European Food Safety Authority

Sharing experience: the re-evaluation of colours by the Panel on Food Additives and Nutrient Sources added to Food

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Why was a review needed?

- Nordic Council of Ministers report
  "Food Additives in Europe 2000"
- Reviewed the status of safety assessments of all food additives permitted in the EU
- Concluded
  - No need for urgent action on any additives
  - Noted many not re-assessed for many years
  - In some cases new literature warrants re-assessment
  - In some cases uses should be re-assessed to ensure exposure complies with SCF recommendations

Changed expectations

- Greater emphasis on transparency
- Expectations of stakeholders
- Data requirements for botanicals published
- Scientific understanding has moved on

Why start with colours?

- Scientific Committee on Food (SCF) established in 1974 – colours evaluated first
- Most SCF opinions on colours for foods now 20-30 years old
- European Parliament (EP) has taken particular interest in colours and sweeteners
- In 2004 EP asked for all permitted additives to be reviewed

Likely issues for natural colours envisaged in 2004

- Methods of production that go beyond physical processes
- Production from non-edible sources
- Inadequate specifications
- Estimates of intake from normal diet, excluding uses as food colour
- Increases in uses and/or use levels and estimates of intake as food colour
- Toxicity data not previously considered in EU
- Possible need for additional toxicity data to be generated

Likely issues for synthetic colours envisaged in 2004

- New toxicological data may show some effects of concern
- Differences between SCF and JECFA views
- Basis of SCF acceptable daily intake (ADI) unclear
- Possible need for additional toxicity data to be generated
- Some ADI values may need to be changed
- Increases in uses and/or use levels and estimates of intake as food colour

Original concept

- Initial screen to decide if full or partial re-evaluation necessary

Stage 1: Information gathering and report on each additive (contracted out)

- Examine original SCF opinions/dossiers to establish what data were available and what was basis for conclusions
- Brief summary and dates of any JECFA evaluations
- Consider comments in Nordic 2000 report
- Update literature search from 2000

Stage 2: Decision on full or partial re-evaluation

- Critical data gaps
- Uncertainties in existing data
- New evidence of potentially harmful effects

Criteria proposed for a re-evaluation

- Reported adverse effects in humans and new toxicological studies will be given greatest weight
  - intakes are likely to **exceed the ADI**, further consideration
    - » nature of the critical effect(s)
    - » adequacy of the uncertainty factors
  - human case reports of actual or alleged **adverse effects**,
    - » evidence of reproducibility of effects
    - » well-designed and controlled studies
  - **toxicological studies**
    - » results that differ from previous data
    - » equivocal findings

- The **quality** of the data will also be assessed.
  - Routine toxicological studies will be expected to conform to GLP if conducted after 1982

Obtaining further data

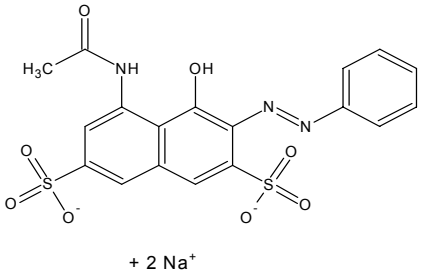
- Provision of data by industry and other interested parties

Manufacturers and users will be given opportunity to provide data within a specified time limit for any data gaps and uncertainties identified at screening stage in:

- Chemistry
- Specifications
- Manufacturing process
- Methods of analysis
- Reaction and fate in foods
- Uses and use levels in foods
- Exposure
- Toxicity data

Expectation meets reality!

- First additive completed was Red 2G



- Breaks down with release of aniline
- New data on genotoxicity and carcinogenicity of aniline
- ADI withdrawn

What were the outcomes?

Can the previous ADI be confirmed?

- Three of the azo dyes were judged to be of safety concern, ADI withdrawn (Red 2G, Brown FK, Litholrubine)
- ADIs reconfirmed for Tartrazine, Azorubine**, Allura Red,** Brilliant Black, Erythrosine, Green S
- ADIs lowered compared with SCF and/or JECFA for Sunset Yellow, Ponceau 4R, Brown HT, Amaranth, Quinoline Yellow, Patent Blue V, Brilliant Blue FCF

Reasons for revoking ADI or establishing a new one?

