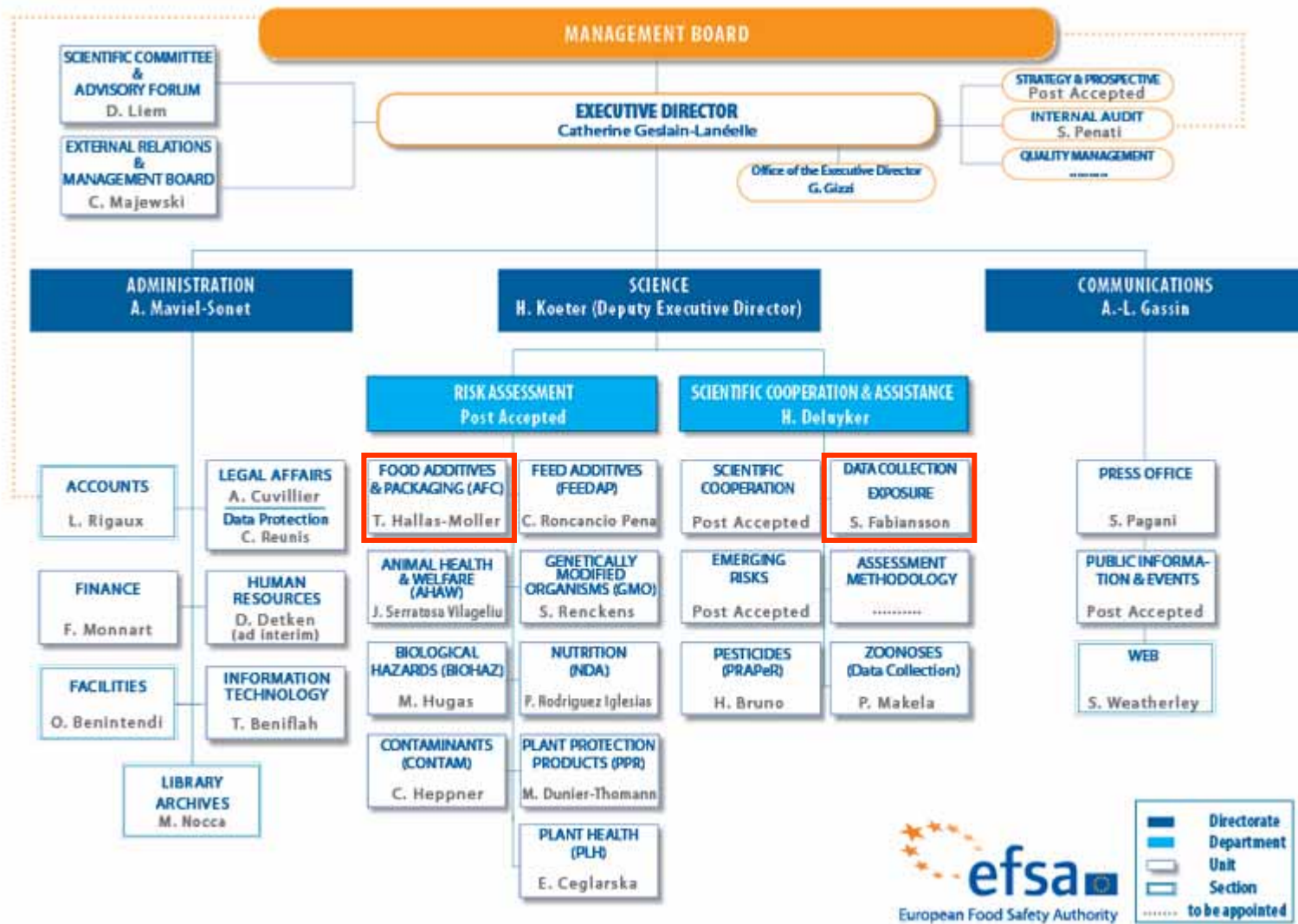




History of exposure assessment of flavourings at EU level

EFSA structure



Once upon a time ...

