

Food additives: an ethical evaluation

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Background: Food additives are an integral part of the modern food system, but opinion polls showing most Europeans have worries about them imply an urgent need for ethical analysis of their use.

Sources of data: The existing literature on food ethics, safety assessment and animal testing.

Areas of agreement: Food additives provide certain advantages in terms of many people's lifestyles.

Areas of controversy: There are disagreements about the appropriate application of the precautionary principle and of the value and ethical validity of animal tests in assessing human safety.

Growing points: Most consumers have a poor understanding of the relative benefits and risks of additives, but concerns over food safety and animal testing remain high.

Areas timely for developing research: Examining the impacts of food additives on consumer sovereignty, consumer health and on animals used in safety testing should allow a more informed debate about their appropriate uses.

Keywords: food ethics/food safety/consumer sovereignty/ADHD/cancer/animal experiments/precautionary principle

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Introduction

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Several thousand different chemicals are added to processed food. The vast majority of additives raise few concerns in terms of consumer health, but for a significant number their use is ethically problematical. According to Millstone and Lang,¹ doubts have been raised about approximately 200 food additives, which for certain consumers have been claimed to cause acute intolerance or allergic reactions, or to significantly increase risks of serious long-term harms, such as cancer.

A food additive is defined in European Community (EC) legislation as 'any substance not normally consumed as a food in itself... the intentional addition of which to food for a technological purpose...'

Table 1 Categories and examples of food additives regulated for use in the EU

E numbers	Category	Examples
100–199	Colourants	Sunset yellow, tartrazine
200–299	Preservatives	Sulphites, benzoates
300–399	Antioxidants, acidity regulators	Ascorbates, phosphates
400–499	Thickeners, stabilizers, emulsifiers	Alginates, natural gums
500–599	Acidity regulators, anti-caking agents	Mineral acids and bases
600–699	Flavour enhancers	Glutamates, inosinates
700–999	Miscellaneous	Waxes, cyclamates, saccharin
1000–1999	Additional chemicals	Lipases, ethanol

results . . . in it or its by-products becoming directly or indirectly a component of such foods'.²

In the European Union (EU), additives are assigned E numbers (Table 1).³ Some additives are natural substances and others synthetic, but the distinction is blurred when naturally occurring substances are synthesised in the laboratory, and might thereby acquire unwelcome contamination. Perhaps more problematical are those additives that are xenobiotics, i.e. substances not normally produced or present in the human body, the metabolism of which might be considered of greater concern for consumers' health.

In terms of a global market approaching \$30 billion p.a., ~40% of additives are used to affect the taste, 30% the texture and 5% the appearance of food. Nearly 20% serve as processing aids, and only about 5% are added for safety reasons, to protect consumers from bacterial food poisoning and rapid deterioration of food quality.¹ The latter are crucially important in inhibiting the growth of bacteria causing conditions such as botulism, which is a serious form of food poisoning. On average, in industrialised countries, each consumer ingests 7–8 kg of food additives p.a., an amount costing food manufacturers about £12.

The legal definition of food additives is in a state of flux because in 2011 the EU will introduce a new list of authorised flavourings.⁴ About 5000 artificial flavourings are currently permitted,⁵ largely according to the criterion that the US Food and Drugs Administration (FDA) designates 'generally recognised as safe' (GRAS). The term 'additive' does not generally apply to substances added to food unintentionally, such as packaging migrants, agrochemicals used in crop production or drug residues resulting from treatment of farm animals. Although these substances are often matters of ethical concern,⁶ neither they, nor substances intentionally added to so-called functional foods,⁷ are discussed here.

Ethical prisms and principles

Virtually any public concern can be viewed through a range of metaphorical prisms, which despite some overlap, provide distinct perspectives, and may lead to different courses of action. For example, food additives can be viewed through commercial, sociological or legal prisms. The issues discussed here, viewed through an ethical prism, are aspects of food ethics⁸—itself a branch of applied ethics. An important aim of applied ethics is to assess the extent to which generally accepted ethical principles are respected when applied in a specific context.

