# Navigating the EU regulatory system - how to capitalize the learnings from the lycopene authorisations

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IACM Global Color Conference, Arlington, VA, USA





**EU Regulatory System** 

**Regulatory History of Lycopene** 

What can we learn from lycopene?

- legal names
- formulations
- specifications





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#### The principal rulemaking process of the EU (new/amended regulation) Stakeholder interaction/lobbying



- executive body of the EU
- propose legislation

The European

parliament (EP)

directly elected

parliamentary

represents the

interest of the

**European citizens** 

- implementing decisions
- upholding EU treaties
- day-to-day business of the EU



#### Proposal for a legislation



The Council of the European Union (Council of Ministers, Council, Consilium)

NATCOL

Natural Food Colours Association

on technical issues

- represents the executive governments of the EU MS



**New/amended regulation** 

#### The three pillars of EU risk analysis



#### Who is involved?

### **Regulatory event**

- change in existing legal specification of a food colour
- new entry of a legal specification
- change in the use conditions of a food colour in finished foods
- change in the additives/carriers than can be used in a food colour formulation







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50 ppm lycopene













# Synthese (Chemie)



Fungus Blakeslea trispora



Tomato fruit





#### Lycopene dispersion in a beverage





#### Carotenoids regulatory history – more than 50 years

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COUNCIL DIRECTIVE	•
on the approximation of the rules of the Member States concerning the colouring matters authorised for use in foodstuffs intended for human consumption	
THE COUNCIL OF THE EUROPEAN ECONOMIC COMMUNITY, being understood that during that period the Council may, in the light of any scientific research carried out, take decisions as to the authorisation of such colour-	
Having regard to the Treaty establishing the Euro- pean Economic Community, and in particular Ar- ticles 100 and 227 (2) thereof;	
HAS ADOPTED THIS DIRECTIVE:	-

NATCOL

1962 - Commission Directive 62/2645/EEC on the approximation of the rules of the member states concerning the colouring matters authorised for use in foodstuffs intended for human consumption:

*Synthetic chemical products which are identical to the natural colouring matters listed below are also authorised.* 

...Carotenoids

(d) lycopene (all the trans forms)



#### Lycopene – safety assessment followed after its authorisation

#### First scientific (safety) assessment in 1975 by the SCF, later on in 1983 and 1987

1975 statement: "Colours for which an ADI could not be established but which are nevertheless acceptable for use in food:.. for use in foods generally: ...lycopene (from natural foods)

1983: reiteration of the 1975 opinion explaining that...

the use of colouring matters extracted from foods would not be expected to result in ingestion differing substantially from the amount likely to be ingested from the normal consumption of the foods in which they occur. The Committee continues to hold the same opinion.



And what else happened between 1975 and 1983?





1979 founding year of NATCOL in Basel, Switzerland by Hoffmann-La Roche





#### Lycopene – safety assessment followed its authorisation

#### SCF's view on "natural materials" expressed 1987

Most of the substances examined by the SCF during their review were extracts of materials the *chemical composition of which was not well defined*. SCF has insisted on several occassions that colourings isolated from *natural materials*, even if they are derived from foods, *cannot be held to be safer a priori than synthetic material*.....The SCF reaffirms that whilst it could accept a number of colouring matters from food without a formal ADI it draws attention to the fact that the *acceptance is limited* to situations under which the use of colouring matters extracted from foods would *not* be expected to result in ingestion *differing substantially* from the amounts likely to be ingested from *normal consumption* of the foods in which they occur. .....



#### Lycopene – the risk assessors desire for modern safety assessment

SCF's view on lycopene, expressed 1987

The Committee has already in 1975 accepted the use of lycopene obtained from foods by physical means although it had been unable to set an ADI. The committee has no objection to the continued use of such material but points out that it has already commented about the use of natural products and the possible extension of their use in the present report. If a synthetic substance would become available, the Committee would expect to evaluate it in terms of a modern toxicological data base appropriate to the substance and its intended use.





#### 1995: Revision of legally binding food colour specifications

Commission Directive 95/45/EC laying down specific purity criteria concerning colours for use in foodstuffs:

Whereas it is necessary to revise the purity criteria for colours mentioned in the Council Directive of 23 October 1962....

Whereas food additives, prepared by production methods or starting materials significantly different from those included in the evaluation of the Scientific Committee for Food, or different from those mentioned in this Directive, shall be submitted for evaluation by the Scientific Committee for Food for the purposes of a *full evaluation with emphasis on the purity criteria...* 

In the annex of Directive 95/45/EC, only lycopene from tomatoes listed.