- Flavourings are agents that are intentionally added to food with the sole intention of imparting flavour.
- Flavouring substances are volatile organic chemicals and they are not used alone (Cadby, 2004).
Most flavourings added to foods and drink contain 50–100 substances.
- Nature is the biggest producer of flavourings but the mere presence in nature can of course not be taken as any reason to presume safety.

Flavouring substances in the European Union

- 1996 the European Parliament and the Council lays down a procedure for the establishment of a list of authorised flavouring substances in the European Union.
- 1999 adoption of a register of about 2,700 flavourings used by the food industry in or on foodstuffs in the Member States (amendments in 2002).

The procedure for the safety evaluation of flavourings

In order to establish a positive list of flavouring substances, the European Commission (2000) adopted the approach developed by the Joint FAO/WHO Expert Committee On Food Additives (JECFA, 1997).

The procedure integrates information on

- intake from current uses,
- structure - activity relationships,
- metabolism and
- toxicity.

In addition, information on purity and chemical specification is assessed.

- European Commission (2000) Commission Regulation No 1565/2000 of 18 July 2000 laying down the measures necessary for the adoption of an evaluation programme in application of Regulation (EC) No 2232/96. Official Journal of the European Communities, L 84, 8-16.
- JECFA (1997) Safety evaluations of groups of related flavouring agents: forty-six report of the Joint FAO/WHO Expert Committee on Food Additives. Safety evaluations of groups of related flavouring agents: forty-six report of the Joint FAO/WHO Expert Committee on Food Additives., Volume IPCS - WHO, Geneva.