Reference to such ethical principles is tantamount to acknowledging that within any society there is almost universal acceptance of a set of normative standards, which may be said to constitute that society's 'common morality'. These principles are derived from a combination of utilitarian and rights theories, in an approach which has been systematically developed in the field of biomedical ethics by Beauchamp and Childress⁹ and extended into non-medical fields of the biosciences by Mepham.¹⁰ To be more specific, acting ethically usually requires that account be taken of both the consequences of prospective actions, such that the intended aggregate benefits clearly exceed any harms that might be caused, and that due respect is shown for individual rights, e.g. in terms of autonomy, privacy and fair treatment. Unsurprisingly, strict adherence to the two principles (viz. utilitarianism and deontology, respectively) often suggests conflicting courses of action, so that it is more satisfactory to consider them as *prima facie* principles. This acknowledges that in making an ethical judgement (perhaps best considered as 'acting in the morally right way, all things considered'), it is widely acknowledged that respect for one or more principles, and/or specific interest groups, should be accorded greater weight than others—although there are frequently sincerely held differences of opinion on this point. In sum, the importance of applied ethics lies in objectively and transparently assessing the extent to which different *prima facie* ethical principles are observed in specific contexts.

Building on this approach, ethical concerns are here examined in relation to the potential of food additives to affect respect for three principles viz. (i) consumer sovereignty, (ii) consumer health and (iii) the rights and welfare of animals used in food safety evaluations. Within the space limits of this review and the biomedical focus of its readers, these have been selected as matters of major ethical concern, but they do not encompass all such concerns. For example, as discussed below, food additives are claimed by many nutritionists to be an essential element of the commercial success of so-called junk foods, which are often held to be responsible, at least in part, for public health concerns such as the increasing incidence of obesity, coronary heart

disease, type 2 diabetes and certain cancers. Or, if commercial criteria were included, with all the associated concerns over financial returns on investment and implications for employment, the remit of the ethical analysis would be even more extensive.

Background

In the prehistoric era, the compelling biological need for food was generally satisfied by the potent biological stimulus of hunger. Subsequently, with the emergence of role-differentiated societies, food provision for all was accomplished by a network of specialized activities subject to the strictures of market economics. But once food had essentially become a commodity it often fell victim to the temptations of profitable deception, such as adulteration, short measures and laxity in observing safety rules—practices that were progressively curbed by tighter regulation and surveillance.

However, concerns over the chemical modification of food have not evaporated. For example, in the EU in 2010, ‘25% of people surveyed were “very worried” about food additives, and a further 41% were ‘fairly worried’¹¹—data that are of undeniable ethical import. The use of food additives has been integral to developments in the global food industry over recent decades, which are characterized by terms such as ‘agribusiness’ and ‘food processing’. The traditional links between agricultural raw materials and food products have been progressively eroded in a process in which farm products are reduced to simple industrial inputs such as proteins, carbohydrates and fats. These inputs are then reconstituted in, so-called, manufactured foods, which possess many commercial advantages, such as longer shelf-life, convenience in processing and standardized composition. As a result, food has become more heterogeneous, with specific products formulated by novel processing techniques that allegedly impart the products with ‘added-value’.

To quote Roberts¹², ‘as production has become almost entirely automated, with vegetables diced, meats ground, batters mixed, doughs extruded, and ready-to-serve dinners assembled, all by computer-controlled robots at rates of thousands of units per minute, the food itself has had to be amended, often significantly, to tolerate the process’. The employment of additives has thus served to ‘repair the damage done to the food during manufacturing’, e.g. with artificial colours added to restore those lost in cooking and pulverizing, and synthetic flavours used to replace the easily damaged natural flavours. Often the addition of a single substance, like monosodium glutamate, can substitute for the range of natural flavours of meat without most

consumers noticing the difference. Additives also allow manufacturers to economize on the cost of natural ingredients and avoid the problem of their frequently limited supply, extend food's shelf life and make considerable economic savings by simplifying the complex procedures involved in cooking.

Indeed, as noted above, to the extent that nutritionists categorize some processed food as 'junk food', additives may be considered to be implicated in the adverse effects of its consumption, quite apart from the more specific effects of the additives considered here.

Defining the ethical issues

EU legislation on food additives requires that only those additives that have been explicitly authorized may be used, which depends on their satisfying three conditions:

- (i) there is a technological need for their use,
- (ii) consumers are not misled,
- (iii) additives present no hazard to consumers' health.¹³

Authorization for the sale of foods containing additives is only granted after they have been evaluated for their safety by the expert panel advising the European Food Safety Authority (EFSA). But other regulatory bodies also exercise jurisdictions over food additives, which not only define additives differently but also set standards that may differ appreciably from each other, a situation that inevitably complicates matters in a globalized food market. A body established to develop uniformity of standards for international food trade is the Codex Alimentarius Commission, which is advised in this case by the Joint Expert Committee on Food Additives (JECFA).

