hazards (although not necessarily a greater risk), much of the risk assessment methodology has been formulated around the risk associated with chemicals.

Hazard Identification

11. Hazard identification is *the qualitative evaluation of the adverse health effects of a substance(s) in animals or in humans*. For chemicals, hazard identification establishes the toxicity of a substance and may identify the set of inherent properties which make it capable of causing an adverse effect. For new chemicals, this is established through a consideration of: (i) the structure and associated physicochemical properties; (ii) the metabolism and toxicokinetics of the substance; and (iii) the results of a series of toxicity tests conducted both in animal models and in *in vitro* systems. The extent of the toxicity tests required is determined on a case-by-case basis, and will be dependent on the nature of the substance and the anticipated level of human exposure. Animal toxicity studies are designed to investigate the major biological systems and would cover acute toxicity, reproductive toxicity, genotoxicity, embryotoxicity, teratogenicity, carcinogenicity, organ toxicity, and sometimes other specific studies such as neurotoxicity or immunotoxicity.

12. For existing chemicals, toxicology data may also be available from published papers although the quality of this data is variable. In some cases, human toxicology data may be available. This could include: (i) case studies of adverse effects; and (ii) results of epidemiological studies. Individual case studies may not by themselves be highly significant, but a pattern may emerge over a period of time with increasing numbers of reports of adverse effects.

Hazard Characterization

13. Hazard characterization is *the process of estimating the relationship between the dose of a substance(s) and the incidence of an adverse effect*. For chemicals, hazard characterization involves a consideration of the results obtained in the hazard identification phase in relation to the dose levels used. The outcomes should be: (i) identification of the major toxicological endpoints and the dose levels at which they occur; (ii) an estimate of the dose level below which the observed toxicity does not occur; (iii) some understanding of the metabolism and kinetics of the substance in a mammalian system; and (iv) in some cases, information on the mechanism of action of the observed toxicity.

Exposure Evaluation

14. Exposure evaluation is *the evaluation of the magnitude and duration of actual or anticipated human exposure, and the number of persons affected*. For chemicals, exposure evaluation involves estimating the level and extent of human intake of a particular substance in the whole diet. When the exposure evaluation is based on estimated or anticipated exposure, the process is sometimes referred to as dietary modelling. When survey data is available, more accurate exposure evaluations for specified population groups can be made. In general, exposure estimates are based on known or anticipated dietary information for particular foods together with an estimate of the level of the chemical in particular commodities.

Risk Characterization

15. Risk characterization is *the process of estimating the probable incidence of an adverse health effect to humans at various exposure levels, including a description of the uncertainties involved*. Risk characterization brings together the information of the previous steps in order to provide a practical estimate of risk for a given population. It is on the basis of this determination that the risk management strategy is formulated. The degree of confidence in the final estimation of risk will depend on the uncertainty factors identified in previous steps.

16. For chemicals, risk characterization might be expressed in terms of a margin of safety between the acceptable level of intake of an additive or contaminant, based on the known hazard, and the known level of human exposure via the diet.

17. The most prohibitive approach to an unacceptable risk is total restriction of use (for a chemical) or a contamination level of zero (for a chemical or pathogenic organism). This approach may be taken for (i) chemicals or pathogens which should not enter the food supply; (ii) chemicals for which there is no toxicity information; (iii) for certain agricultural chemicals which are no longer in use; and (iv) certain botanicals which are not considered suitable for use in food.

18. The most common approach with chemicals is that the permissible upper level in food is controlled through the Food Standards Code. Thus, food additives are controlled on the basis of the acceptable daily intake (ADI) and technological justification, processing aids are controlled largely on the basis of good manufacturing practice (GMP), agricultural chemicals are controlled on the basis of the ADI and good agricultural practices (GAP), contaminants are controlled on the basis of a tolerable intake together with best management practices.

19. Whether the presence of chemicals, nutrients or micro-organisms is restricted or not, surveys can be a useful tool for monitoring actual levels in food. Such information can then be used in estimating the level of dietary intake of chemicals and nutrients for different population sub-groups, or the adequacy of existing microbiological standards and Codes of Practice in minimizing the level of pathogens in foods. This information is important in providing reassurance to the public regarding the safety and adequacy of the food supply.

20. The concept of a dose-response relationship is fundamental to establishing the safety of chemicals in food. Animal studies may be useful, firstly, to identify the target organs for toxicity and perhaps gain some information on the mechanism of action of the observed toxicity and, secondly, to estimate the dose level below which the adverse effect does not occur. This dose level is referred to as the no-observable-effect-level (NOEL). In order to compensate for the uncertainty in this figure as a measure of safety, the NOEL is generally adjusted by means of so-called "safety factors" to arrive at safe levels of intake for humans. The safety factor (or "uncertainty factor") used may vary from 10 to 2000 depending on the confidence in the available data. For food additives, a safety factor of 100 is generally used which comprises a factor of 10 to account for the species differences between experimental animals and humans, and a factor of 10 for the variation in the human population. If the NOEL is based on human data, a safety factor of 10 may be considered adequate, while on the other hand, if the NOEL is based on less than lifetime studies, a higher safety factor (1000-2000) may be applied. The acceptable daily intake (ADI) is determined by applying the safety factor to the NOEL. For food additives, the ADI is used as the basis for establishing the safe level of human lifetime exposure.