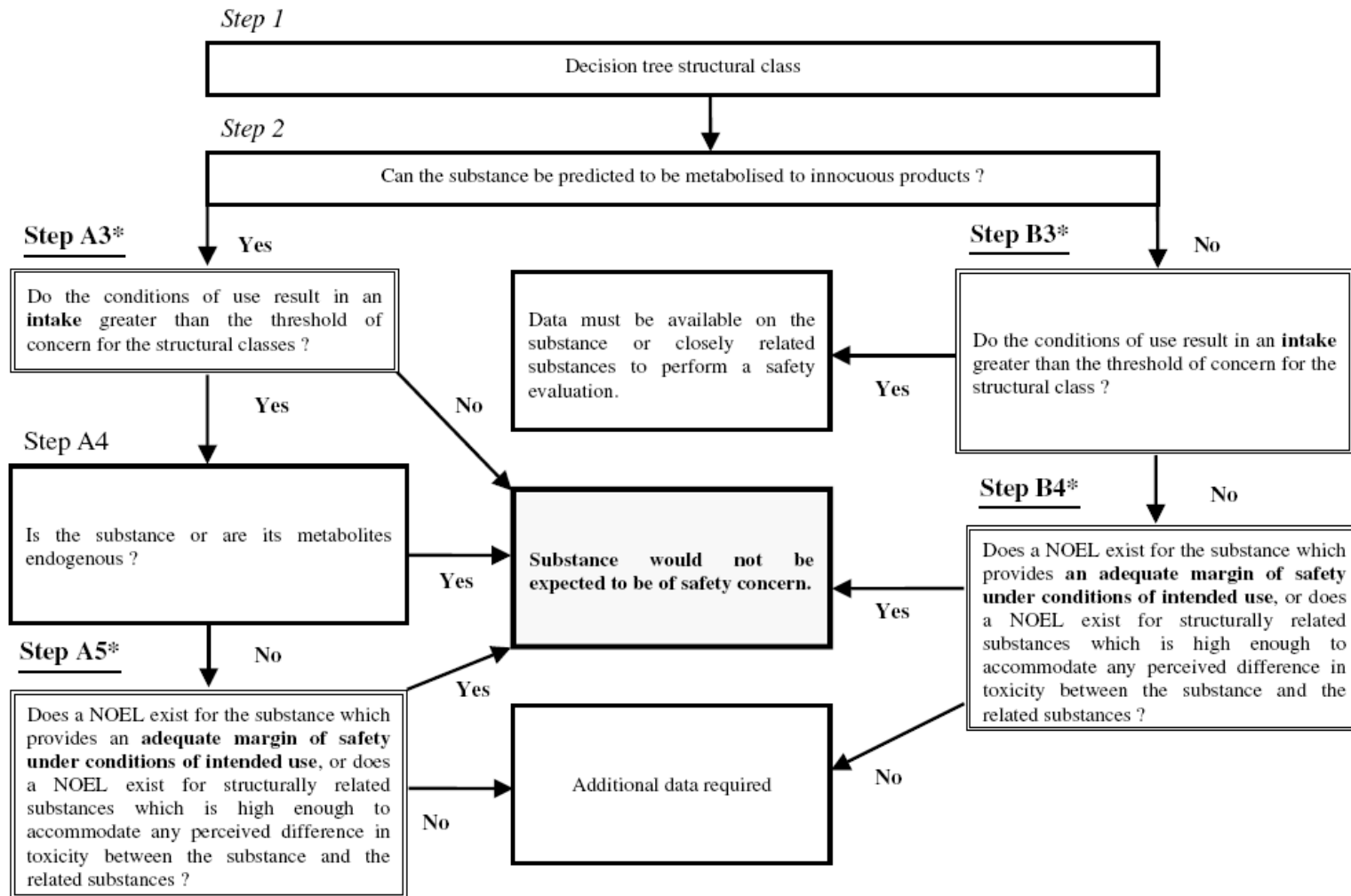
Thresholds of Toxicological Concern

The Threshold of Toxicological Concern (TTC) principle extends the ADI concept by proposing that a threshold value, **below which there is a very low probability of an appreciable risk to human health, can be identified for many chemicals,**

- in the absence of a full toxicity database,
- based on
 - their chemical structures and
 - the known toxicity of chemicals which share similar structural characteristics.

One of the key elements in the procedure for the safety evaluation of flavourings is the subdivision of flavourings into **three structural classes** for which human exposure thresholds have been specified. ,

The procedure for the safety evaluation of flavourings



The **estimation of the intake** is involved in four different steps of the decision tree

Maximised Survey-derived Daily Intake (MSDI) =

Annual production _(kg) **x** **10⁹** _(µg/kg)

Consumers x survey response rate x 365 _(days)

Annual production volume in one year in Europe

Consumers: estimated to be 10% of the total European population (= 32,000,000)

Survey response rate: correction made to take into account that survey data provided by industry could be incomplete (= 0.6 in Europe)

Example

Pentyl isovalerate

Production volume of in Europe in 1995: 77 kg

$$\text{MSDI: } \frac{77 \times 10^9}{32,000,000 \times 0.6 \times 365} = 11 \mu\text{g /day}$$

2003 Scientific Committee on Food (SCF) produces the first two opinions of the related to flavourings (FGE.01 and FGE.02)

Exposure was estimated using the MSDI method calculated on the basis of annual production volumes as reported in a survey conducted in Europe in 1995 by the International Organization of the Flavour Industry.

- Scientific Committee on Food (2003a) Opinion of the Scientific Committee on Food on chemically defined flavouring substances listed in the EU register Flavouring Group Evaluation 1 (FGE.01): Branched-chain aliphatic saturated aldehydes, carboxylic acids and related esters of primary alcohols and branched-chain carboxylic acids from chemical groups 1 and 2 (Commission Regulation (EC) No 1565/2000 of 18 July 2000). SCF/CS/FLAV/FLAVOUR/42 Final. Volume European Commission - Health & Consumer Protection Directorate-General, Bruxelles.
- Scientific Committee on Food (2003b) Opinion of the Scientific Committee on Food on chemically defined flavouring substances listed in the EU register Flavouring Group Evaluation 2 (FGE.02): Branched- and straight-chain aliphatic saturated primary alcohols, aldehydes and related esters of primary alcohols and straight-chain carboxylic acids from chemical groups 1 and 2 (Commission Regulation (EC) No 1565/2000 of 18 July 2000). SCF/CS/FLAV/FLAVOUR/42 Final. Volume European Commission - Health & Consumer Protection Directorate-General, Bruxelles.

Is the MSDI a conservative method?