#### 1999: Scientific Committee on Foods not satisfied with lycopene safety

April 1997: Hoffmann-la Roche AG: Submission of a lycopene dossier for approval of a lycopene specification under Regulation 95/45/EC for food colour use

SCF 1999: The present application seeks an extension of the specifications laid down in Directive 94/45/EC,..., to include lycopene produced by chemical synthesis containing not less than 96% lycopene. The proposed specification `not less than 96 %` lycopene is not acceptable because highly concentrated lycopene is sensitive to oxygen and light, forms degradation products with mutagenic activity, and is not identical with the beadlet formulation that has been tested toxicologically.... The toxicological data provided on the beadlet formulation are insufficient. Therefore, the Committee is not able to allocate an ADI and considers its use in food is unacceptable at present.

→ Regulatory approach of 1962 for chemically synthesised «nature identical» colours is definitely history.





#### 1997 – 2011 : 14 years for lycopene to get approval as a food colour





#### Lycopene as a nutrient- the race to obtain novel food approval





#### NF approval – exemplified timeline

Oct 30 2003: Vitatene dossier lycopene from Blakeslea trispora to UK ACNFP panel,

April 6 2004 UK report, send to EC

April 27 EC to all EU member states for 60 days comment period

May/June reasoned objections raised by EU MS

November 22 2004 dossier to EFSA

April 21 2005 EFSA opinion published

Oct 23 2006 EC decision 2006/721

36 month (3 years)

Approval as a novel food





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- formulations



- specifications

What can we learn from lycopene for the upcoming revision of the legal color specifications as part of the EU food additives reevaluation program?



## Be certain about the desired legal name for your product

Legal names  $\rightarrow$  ingredient list on finished food

Requirements for legal names  $\rightarrow$  regulated in Regulation (EU ) 1169/2011 (Food Information to Consumers)

- not mislead consumers
- legal/customary/descriptive name
- disclose nature of the substance, differentiation from similar substances

Legal name for food additive (incl. colours) provided for in the legal specification in Regulation (EU) 231/2012

Applicant dossier "synthetic XY" → EC/MS likely to follow proposal

But "natural XY"  $\rightarrow$  no definition, Fair information practices (Art 7 Reg (EU) 1169/2011) applies

GM origin/GMM use → GM tracetability regulation applies ((EC) 1830/2003); e.g. colour Riboflavin) Color formulations – choose your own recipe? Industry call: Legal specifications should cover the "pure" substance only

#### Regulators tend to focus more than before on the formulations

Annex III Food Additives Regulation 1333/2008 regulates



- carriers and other food additives in formulations
- permitted carry over into finished food applications
- reverse carry over remains acceptable
- common food ingredients remain permitted

New novel food regulation includes certain nano-sized ingredients in its novelty definition subject to premarket approval  $\rightarrow$  Dual use substances (lycopene, riboflavin,  $\beta$ -carotene)



## Nano-size formulations- what does the future hold?

Food Additive Regulation , Art 12

...significant change in production methods or starting materials ...or change in particle size, for example through nanotechnology, ...shall be considered a different additive ...

→ New pre-market approval required



New Novel Food Regulation , Art 3

Novel food means ...

...food consisting of engineered nanomaterial...

Vitamins...and other substances ...where they *contain* or consist of engineered nanomaterial

→ pre-market approval required



Nanomaterial definition not limited to "solid" particles NF regulation impact on interpretation of Art 12? Impact on dual use ingredients (color/nutrient)

## **Residual solvents**

#### Origin matters and must be recognised case by case

- natural occurring volatile organic compounds (VOC) from the plant used as starting material, e.g. methanol, ethanol, acetone, Stecker aldehydes, dimethylsulfide,...
- solvent used during synthesis
- extraction solvent used to extract color from starting material
- sustainability aspect: solvents are rectified (re-distilled) for continuous use
- → VOC impurity profile of solvent changes

#### Risk based approach

- benchmarking with extraction solvent directive
- for some VOC: no other limit than GMP

- solvents used in the manufacture of a formulation are processing aids subject to the general provisions for processing aids in food additive regulation (EU) 1333/2008. No limits for those in legal specifications





Recital 7 Regulation (EU) 231/2012: legislator intends to reduce maximum limits for heavy metals

Recital 10 same regulation: "heavy metal" parameter to be replaced by individual metals and limits, typically Pb, Cd, As, (Hg)

Oral information from the EC- reduce limits 10-fold



CONCLUSION



## 2017 EU food colours revision of specification