Whether the three pre-conditions for authorization of food additives listed above are adequately observed is ethically contentious. Thus, crucial ethical questions concerning food additives may be classed as:

- (i) consumer sovereignty, i.e. consumers' ability to act on their informed judgements about additives
- (ii) risks of any harms to consumers resulting from additive consumption
- (iii) the adequacy and effects on laboratory animals of mandatory safety evaluation procedures.

Each of these is now considered in turn, although all are closely interrelated.

Consumer sovereignty

This refers to individuals' status in respect of their informed choices over what they consume, the term implicitly echoing the time-honoured maxim 'the consumer is king'. It is thus one aspect of the broader concept of autonomy, a vital feature of human rights. In relation to food, there are strong reasons why consumer sovereignty demands explicit respect. Thus, (i) food has the capacity to profoundly affect consumers' wellbeing, either positively or negatively; (ii) any effects may not be evident until a food has been consumed for a long period (possibly extending over many years); (iii) sensory inspection is not always a reliable means of assessing food safety; (iv) the complex ways nutrition interacts with other factors, such as individual genetic predispositions or lifestyles, coupled with the low precision with which outcomes can be forecast, mean that informed food choices are intrinsically difficult.

Currently, many foods that are widely consumed contain several food additives, which it is necessary to assess in the context of consumer sovereignty. Three ethical principles are customarily taken to define consumer sovereignty¹⁴ *viz.* the target consumer should have:

- (i) the capability to understand the product and any associated risks
- (ii) a choice of goods, provided by competition
- (iii) sufficient information to judge how expectations of the goods are satisfied.

Understanding whether these principles have been adequately respected presents a challenge to consumers, the significance of which varies from, at one extreme, a case in which a familiar, naturally occurring, additive raises no safety concerns, to, at the other extreme, a case in which the additive is an unfamiliar, synthetic chemical (e.g. with an unrecognized E number), employed to impart the food with a vivid colour.

But stating the issue as one of challenges may be deceptive in some cases. This is because food preparation and food distribution in the form of prepared meals often deny consumers any realistic opportunity of making informed choices; and probably in most cases where food is provided in family or institutional settings, no conscious efforts are made to discern the provenance of the meals' constituents. Arguably in such cases, consumers might be thought to forfeit their autonomy. But an alternative interpretation is that their autonomous actions involve placing trust in the regulatory bodies that governments invest with the authority to adjudicate on food safety. The crucial question then

becomes whether the trust demonstrated is justified by the trustworthiness of the appointed trustees.

The question of public trust with respect to developments in science and medicine has received prominent recent attention, e.g. in Onora O'Neill's Reith Lectures. O'Neill pointed out that despite concerns over e.g. food safety, people often conclude that they have very little option but to continue to place trust in the system.¹⁵ In such circumstances they appear to adopt an attitude, or perhaps a culture, of suspicion, in which they are uncertain as to whether they can rely on the trustworthiness of the food industry and its governmental regulation.

Several factors affect the issue of trustworthiness. Notably, consumers' opinions depend on their perceptions of the competence and the motivation of the regulatory authorities. However, large numbers of other individuals are also directly or indirectly involved in ensuring food safety, including scientists gathering test data, technicians responsible for animals used in tests and administrative staff responsible for collating results. The evidence thus obtained is then subject to the judgements of government advisory committees pronouncing on acceptable safety standards, the accuracy of quality control procedures in food manufacturing establishments and the effectiveness of trading standards officers in monitoring international transactions. Sceptical consumers may perhaps justifiably reflect on the intrinsic instability of such long chains of responsibility. Moreover, many additives have not been subjected to recent study, with JECFA indicating that about 30% of safety evaluations are over 30 years old.¹⁶

It is arguable that the central problem of consumer trust is one of the trustworthiness of regulatory authorities¹⁷ and recent history has unfortunately provided numerous examples in which they have fallen short of consumers' expectations. Thus, before the link with new variant Creutzfeldt-Jakob Disease (vCJD) in humans was established there were repeated assertions that beef from BSE-infected cattle (i.e. with bovine spongiform encephalopathy) was safe for human consumption. And there have been many other reports of defective regulation, e.g. concerning *Salmonella*- and *Listeria*-infected meat, melamine-contaminated animal feed and residues in food of various agrochemicals. Arguably, the public trust sought by the policy-makers (the trustees) will only be achieved when trustworthiness is won. This is because people cannot simply *decide* to trust others. The process entails acquiring tacit knowledge—which by definition is almost impossible to put into words (like knowing how to ride a bicycle).

