Food: Flavourings, Ingredients and Processing, 1980 ROE1980A

Copies of printed version not available

EXPERIMENTAL TOXICOLOGY BACKGROUND TO FACC REPORT ON FOOD COLOURS

Author: Francis J.C. Roe
DM(Oxon), DSc (Lond), FRC Path.

I must point out that anything I say is an expression of my personal opinion and does not represent the view of the Committee on the Toxicity of Chemicals in Food (COT) on which I serve.

The FACC Report

The Report concerns 50 colouring matters of which 40 were permitted for use by the 1973 Colour Matter and Food Matter Regulations, and 10 were not permitted by those or subsequent Regulations for food use, but have been requested by the trade (8) or suggested by FACC (2). Of the 40 permitted under the 1973 Regulations, 3 had been banned from use in the UK prior to 1978. Tables 1-4 list the colours in these different categories.

Of the 50 Colours, 19 were eventually classified by the COT in Group A - i.e. as substances that the available evidence suggests acceptability for use in food; 17 were classified in Group B - i.e. as substances that on available evidence may be regarded meantime as provisionally acceptable for use in food, but about which further information is necessary and which must be reviewed within a specified period of time; a further 11 were classified in Group E - i.e. as substances for which the available evidence was inadequate to enable an opinion to be expressed as to their suitability for use in food; 2 were classified in Group F - i.e. as

substances for which no information on toxicity was available; and Chocolate Brown FB was not considered as it was no longer available.

In the case of substances classified in Groups B, E or F, unless more evidence of safety is forthcoming within a prescribed time, permission to use in food will not be granted or possibly withdrawn if presently permitted. It is presumably this requirement for further evidence of safety that has been the stimulus for the present meeting.

General Comments

The whole concept of artificially colouring food is evocative. Food Manufacturers know, or think they know, what the public wants. To be more precise they endeavour to find out what they can sell to the largest number of people. Colours are sometimes used in the belief that they make food appetising. More often, perhaps, they are used to confer on a food a standard appearance which comes to be taken as an index of quality or good condition. Whatever the reasons for adding colours to foodstuffs there is a sizeable minority of the general public whose image of food colours is "candy floss" which they personally regard as both unnecessary and unappetising. However misguided it may be, there is a seemingly growing preference for the 'natural' over the 'artificial' as witnessed by the explosive expansion of sales of health foods; and more and more people are becoming suspicious of foods which are unnaturally coloured. In my opinion the Food Industry has so far done a lousy job in justifying the widespread use of food colours, particularly gaudy and unnatural colours, to members of the public.

Now it isn't within the terms of reference of the Committee on Toxicity to question the need for particular food additives. This is the perogative of the Food Additives and Contaminants Committee. It is noteworthy, therefore, that in paragraph 12 of their report the Committee on Toxicity found fit to remind the FACC of the provision in the Food and Drugs Act 1955 that requires "regard to be given to the desirability of restricting, so far as practicable, the use of substances of no nutritional value as foods or as ingredients of foods". They further went on to recommend that the addition of colouring matter to foods specially prepared for infants and young children under 12 months old, should no longer be permitted.

How does one assess the likely safety of a Food Colour?

The principles to be followed in the assessment of the safety of a food colour are the same as those for any other food additive. In simple terms answers are sought to the following questions:-

(i) What are its use and purpose?

(ii) What is its chemical structure?

(iii) How pure is it? What are the known contaminants? Does the method of its manufacture suggest the possibility of contamination with toxic substances?

(iv) How is it metabolised in animals and man? Is the formation of toxic metabolites a possibility?

(v) Is it a secondary amine that could react with nitrites to form a carcinogenic nitrosamine?

(vi) What are the target organs for toxicity if animals are exposed to very high doses?

(vii) Is there an adequate margin between proposed use levels in human food and minimum toxic dose levels as predicted from animal studies?