In view of the large number of flavouring substances in current use, it is essential to have exposure assessment methods that are relatively rapidly performed.

At the same time, in the interests of protecting public health, these methods should not underestimate exposure by the higher consuming groups of the population.

Is the MSDI a conservative method?

- Hall, R. L. and Ford, R. A. (1999) Comparison of two methods to assess the intake of flavouring substances. *Food Addit Contam*, 16, (11) 481-95.
- Lambe, J., Cadby, P. and Gibney, M. (2002) Comparison of stochastic modelling of the intakes of intentionally added flavouring substances with theoretical added maximum daily intakes (TAMDI) and maximized survey-derived daily intakes (MSDI). *Food Addit Contam*, 19 (1) 2-14.
- Arcella D. and Leclercq C. (2005) Assessment of dietary intake of flavouring substances within the procedure for their safety evaluation. Advantages and limitations of estimates obtained by means of a per capita method. *Food and Chemical Toxicology* 43 (1), 105:116.
- Munro IC, Danielewska-Nikiel B. (2006) Comparison of estimated daily intakes of flavouring substances with no-observed-effect levels. *Food Chem Toxicol*. 2006 Jun;44(6):758-809.
- Leclercq C. (2007) Issues arising when methods used to assess dietary exposure to flavouring substances are compared. *Food Chem Toxicol*. 2007 May 18;

Hall and Ford (1999)

This study carried out in the United States, for **10 flavourings**, comparison between the estimated intakes calculated by means of:

- the MSDI method and
- 14-day food frequency data combined with mean portion sizes and presence/concentration data provided by experts from the flavour industry.

The MSDI method was asserted to be “a **conservative and practical approach to assessing exposure to flavouring substances and other food ingredients**”, based on the results of a study.

Estimates of exposure, for **12 flavourings**, based on the MSDI method were compared with exposure estimates based on a **stochastic model** using:

- food consumption data of British males (16-24 years old).
- Over 40,000 flavour formulae were examined to provide distributions of concentrations in 31 different categories of food and beverages.
- % of flavoured brands within food groups was estimated using the Irish National Food Ingredient Database.

This study confirmed the findings of Hall and Ford (1999) that “**the MSDI appeared, within the limits of the studies, to be a practical and conservative method for assessing exposure to intentionally added flavouring substances**”.

Arcella D. and Leclercq C. (2005)

This paper reviews the MSDI method in order to check if it can provide conservative intake estimates as needed at the first steps of a stepwise procedure.

In particular,

- 1) Scientific papers and opinions dealing with the MSDI method were critically reviewed.
- 2) Concentration levels reported by the industry were compared with estimates obtained with the MSDI method.

“The present paper suggests that the MSDI method is not sufficiently conservative”.

In order to enable the evaluation of a substance, the **EC Regulation requires** that the person responsible for placing on the market a flavouring substance has to provide:

- total amount of the substance which is added to foods in the Community,
- normal and maximum use levels of the substances according to specific food categories, if available.

Food categories as outlined in Commission Regulation

1. Dairy products, excluding products of category 2.
2. Fats and oils, and fat emulsions (type water-in-oil).
3. Edible ices, including sherbet and sorbet.
4. Processed fruits and vegetables (including mushrooms and fungi, roots and tubers, pulses and legumes), and nuts and seeds.
 - 4.1 Fruit.
 - 4.2 Vegetables (including mushrooms and fungi, roots and tubers, pulses and legumes), and nuts and seeds.
5. Confectionery.
6. Cereals and cereal products, including flours and starches from roots and tubers, pulses and legumes, excluding bakery.
7. Bakery wares.
8. Meat and meat products, including poultry and game.
9. Fish and fish products, including molluscs, crustaceans and echinoderms (MCE).
10. Eggs and egg products.
11. Sweeteners, including honey.
12. Salts, spices, soups, sauces, salads, protein products, etc.
13. Foodstuffs intended for particular nutritional uses.
14. Beverages, excluding dairy products.
 - 14.1 Non-alcoholic ('soft') beverages.
 - 14.2 Alcoholic beverages, including alcohol-free and low-alcoholic counterparts.
15. Ready-to-eat savouries.
16. Composite foods (e.g. casseroles, meat pies, mincemeat), foods that could not be placed in categories 1 to 15.