These difficulties are undoubtedly compounded by the effects of food advertising, which exerts a significant influence on food choices. For example, it was estimated that in 2004 US\$512 billion was spent globally on food advertising, an amount exceeding the national

economies of the majority the world's countries.¹⁸ Given this enormous investment, the authenticity of the concept of consumer sovereignty must surely be questionable.

An early publication specifically addressing the ethics of food additives¹⁹ claimed that it was important to invoke minority rights in considering risks to consumer health from allegedly carcinogenic additives. Such rights were, it was argued, universal and should not be thought of as only applicable to particular, disadvantaged, people: anybody might need to invoke them in certain circumstances. But the fact is that for certain people consumer sovereignty is more dependent on such rights than for others. For example, wealthy, well-educated, people might easily satisfy their food needs by only consuming expensive organic food, from which additives are excluded, whereas poor people, without private transport and with few cooking skills, might be forced to rely unduly on processed food from the corner shop, thereby often being exposed to allegedly harmful additives.

In summary, critical ethical issues concern (i) the extent to which all consumers are able to make and act on sound judgements on the safety and acceptability of food and (ii) the perceived trustworthiness of regulatory authorities and of the many components of the food supply chain.

The risks of harm to consumers

Additives have been claimed directly responsible for a wide range of disease conditions (i.e. apart from those allegedly attributable to excessive consumption of junk food). Although some of the alleged associations are probably ill-founded, there seems to be strong *prima facie* evidence for certain claims. Several public interest groups have drawn up lists of additives they consider should generally be avoided or treated with caution, especially by sensitive individuals. A prominent example is the Center for Science in the Public Interest,²⁰ whose directors include a former FDA commissioner.

In theory, safety assessments of food additives might be based on two types of evidence, *viz.* epidemiological data and results of toxicological tests. In practice, because of the complexity of people's diets, lifestyles and genetic predispositions, it is only rarely possible to derive useful data on the risks of consuming food additives from epidemiological studies. Exceptions to this generalisation almost prove the rule. For example, acute adverse reactions to foods known to contain certain substances (as in the rapid onset of asthma attacks or other allergic reactions to certain colourants) may be strongly suggestive of causal links. Some acute reactions suggest an allergic response, others may

Table 2 Alleged acute adverse reactions to consumption of certain food additives

Organ/system	Examples
Heart	Palpitations; arrhythmias
Skin	Urticaria; angiodema; pruritus; eczema; rashes
Digestive	Abdominal pain; nausea; vomiting; colic; flatulence; diarrhoea
Respiratory	Asthma; coughing; wheezing; rhinitis
Musculoskeletal	Muscle/joint aches; fatigue; weakness
Nervous system	Behaviour/mood changes; ADHD; migraine; numbness

imply intolerance. Current estimates are that food allergies affect 3–7% of young children and about 2% of adults in European countries.²¹ Table 2 lists examples of alleged reactions.

Acute effects

In 1973, Californian paediatric allergist Ben Feingold proposed that certain artificial colours and flavours cause hyperactivity in children, now classed as ‘attention deficit hyperactivity disorder’ (ADHD). His recommended additive-free diets found support from many, but were often disparaged by mainstream medical practitioners.

Recently, more substantial evidence has been provided, notably by a dietary intervention study funded by the Food Standards Agency (FSA). The study involved 153 three-year olds and 144 eight-to-nine year olds who received fruit drinks containing various levels of six colourants and one preservative additive. The researchers found that the groups of children consuming all of the additive-enhanced drinks showed significantly higher hyperactivity scores than those shown by children consuming placebos, and stated that ‘artificial colours or a sodium benzoate preservative (or both) in the diet result in increased hyperactivity in 3-year-old and 8/9-year-old children in the general population’.²² It now appears that the variability in response to additives in the study was moderated by histamine degradation gene polymorphisms.²³ The colourant additives identified as potential causal factors in ADHD responses were sunset yellow (E110), quinoline yellow (E104), carmoisine (E122), allura red (E129), tartrazine (E102) and ponceau 4R (E124).