(viii) Is it without detectable toxic effect in short-term studies (e.g. 90 days in the rat) at dose levels up to 100 times the maximum levels to which humans are likely to be exposed?

(ix) Is it without detectable toxic effect in long-term studies (e.g. 2 years or life-span rat) at dose levels up to 100 times the maximum levels to which humans are likely to be exposed?

(x) Is it a teratogen? Is it without adverse effect on reproduction?

(xi) Is it a mutagen?

(xii) Is it a carcinogen?

(xiii) Is it an allergen or sensitizer?

(xiv) Is it likely to interact with food constituents, other food additives or drugs to produce toxins?

(xv) Does it belong to a class of similar food chemicals which need to be regulated as a group because the effects of individual substances are likely to be additive?

This list of questions is not necessarily to be translated directly into demands for relevant laboratory studies. Every effort should be made to apply common sense in relation to every aspect of safety assessment. The fact that a particular food colour is of natural origin and/or is identical chemically to a colour occurring naturally does not automatically mean that it is free from toxicity and could not constitute a cancer hazard. On the other hand, it would be absurd to ask for tests on chlorophyll since there is no conceivable regulatory action that could prevent exposure to it.

In the case of artificial colours it is more likely that a fairly complete shopping list of tests would be deemed necessary. However, in this country at least, the costs and wastefulness of unnecessary tests are well appreciated, so that 'clearance by analogy' is sometimes practiced if toxicologically justifiable and commercially fair.

The Committees on which I serve take great pains to avoid unnecessary and costly testing, and sometimes, if they do slip up, it is because they do not have available to them all the information available to the prospective user. In such cases the latter should not hesitate to bring the missing information to the notice of the appropriate authorities. There will in fact have been plenty of opportunity to do this before the publication of FACC/Rep 29.

Failure to undertake tests

During the recent Review of Food Colours, it was apparent that Industry had, in some cases, made little or no attempt to provide information requested at the time of the previous Review. This has been a cause for concern but not by itself

a reason for downgrading any food colour in the present Review. Whether a less lenient policy will be followed in future, I cannot say.

Quality of data provided

I should emphasise that what Regulatory Committees ask for is evidence of safety in relation to particular potential kinds of toxicity rather than for particular tests to be carried out. In some cases of course there may be no way of answering a question other than by carrying out a test of a routine nature (e.g. standard 90-day test, standard teratogenicity test, etc). Even so, it is a satisfactory negative from such a test that is needed not merely evidence that an appropriate test has been carried out.

During recent years the quality of test data required has risen steeply. This has affected the numbers of animals used, their randomization between groups, the range of observations made, the standard of observation and the method of statistical evaluation. In a few instances this has meant that tests regarded as adequate at the time of an earlier Review are no longer regarded so, with the result that new tests using modern techniques are deemed necessary. However, in cases where new tests have been asked for, there is usually some additional reason behind the decision (e.g. positive results in mutagenicity tests).

The Committees on Toxicity, Carcinogenicity and Mutagenicity are presently preparing guidelines for the conduct of tests. Perusal of these will help to clarify how and why data from tests are sometimes regarded as inadequate.

Route of administration and dose

It is now generally accepted that oral administration is normally appropriate for tests on prospective food additives. The days of testing food colours by subcutaneous administration in rats are over, except perhaps in peculiar and special circumstances. Admixture with diet or administration in drinking water is usually preferable to administration by gavage for a food additive. In the case of essentially non-acutely-toxic materials, it is now generally accepted that giving them at such high concentrations in food (e.g. 5%) that the nutritional status of animals is interfered with, is neither, as a rule, necessary nor sensible.