21. Carcinogenic chemicals which are also genotoxic present a particular problem with regard to safety assessment. Because of their ability to produce DNA damage at very low dose levels, a NOEL cannot easily be established for such chemicals. In general, the approach has been to disallow the use of such chemicals in food. When their occurrence in food is unavoidable, either because they are naturally-occurring or are produced during processing, levels should be kept to a minimum. Carcinogenic chemicals which are non-genotoxic can generally be regulated in a similar manner to other chemicals with the establishment of a NOEL and an ADI.

22. Environmental contaminants cannot be regarded in the same way as food additives since they are not intentionally added to food and the levels cannot necessarily be controlled to provide the same margin of safety which can be achieved with a food additive. Thus, assessments must be done on the basis of the lowest achievable level. Maximum permissible concentration (MPCs) are established generally on the basis of the lowest achievable levels of contamination which is consistent with protection of public health and safety.

Determination of the ADI

23. One of the criticisms of the ADI approach is that the value of the NOEL is dependent on the dose levels chosen for the study and, in some cases, an overly conservative ADI may result. This uncertainty factor is difficult to correct except by repeating the experiment at different dose levels, but needs to be considered when questions of safety arise for chemicals for which the intake is approaching the ADI.

Toxic effect upon which the ADI is based

24. The nature of the toxic effect upon which the ADI is based is important when considering the health implications of a dietary intake above the ADI. This may be an important consideration when concern is expressed regarding excessive intake. Chemicals which cause, for example, a neurotoxic effect or a retinal disorder, should be monitored more closely in relation to the ADI than one which caused a slight liver weight increase.

Use of safety factors

25. Safety factors (or uncertainty factors) are one way of dealing with the uncertainty arising from, firstly, species extrapolation of toxicity studies and, secondly, human heterogeneity with regard to response to the toxicity of chemicals, and are designed to protect the more sensitive members of the population. If the toxicity to humans is known, and also the most susceptible groups within that population can be identified, the safety factors can be smaller.

Dose-response relationships and thresholds

26. The advantage of the ADI approach to establishing a safe level of exposure is that it avoids extrapolation of the dose-response curve beyond the dose levels used in the study. Where no threshold dose level is evident to establish a NOEL, it may be necessary to extrapolate to a so-called virtually safe dose level. While mathematical models are available to perform such extrapolations, these are not considered particularly reliable since they themselves make assumptions regarding the shape of the dose-response curve. The only situation where it may be necessary to consider extrapolation to a virtually safe dose level is for the naturally-occurring genotoxic chemicals in food.

Measurement of exposure

27. Uncertainty in the measurement of dietary exposure to chemicals can be due to lack of knowledge in a number of areas. Firstly, variable dietary consumption of particular foods by different groups of the population. Secondly, information on the level of the chemical in the different food commodities. Thirdly, information regarding the level of absorption from the gastrointestinal tract and its distribution in the body prior to excretion.

Chemical risk management

28. There are a number of approaches to managing the risks associated with the presence of chemicals in food, including: (i) restricting the level of the chemical in food, if necessary; (ii) appropriate labelling to indicate the presence of the chemical; and (iii) an education programme to make the public aware of potential risks associated with excessive consumption. The general principle of minimizing unnecessary exposure to chemicals underlies each of the above approaches.

29. The most common management approach with chemicals is to establish a permissible upper level in food. The basis on which this permissible level is established will depend on the nature of the chemical and the type of food in which it occurs, as discussed below. Labelling of food is used to identify the presence of food additives and may also be used to highlight the potential for adverse reactions to particular foods or food components.

30. Unrestricted use may be suitable for chemicals of very low toxicity, and for some chemicals which have been used traditionally in foods with no evidence of adverse health effects. This is similar to the US "generally regarded as safe" or GRAS classification. Unrestricted use of a chemical may or may not also need to be accompanied by a public education programme. Chemicals for which better understanding of the risk associated with their consumption is needed are: (i) the naturally-occurring toxic chemicals in food, e.g. pyrrolizidine alkaloids; and (ii) those potentially hazardous chemicals which are formed during cooking or food processing, e.g. heterocyclic amines.

31. Surveys, such as the Australian Market Basket Survey, are a useful tool for monitoring actual levels in food, as consumed. The objective of monitoring and evaluation activities is to assess the public health and safety impact of individual food standards, and also to assess the cumulative impact of food standards, especially over an extended time period. The development of indicators and guidelines

for the monitoring and evaluation of the cumulative influence of food standards on the food supply and possibly on public health and safety is a key responsibility of the Authority.