Regulatory authorities reacted differently to these results. The FSA recommended that manufacturers and retailers find alternatives, and that parents avoid them if concerned about their children’s behaviour.²⁴ By contrast, the EFSA claimed that the results were ‘ambiguous and inconclusive’ and recommended no changes to current EU regulations pending further research.²⁵ Even so, since July 2010, use of the

six food colourants in any food requires a mandatory warning on the food label.²⁶

Chronic effects

But if establishing causal factors of acute effects is problematical, doing so for chronic effects is usually even more difficult; and the intrinsic imprecision of many evaluations is compounded by the fact that tests on individual additives take no account of synergies with other additives and dietary components. In consequence, there is an almost complete reliance on toxicological studies on animals to provide quantitative evidence.

The so-called Delaney Clause, introduced into US food safety legislation in 1958, which stipulated that ‘no additive shall be deemed to be safe if it is found to induce cancer when ingested by man or animal,’ has been a matter of contention ever since. In part, this is because it is now realized that virtually any chemical, even at a low level of exposure, might prove carcinogenic in some individuals. In practice, although some modifications to US law now permit use of certain agrochemicals that might otherwise have been banned, the clause still stands—although the *de-minimus* principle is often applied, whereby a risk of less than 1 in 1 million is considered negligible.²⁷

However, a recent illustration of the possible relevance of animal studies is the report that high dietary inorganic phosphate (Pi) levels in mice stimulate tumorigenesis, by influencing the activity of pivotal genes for lung cancer.²⁸ These appear to be important findings because (i) this condition has the highest global mortality rate of all cancers and (ii) as the authors noted, between 1983 and 1993 there was a 17% increase in addition of Pi to processed foods (e.g. meats and cheeses) to increase water retention and texture—a trend that seems likely to continue. In fact, a large number of other food additives (or their metabolites²⁹) have also been alleged to be potential carcinogens in humans, including sweeteners (like saccharin, cyclamates and aspartame), xenobiotic colourants (including the six listed above) and preservatives (such as nitrates and nitrites, which by reacting with amino acids form carcinogenic nitrosamines).³⁰

Risk assessment

The standard approach to addressing the safety of chemical hazards comprises four elements: (i) hazard identification; (ii) risk assessment; (iii) risk management and (iv) risk communication. Historically, the

elements were thought to provide a necessary separation between the scientific domain (i and ii) and the policy-makers' domain (iii and iv), thus leaving politicians with the task of managing the policy implications of the, allegedly objective, facts the scientists produce.

Accepting the insight of Paracelus ('the father of toxicology') that everything is a potential poison—the dose being the crucial factor, we can swiftly move to risk assessment as a major concern, on which the subsequent elements are highly dependent. However, matters are complicated by the ways the body reacts to ingestion of a chemical. Thus, toxicokinetic studies reveal that different dose levels can produce varying responses in factors such as stability, solubility, absorption, protein binding and metabolism—which may elicit markedly different end results.

Defined as 'the probability of harm', the significance of risk is most meaningfully expressed as the product of probability and severity. But other relevant features include the intensity, duration and reversibility of the harm, and whether it might be offset by other practices or mitigated by compensation. An important consideration is the manner in which scientific assessments of risk are employed in circumstances in which legal criteria might be more appropriate. For example, it is generally accepted that in law it would be a more grievous error to convict one innocent person of murder than to let 10 guilty persons go free. Yet scientific standards insist that a causal relationship between a chemical agent and human mortality requires that the odds be, at least, reversed. Arguably, with respect to the burden of proof, the current situation for the safety evaluation of additives should accord much more with the legal approach than with that standard in scientific research.³¹

Moreover, the traditionally acknowledged distinctions between risk assessment, management and communication are open to severe criticism. While risk assessment is often considered an objective process that necessarily entails the rigorous application of scientific methods and probability theory, it would be false to assume that the resulting recommendations are indisputable. This is because risk assessment is far from being value-free. Rather, the experts who produce the data for the risk analysis are constrained by the framing assumptions of their enquiries, which include: the types of question they seek to answer and those they neglect, the types of evidence deemed relevant and those discounted or ignored and the ways the evidence is interpreted.³² These assumptions might seriously affect (i) the reliability of extrapolating from laboratory test results to conditions in which people consume food in the real world, (ii) the time and resource investments considered appropriate for adequate testing and (iii) the skills, experience

and presumptions of the experts chosen to make policy recommendations.