Interpretation

It is sometimes debatable whether an effect recorded (e.g. simple enlargement of an organ such as the liver) is a manifestation of toxicity or merely an adaptive response. In the case of enlargement of the caecum as occurs in animals exposed to caramel colours, it is now generally accepted that this is merely a consequence of the inability of animals to break down certain moieties of the colourant except as a result of bacterial degradation in the large bowel. This change is therefore not to be regarded as a manifestation of toxicity. However, it is usually an indication that humans exposed to similar concentrations might suffer from bulky and/or offensive stools or even frank diarrhoea. Caecal enlargement might also be associated with disturbance of mineral metabolism. Thus, in high concentrations in the diet, lactose predisposes inter alia to increased calcium absorption and excretion. Under extreme conditions this change in calcium metabolism results in various manifestations of nephrocalcinosis. In other cases, however, it seems that caecal enlargement is

associated with decreased calcium absorption, perhaps because carbohydrates which even large-bowel bacteria can't get their teeth into, chelate calcium and prevent its absorption. There is, I hasten to add, no evidence that any of the caramel colours influences calcium metabolism in either direction. I will say nothing more about caramel colours since Mr Barber is speaking at length on this subject.

Absorption

It is not infrequently suggested that elaborated tests are not necessary because a substance is not absorbed. Regulatory Committees should be forgiven for being skeptical about this unless sound evidence of non-absorption, based on the use of sensitive methods, is provided. Notwithstanding this you will note that gold was permitted for use on the grounds that it is not absorbed. I cannot remember how good the evidence for non-absorption is, but personally I remember feeling rather sorry that I don't absorb this precious metal!

Sensitization

I propose to duck saying anything about hypersensitivity reactions since Miss Whitehall from BIBRA is dealing with this topic at length.

Concluding remarks

For those who have studied the FACC Report, I doubt very much whether I have said anything useful. For those who haven't read it but feel aggrieved by its conclusions I can only advise that they read it in the knowledge that those who contributed to the decisions are, in the main, reasonable people making great efforts to come to reasonable conclusions.

FJCR
23-10-79

TABLE 1 - Colours permitted under the Colouring Matter in Food Regulations, 1973 and not subsequently banned

E100	Curcumin
E101	Riboflavin
E102	Tartrazine
E104	Quinoline Yellow
	Yellow 2G
E110	Sunset Yellow FCF
	Orange G
E120	Cochineal
E122	Carmoisine
E123	Amaranth
E124	Ponceau 4R
E127	Erythrosine BS
	Red 2G
E131	Patent Blue V
E132	Indigo Carmine
	Brilliant Blue FCF
E140	Chlorophyll
E141	Copper complexes of chlorophyll and chlorophyllins
E142	Green S
	Brown FK
	Chocolate Brown FB
	Chocolate Brown HT
E150	Caramel
E151	Black PN
E153	Carbon black
E160(a)	alpha-, beta- and gamma-Carotenes
E160(b)	Annatto, bixin and norbixin
E160(c)	Capsanthin or Capsorubin
E160(e)	beta-apo-8-Carotenal (C30), (8'-Apo-beta-caroten-8'-al)
E160(f)	Ethyl ester of beta-apo-8'carotenoic acid (C30), (Ethyl 8'apo-beta-caroten-8'oate)
E162	Beetroot Red
	Paprika
	Tumeric
E171	Titanium dioxide
E172	Iron oxides and hydroxides
E175	Gold
	Methyl violet

TABLE 2 - Colours permitted under the 1973 Regulations but subsequently banned from use in food

E105	Fast Yellow AB
E130	Solanthrene Blue RS
E152	Black 7984

TABLE 3 - Colours not permitted for use in 1978 but requested by the Trade

Allura Red AC
Antheraxanthin
Citranaxanthin
Red 10B
Stabilised blood pigment
Ultramarine
Violet BNP
Violet 6B

TABLE 4 - Colours reviewed by COT at the request of FACC

Methyl ester of beta-apo-8' carotenoic acid (C30), (Methyl 8'-apo-beta-caroten-8'-oate)

Riboflavin-5'-phosphate, (Riboflavin 5'-[sodium phosphate])