6 Risk assessment: alternatives to animal testing
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6.1 Introduction

All new chemicals manufactured specifically for use in food are required to be evaluated for safety. Such chemicals which are intentionally incorporated into foods are additives, and this chapter focuses on their safety assessment. Each proposed food additive is subjected to various in vivo and in vitro assays, which may include tests for genotoxicity, acute and subchronic toxicity, carcinogenicity and teratogenicity (Chapter 2). In the UK, on the basis of the results obtained and the estimated daily intake, the additive is assigned an acceptable daily intake (ADI) value as an indication of the levels which may be consumed without the likelihood of adverse effects.

The public is becoming increasingly concerned about the use of large numbers of animals in the safety testing of what are perceived to be ‘luxury’ products, e.g. cosmetics and toiletries. Intense public pressure has forced cosmetics and toiletries manufacturers to seek alternative methods of testing their ingredients and products. This demand has been recognized by the EU, and the Cosmetics Directive (76/768/EEC) (European Economic Community, 1976) has been amended to include the statement: ‘testing on animals of ingredients or combinations of ingredients should be banned as from 1 January 1998; ... that date should be postponed where alternative methods of testing have not been scientifically validated’ (European Economic Community, 1993). The numbers of animals used in regulatory food toxicity testing are greater than the numbers used in the testing of cosmetics and toiletries. Therefore, the public may soon refocus its attention on the use of animals in food toxicity testing, and demand that food additives also be tested by alternative methods which can reduce the numbers of animals, refine the experimental procedures used and, in some cases, totally replace the use of animals.

As very few, if any, serious instances of toxicity have arisen due to the consumption of specific food additives, it might be claimed that the current methods for food additive safety assessment are reliable. However, food additives pose a number of special problems for toxicity testing. Foods are complex mixtures of many potentially toxic compounds and the testing of a single additive is unlikely to predict its effects when combined with other food constituents. Humans are subjected to highly variable, repeated
low-dose exposures to food additives over long periods of time. This means that it is difficult to attribute a disease or toxicological effect to any specific food component. In addition, the possible long-term effects of food additives cannot be accurately predicted in 2-year animal bio-assays. Finally, many of the animal tests used have not been adequately validated for the specific purpose of food toxicity testing. Therefore, the data they provide may be scientifically inadequate, and the subsequent risk assessments based on such data are therefore of dubious value. Thus, it is not unreasonable to assume that current animal studies for the purpose of food additive safety assessment are far from ideal.

The main issue that needs to be addressed is how to develop methods for assessing the effects of long-term, low-dose (chronic) exposure to food substances, by using refined procedures and minimum numbers of animals in experiments which are only carried out when absolutely necessary. The eventual goal should be the development of assays which can completely replace the need for animal studies in food additive safety evaluation.

6.2 The Three Rs concept


The UK Animals (Scientific Procedures) Act 1986 contains a commitment to replacement alternatives in the following important clause:

5(5). The Secretary of State shall not grant a project licence unless he is satisfied that the applicant has given adequate consideration to the feasibility of achieving the purpose of the programme to be specified in the licence by means not involving the use of protected animals.

In Europe, Directive 86/609/EEC (European Economic Community, 1986) states that:

7.2. An experiment shall not be performed if another scientifically satisfactory method of obtaining the result sought, not entailing the use of an animal, is reasonably and practicably available.

Thus, the concept of alternatives is promoted via UK and European legislation and the use of animals has fallen significantly since the mid-1970s. However, there is still considerable room for progress and improvement. At a workshop (Balls *et al.*, 1995), the current status of the Three Rs was discussed and recommendations were made which aim to achieve greater acceptance of the concept of humane experimental technique and the more active implementation of alternatives. This chapter aims to highlight the areas within food safety assessment where there is potential, both in