At issue here is the appropriate application of the precautionary principle, which states that lack of scientific certainty should not be used as a reason to ignore or postpone preventive or remedial action when there are other good reasons to do so, i.e. the principle aims to address the problems of uncertainty. The sheer complexity of the cocktail effect of a wide range of diverse individuals consuming *inter alia* numerous food additives exemplifies the latter factor. The issues of uncertainty and variability in response to chemicals in food were addressed recently in the UK in a report of the Committee on Toxicology (COT).³³ This noted that while both toxicokinetic and toxicodynamic variability arise from a combination of inherent factors (e.g. gender and genotype) and factors related to physiology and the environment, which change over time, these are modulated by a range of other circumstances such as age, stage of development and functional maturation of organs and systems, co-exposure to other agents and compounds (e.g. nutrients), lifestyle, environmental factors and disease. While in theory this variability is measurable, in practice the virtual impossibility of collecting and interpreting the data accurately for any individual means that variability usually equates with uncertainty.

But the precautionary principle 'is not only about uncertainty, ignorance and caution, but also about policy and action',³⁴ The principle has several forms,³⁵ but, with different degrees of emphasis, all address questions relating to the importance to be assigned to health and sustainability, proactive approaches to acceptable risk and the location of the burden of proof. It is surely an accurate assessment that 'however the principle evolves, the value of acting in a precautionary manner is obvious to those in public health'.³⁶

In summary, the critical ethical issue relating to human health concerns the effectiveness of risk assessment and management procedures employed in evaluating the safety of food additives.

The validity of safety evaluations and their effects on test animals

Risk analysis is conventionally divided into dose-response evaluation and human exposure evaluation. A notionally ideal system of safety testing would entail recruitment of a large number of human volunteers, representative of the whole population, whose biochemical, physiological and pathological responses to long-term consumption of additives in all feasible combinations (extending over more than a

single generation) were studied in fine detail. Because the scenario is clearly both ethically and practically unrealistic, the principal alternative approach involves tests on non-human animals, the use of which is mandatory.

The current EC guidelines on the evaluation of food additives consist of a set of core studies (Table 3),³⁷ but others may also be required in specific cases, including those that aim to evaluate responses in the following categories: immunotoxicity, allergenicity, neurotoxicity and intolerance reactions. The use of rigorous scientific tests might suggest that consumers can be reassured as to the safety of food additives. Thus, according to the European Food Information Council, 'Thanks to strict regulation and thorough testing, food additives can be considered safe components of our diet that are contributing to the rapid evolution of the food supply in Europe and throughout the world'.³⁸

Arguably, however, this opinion is highly questionable. For example, dose-response evaluations often entail feeding to laboratory animals (in the diet or by gavage) a range of amounts of the test substance, followed by *post-mortem* examination of body tissues. As few as 2–3 dose levels may be used, generally at high levels. From these few points, it is standard practice to extrapolate the response curve to determine the level at which no adverse effects are observed (the NOAEL). By convention, the safe level to which humans should be exposed in their diets, over a lifetime, is calculated by dividing the NOAEL, expressed per kg body weight, by one hundred. The amount calculated is the acceptable daily intake (ADI). This rule of thumb allows a factor of 10 to account for possible inter-species differences in responses, and a further factor of 10 to account for different degrees of sensitivity to potential toxins within the human population. The COT

Table 3 EC guidelines for core studies to evaluate the safety of food additives

Study objective	Nature of studies
Metabolism and toxicokinetics	Animal studies with single or repeat dosing
Subchronic effects	Two species (rodent and non-rodent) over at least 90 days
Genotoxicity	A battery of three tests investigating: <ul style="list-style-type: none"> Gene mutations in bacteria Gene mutations in mammalian cells <i>in vitro</i> Chromosomal aberrations in mammalian cells <i>in vitro</i> with genotoxicity testing <i>in vivo</i> when positive results to above are obtained
Chronic toxicity and carcinogenicity	Dietary administration to two species (rodent and non-rodent) over the majority of life spans (~18–24 months)
Reproductive toxicity	Multigeneration studies (dietary administration) in one species (usually rat) for at least two generations, with at least one litter per generation
Developmental toxicity	Two laboratory species (rodent and non-rodent), with administration by diet or gavage

report claimed that these factors are adequate in allowing for interspecies differences and differential vulnerability, but also suggested that they were capable of refinement, and recommended that ‘this area be kept under review’. As an alternative to the NOAEL, the report also discussed the benchmark dose level, for assessment of risks where no specific thresholds have emerged (such as carcinogenicity), which is claimed to make use of all the dose-response data and reduce the degree of uncertainty.³⁹

