9 Assessing risks to infants and children

N.R. REED

9.1 Introduction

The approach to assessing the risk to infants and children has been one of the key issues in risk assessment over the last decade. Occasional reports of unexpected adverse effects in these younger subpopulations from the exposure to pharmaceutical agents or environmental chemicals has heightened the awareness that the risk to the younger subpopulations can differ substantially from those to the adults. The need for a special approach to account for the unique characteristics of the younger subpopulations in risk assessment was clearly outlined in a joint report by the International Programme on Chemical Safety (IPCS) and the Commission of the European Communities (CEC) (World Health Organization, 1986). The similarities and differences between children and adults were further documented in a conference sponsored by the International Life Sciences Institute (ILSI) and US Environmental Protection Agency (USEPA) (Guzelian et al., 1992).

Pesticides have been the focus of food safety evaluations due to their purposeful and widespread use. Designed to be poisonous, pesticides used in agricultural crops and foodstuffs have the potential to adversely affect human health if not appropriately controlled. However, pesticides are not the only chemicals present in foods that have the potential to cause adverse effects. The presence of other chemicals in foods can also render them unsafe for consumption. Food additives (e.g. preservatives, supplements, stabilizers), therapeutic drugs used on livestock, naturally occurring toxicants, mycotoxins produced by molds growing in or on foods and enterotoxins (e.g. Clostridium botulinum toxin) have all been subjected to food safety investigations.

Concerns have been raised over whether regulations concerning food chemicals based on the current approach to risk assessment are sufficient to protect the health of infants and children (National Research Council, 1993). The concerns for the young are not just about the body size, but also about the varying sensitivity to risk agents. Infants and children differ from adults physiologically and developmentally. Rapid growth and functional development mark the first 2–3 years of life. These developmental changes affect the ways in which the body handles and responds to xenobiotics. The young individuals also differ from the adults in the pattern
of exposure to chemical toxicants in the environment and in food. With regard to exposures to food chemicals, infants and children generally have higher exposures due to the higher food intake rates per unit body weight. The younger subpopulations may also have preferences for certain foods or forms of food. It is apparent that the human adult model is inadequate for the evaluation of risk in infants and children.

The safety evaluation of food chemicals in infants and children should not be focused only on the potential harm from direct exposures to foods containing chemical residues and from the exposure of a single chemical. Developmental effects as a result of in utero exposures and the reality of concomitant exposure to more than one chemical in foods are two aspects that are important to the overall evaluation of food safety for infants and children and could have significant impacts on the health of these younger subpopulations.

This chapter begins with a description of the unique characteristics of infants and children. The implications of their unique characteristics for risk assessment will then follow. The two important subjects, in utero exposure and multiple chemical exposures, are presented last.

9.2 Infants and children – unique population subgroups

In the literature, young individuals undergoing developmental changes are categorized into different groups based on somewhat different ranges of age. In this chapter, ‘infants’ refers to individuals from birth up to 1 year of age, and ‘children’ includes individuals beyond 1 year and up to 12 years old. Infants and children are distinctly different from adults in terms of physiology, development and size. The significance of these differences with regard to the evaluation of risks to food chemicals is two-fold: one is in the differential sensitivity in response to xenobiotics and the other is in the different levels of exposure to food chemicals. The issue of differential sensitivity pertains to both the pharmacokinetic and pharmacodynamic characteristics and the manifestation of toxicity. The issue of exposure pertains to both the amount and the pattern of food intake.

The unique ways in which infants and children handle and respond to xenobiotics are well recognized in the field of therapeutics. Incidents of unexpected toxicological response have occurred in the pediatric population towards drugs that have been tested only in adults. The concern of untoward toxicity to the pediatric population prompted the issuance of warnings for drugs that have not been tested in the young subpopulation. Thus, over three decades ago, it was realized that infants and children became ‘therapeutic orphans’, deprived of therapeutic drugs that may be beneficial to them (Yaffe and Aranda, 1992). This awareness has led to a greater effort toward pediatric drug monitoring and research