Example: Pentyl isovalerate (FGE.01)

Normal use levels:	1-20	mg/kg food
MSDI:	11	µg/day

A quick “back calculation” shows that 11 µg/day would be the intake in a person consuming approximately:

- 3 yoghurts every month (125 g each) containing 1 mg/kg of the substance
- or
- 1 glass of non alcoholic beverage every year (200 g) containing 20 mg/kg of the substance

Exposure estimates in the AFC panel evaluation (1)

In its evaluation, the Scientific Panel on Food Additives, Flavourings, Processing Aids and Materials in contact with Food (AFC) as a default used the MSDI approach to estimate the per capita intakes of the flavouring substances in Europe.

The AFC Panel (EFSA, 2005) expressed reservations about the data on use and use levels provided and the intake estimates obtained by the MSDI approach.

The MSDI approach in a number of cases may grossly underestimate the intake by regular consumers of products flavoured at the use level reported by the industry, especially in those cases where the annual production values were reported to be small.

EFSA (2005) Flavouring Group Evaluation 20: Benzyl alcohols, benzaldehydes, a related acetal, benzoic acids, and esters from chemical group 23. The EFSA Journal (2005) 296, 1-117.

In the absence of more precise information that would enable the Scientific Panel to make a more realistic estimate of the intakes of the flavouring substances, the Scientific Panel has decided also to perform an estimate of the daily intakes per person using an approach based on the normal use levels reported by industry.

A modified version of the TAMDI-approach based on normal use levels was added to the procedure for the safety evaluation of flavourings.

The TAMDI method (Cadby, 1996) assumes that:

- the hypothetical consumer will day in day out consume a fixed amount (standard portions) of flavoured food and beverages and
- that these items will always contain the specific flavouring at its specified Upper Use Level.

TAMDI basic assumptions

Foods and beverages	Consumption (g/day)	Content (mg/day)
Beverages (not alcoholic)	324	Upper Use Level
Foods	133	Upper Use Level
Exceptions:		
Candy, confectionery	27	Upper Use Level
Condiments, seasonings	20	Upper Use Level
Alcoholic beverages	20	Upper Use Level
Soups, savouries	20	Upper Use Level
Other exceptions (e.g. chewing gums)	2	Upper Use Level

TAMDI - Example

Foods and beverages	Consumption (g/day)	Upper Use Level (mg/kg)	Estimated intake (mg/day)
Beverages (not alcoholic)	324	0	0.000
Foods	133	3.5	0.465
Exceptions:			
Candy, confectionery	27	0	0.000
Condiments, seasonings	20	2.75	0.055
Alcoholic beverages	20	0.1	0.002
Soups, savouries	20	1	0.020
Chewing gums	2	0	0.000
Total			0.542

Modified TAMDI (mTAMDI)

Foods and beverages	Consumption (g/day)	Content (mg/day)
Beverages (not alcoholic)	324	Normal Use Level
Foods	133	Normal Use Level
Exceptions:		
Candy, confectionery	27	Normal Use Level
Condiments, seasonings	20	Normal Use Level
Alcoholic beverages	20	Normal Use Level
Soups, savouries	20	Normal Use Level
Other exceptions (e.g. chewing gums)	2	Normal Use Level

IMPORANT:

The mTAMDI **does not replace the MSDI method** but is used to **screen** and **prioritise** the flavouring substances according to the need for refined intake data.

The End

Thank you

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The author of this presentation is not currently involved in the procedure for the safety evaluation of flavouring substances. His interest in the field of exposure assessment to flavouring substances mainly comes from research project carried out before joining EFSA.

The EFSA Panel on Food Additives, Flavourings, Processing Aids and Materials in Contact with Food (AFC) is responsible for carrying out a risk assessment on flavouring substances prior to their authorisation and inclusion in a positive list according to Commission Regulation (EC) No 1565/2000.