Unfortunately, the NOAEL approach relies on several questionable assumptions. For example, (i) for some substances, such as genotoxic carcinogens, there is no definable NOAEL; (ii) different end-points give very different NOAELs; (iii) to limit costs, testing is typically performed with the maximum doses that can be tolerated, a strategy of questionable validity from both ethical and scientific perspectives. Moreover, ‘we are not 70-kg rats: we take up substances differently, we metabolize them differently; we live longer’.⁴⁰ For these and other reasons, current procedures used to evaluate the safety of food additives are ethically problematical. According to Thomas Hartung, former director of the European Centre for the Validation of Alternative Methods (ECVAM), ‘There is almost no other scientific field in which the core experimental protocols have remained unchanged for more than 40 years’,⁴⁰ a situation which has been prolonged by resistance to changes necessary for international harmonization.

The imprecision of standard procedures is compounded by the reliance on animals when the moral standing of non-humans is commanding increasing recognition. For example, the three Rs criteria, which are enshrined in EU law, stipulate that experimental use of animals may only be allowed when consideration has been given to: (i) *replacing* conscious animals by insentient material; (ii) *reducing* the numbers of animals used to obtain information of a given amount and precision; and (iii) *refining* the tests in order to decrease the incidence or severity of stressful procedures.⁴¹ Few would deny that these provisions represent an ethical advance in the treatment of animals. Even so, certain tests still entail high animal usage, e.g. a single two-generation test for reproductive toxicity requires an average of 3200 animals.⁴⁰ Moreover, food additive testing is open to the serious criticism that it is often performed for agents employed for purely cosmetic purposes, e.g. colourants, when animal testing of cosmetics *per se* is now illegal in the EU. The ‘particular concern about toxicity testing of what many perceive to be trivial products’ was identified in an informative report of the Nuffield Council on Bioethics.⁴²

Tests on animals have other serious limitations. Usually they are only performed once, and are not open to scrutiny by others, which is the normal quality control procedure employed for scientific publications.

Moreover, to calculate ADIs tests are generally performed on single substances. But because there can be no control over individual's consumption patterns, which might often include a range of foods containing the same or interacting additives, the mere citation of individual ADIs would demand that in order to 'play safe' consumers would need to pay unrealistic attention to food labels.

Alternatives to animal tests

Several organizations in the EU, notably ECVAM, have been established to replace animals in experiments and safety testing by developing alternative methods, such as cell and tissue cultures, molecular research, computer modelling, use of microbes, improved literature searching and clinical research with human volunteers. In the UK, this role is performed by the National Centre for the three Rs. But it is clear that one way to reduce animal testing would be to limit use of unnecessary, potentially hazardous chemicals.

In summary, large numbers of animals are used in safety evaluations of food additives. In view of the legal requirement to observe the three Rs, it is questionable whether the current practice is justifiable in terms of the suffering inflicted on the animals, the infringement of their putative rights or the claimed benefits for consumers.

Conclusions

The aim in this review has been to examine food additives through an ethical prism, i.e. one that prioritizes concern for respecting key ethical principles, focusing on the ethical impacts of direct effects of their presence in food. Thus, the central issues concern the alleged 'technological need' for additive use, the degrees of consumer safety and sovereignty that can be guaranteed, and the justifiability of using sentient non-human animals in toxicity tests.

The analysis presented suggests there is a strong case for significant changes in food manufacturers' employment of certain food additives, in the levels of precaution adopted in their legal authorization and in the reliance placed on, and conduct of, tests performed on animals. Or, adopting a more rhetorical tone, it is arguable that in some cases the current evaluative procedures are blunt instruments that entail unwarranted animal suffering, in pursuit of trivial aims and without due regard to longer term public health outcomes.

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