- Genotoxicity (Red 2G)
- Data quality (Brown FK, Litholrubine BK)
- New data (Sunset Yellow, Allura Red)
- Different conclusions drawn from same data set
  - **Ponceau 4R: SCF/JECFA NOAEL 375 mg/kg bw/day, EFSA 70 mg/kg bw/day**
  - **Amaranth: JECFA NOAEL 50 mg/kg bw/day, SCF 80 mg/kg bw/day EFSA 15 mg/kg bw/day**
  - **Brown HT SCF NOAEL ??, JECFA and EFSA 143 mg/kg bw/day)**

Natural colours

- Few toxicity data were available to SCF

- Evaluations were based on
  - assumption that they originate from food
  - amounts consumed would not differ significantly from that obtained naturally from foods in a normal diet
  - specifications and use levels agreed subsequently would reflect these presumptions

SCF opinions on natural colours

- First series report (1975) classified colours into those for which:

  1. An ADI could be established
  2. A temporary ADI could be established
  3. An ADI could not be established but the colour was acceptable or temporarily acceptable
  4. An ADI could not be established and the colour was not toxicologically acceptable for use in food

- Third category seen as exception needed for colours that are **constituents of foods** and **derived from coloured natural foods by purely physical processes**

The SCF caveats

- If natural colours are
  - In widespread use
    (i.e. consumed in amounts significantly greater than that obtained from the normal diet)
  - From natural sources but not from natural foods
  - Prepared synthetically
    (method other than physical extraction)

  Then they need to be tested adequately for safety before being accepted

Reality

- Evaluations of natural colours have been more challenging than envisaged
- Why?
  - Range of sources
  - Differences in production methods
  - Unsuitable models
  - Limited exposure data
    - Uses and use levels
    - Dietary intake
- Elephant in the room

Finished evaluations

- Lutein
  - ADI of 1 mg/kg bw/day refers to lutein derived from *Tagetes erecta* containing ≥80% carotenoids consisting of lutein and zeaxanthin (79 and 5% respectively) and to lutein with high concentrations of total carotenoids extracted from *Tagetes erecta* and present as esters at levels of at least 60%.
  - toxicological data-base available is too limited to conclude that the ADI also applies to lutein preparations of lower purity or from other sources.
- Caramel colours
  - group ADI of 300 mg/kg bw/day for the caramel colours, Within this group ADI, the Panel establishes an individual ADI of 100 mg/kg bw/day for Class III due to new information regarding the immunotoxicity of THI
- Lycopene
  - ADI of 0.5 mg/kg bw/day

Unsuitable and suitable models

- Carotene
  - The Panel concluded that based on the presently available dataset, no ADIs for mixed carotenes and β-carotene can be established and that the use of (synthetic) β-carotene and mixed β-carotenes obtained from palm fruit oil, carrots and algae as food colour is not of safety concern, provided the intake from this use as a food additive and as food supplement, is not more than the amount likely to be ingested from the regular consumption of the foods in which they occur naturally (5-10 mg/day). This would ascertain that the exposure to β-carotene from these uses would remain below 15 mg/day, the level of supplemental intake of β-carotene for which epidemiological studies did not reveal any increased cancer risk. Furthermore, the Panel could not conclude on the safety in use of mixed carotenes [E 160a (i)]
- ß-apo-8'-carotenal (E 160e)
  - ADI for β-apo-8'-carotenal of 0.05 mg/kg bw/day established

Complex conclusions

- Anthocyanins
  - currently available toxicological database was inadequate to establish a numerical ADI for anthocyanins
  - For anthocyanins extracted from edible fruits and vegetables by aqueous processes, changes in composition would not be expected. The Panel concluded that provided exposure from use as a food additive was comparable to that from the diet the underlying conclusion in the 1975 SCF opinion that such food additives derived from natural sources would still apply. The majority of data are on aqueous grape skin extract (GSKE) and blackcurrant extracts and the Panel considers that exposures estimated from current uses and use levels these extracts are unlikely to be of safety concern.
  - For anthocyanins extracted from other sources and/or using non-aqueous extraction methods the absence of characterisation does not allow verification that this conclusion in the 1975 SCF opinion could be applied.

ADI unchanged

- Canthaxanthin

  ADI of 0.03 mg/kg bw/day

- Curcumin

  ADI of 3 mg/kg bw/day

- Vegetable Carbon

  at the reported use levels vegetable carbon (E 153) containing less than 1.0 µg/kg of residual carcinogenic PAHs expressed as benzo[*a*]pyrene is not of safety concern

Still on-going

- Sunset yellow E110
- Indigotine, indigo carmine E132
- Titanium dioxide E171
- Chlorophylls E140i
- Iron oxides E172
- Beetroot Red E162
- Annatto E160b
- Copper complexes of Chlorophylls E141i
- Chlorophyllins E140ii
- Copper complexes of Chlorophyllins E141ii
- Paprika extract E160c
- Cochineal E120

Conclusions

- Re-evaluation has been more challenging than expected:
  - Expectations on transparency are higher
  - Incomplete databases
  - Availability of original data is poor
  - Newer published studies not always relevant
  - Limited exposure data
  - Societal appetite for risk is generally low