

# **RISK ASSESSMENT STRATEGIES OF CHEMICALS IN FOOD AND DIET TO SUPPORT HEALTH AND SAFETY DECISIONS**

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# European legislation (Regulation No 178/2002 of the European Parliament and of Council of 28 January 2002)

❖ **Food** means any substance or product, whether processed, partially processed or unprocessed, intended to be, or reasonably expected to be, ingested by humans



**Food should not be placed on the market if it is “unsafe”, i.e. it is injurious to human health or unfit for human consumption**



**In determining whether any food is injurious to human health, regard shall be had:**

- (i) not only to the probable immediate or short term or long term effects on the health of a person consuming it, but also on subsequent generations**
- (ii) to the probable cumulative toxic effects**
- (iii) to the particular health sensitivities of the specific**



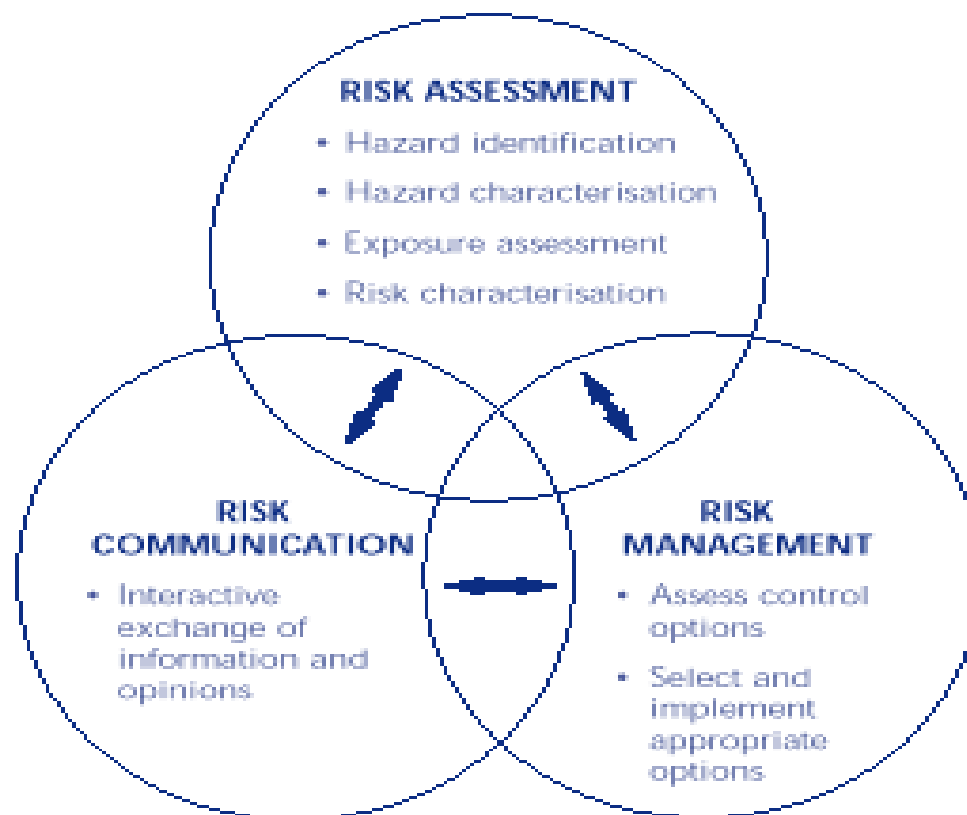
**The operational tool developed to achieve  
the goal of food safety:  
Risk analysis**

**A process based on three components:**

- ❖ risk assessment,
- ❖ risk management
- ❖ risk communication



**FIGURE 1**  
**Risk analysis framework**



Risk assessment and management also need to take into account the public's perceptions of the acceptability of risk in different situations.



## **Chemicals in food and diet main categories of concern:**

- ❖ **natural toxins**
- ❖ **additives**
- ❖ **contaminants migrating from packaging**
- ❖ **contaminants from water**
- ❖ **environmental contaminants, including pesticide residues**
- ❖ **medicines, hormones and growth factors**



**Additives (colouring and flavouring agents):  
deliberately added to food**

**All the other chemicals: “unwanted”  
components of foods, the presence of which  
has to be controlled and reduced to a  
minimum**

**Main effort of the current regulations: to  
assess the health risk posed by each  
individual component and set limit values  
that can be tolerated in the diet**



# **Risk assessment of chemicals in food in the European Union is a multi-step process that includes:**

- ❖ definition/identification of the substance to be assessed**
- ❖ characterisation of its hazardous properties in terms of type of effects and dose-response relationship**
- ❖ assessment of the dietary exposure (current or future)**
- ❖ risk characterisation**



**The process provides for a 'one-by-one'  
substance risk assessment**

**Combined or multiple exposures to  
different substances in the diet requires a  
further iteration of the process taking into  
consideration all the mixtures and their  
environmental and metabolic interactions**



# **EXAMPLE: the case of pesticide residues**



# Pesticide Hazard Identification

The data used in hazard identification may include results from many different types of study:

- ❖ human studies – epidemiology, case reports or volunteer studies
- ❖ toxicity studies conducted in laboratory animals
- ❖ alternative approaches, including use of in vitro models such as cell cultures or tissue slices, and comparisons with structurally-related chemical substances



# Examples of types of adverse effect caused by chemical agents (1)

<b>Functional changes</b>	<ul style="list-style-type: none"><li>❖ Reduced weight gain</li></ul>
<b>Morphological changes (other than cancer)</b>	<ul style="list-style-type: none"><li>❖ Organ enlargement</li><li>❖ Histopathological lesions</li></ul>
<b>Mutagenicity</b>	<ul style="list-style-type: none"><li>❖ Heritable changes in DNA, genes and chromosomes, with the potential to cause cancer or foetal abnormalities</li></ul>
<b>Carcinogenicity</b>	<ul style="list-style-type: none"><li>❖ Cancer</li></ul>



## Examples of types of adverse effect caused by chemical agents (2)

<b>Immunotoxicity</b>	<ul style="list-style-type: none"><li>❖ Sensitisation (leading to hypersensitivity or allergy)</li><li>❖ Depression of the immune system (leading to increased susceptibility to infection)</li></ul>
<b>Neurotoxicity</b>	<ul style="list-style-type: none"><li>❖ Behavioural changes, deafness, tinnitus, etc.</li></ul>
<b>Reproductive effects</b>	<ul style="list-style-type: none"><li>❖ Impaired fertility</li><li>❖ Embryotoxicity (spontaneous abortion)</li><li>❖ Teratogenicity (foetal deformities)</li><li>❖ Other developmental effects</li></ul>



# Expert committees

**review all the reported effects to establish whether they can be considered:**

- ❖ directly attributed to the chemical
- ❖ relevant to man
- ❖ “adverse”

**Identify the “critical effect”**

**Determine the NOEL and/or the NOAEL**



# Hazard characterisation – the pesticide

- ❖ Consider whether toxicokinetic data and current understanding of the toxicological mechanism indicate that humans are similar, less or greater in sensitivity to the critical effect, compared with the test species
- ❖ Consider whether to use a default safety (uncertainty) factor (100) or if data support selection of a lower factor, or level of uncertainty warrants selection of higher factor
- ❖ Establish acceptable daily intake (ADI), where:  
$$\text{ADI} = \text{NOAEL} / \text{safety factor}$$



# Exposure assessment – food

## Estimation of maximum daily intake from foods (TMDI)

- ❖ Content in foods based on Maximum Residue Level (MRL), determined in studies of pesticide application to various crops, using principles of best agricultural practice
- ❖ High level consumption of different contaminated food commodities estimated from survey data
- ❖ Calculation of maximum daily intake (worst case)

## Estimation of potential daily intake from foods (EDI)

- ❖ Content in range of foods based on chemical analysis
- ❖ Consumption of different food commodities estimated from dietary records
- ❖ Calculation of potential daily intake (more realistic)



# Exposure assessment – drinking water

## Pesticide residues in drinking water

- ❖ Based on worst case maximum of drinking water quality standards where available
- ❖ Analytical data on surface water in vicinity of pesticide trials
- ❖ Assume 2 litres consumed per day for adults



# Exposure assessment – total intake

## Calculation of total intake from food and/or drinking water as appropriate

- ❖ Maximum or potential intake, depending on nature of the available data and the assumptions made



# Risk characterisation

Qualitative and/or quantitative estimation, including attendant uncertainties, of the probability of occurrence and severity of known or potential adverse health effects in a given population based on hazard identification, hazard characterisation and exposure assessment

In simple terms: estimating how likely it is that harm will be done and how severe the effects will be

The outcome may be referred to as a risk estimate, or the probability of harm at given or expected exposure levels



# Risk assessment as a supportive tool for risk management

## Factors to take into account:

- ❖ Availability of alternative pesticides for the specific application
- ❖ Economic aspects in different regions

## Risk management options might include

- ❖ Ban usage if alternatives are available
- ❖ Permit restricted usage to limit exposure



# Food residues risk: single meal versus lifetime dietary intake

Some pesticides possess high acute toxicity or can induce severe, long-lasting toxic effects even after a single dose when this is taken on sensitive time windows, for example during the pregnancy

Under special dietary conditions [single meals with only one food item or closely spaced meals with the same food item], residues can reach an exceptionally high intake in some individuals, entering in the dose range sufficient to cause acute or severe toxic effects



# Acute Reference Dose

To prevent the occurrence of these effects, risk assessment should identify the Acute Reference Dose (ARfD) that should not be exceeded in a single day (meal)

Maximum possible intake should be compared with ARfD

Risk managers should adapt the MRL to a value consistent with such an ARfD



# Different meaning of ADI and ARfD

## ADI

protection of the population for lifetime exposure

Occasional exceedance of ADI : no problem if average  
daily intake is within ADI

## ARfD

protection of the single person for occasional  
“special meal”

Exceedance of ARfD may cause adverse effects



# Issues related to Risk assessment for chemicals in food

- ❖ The adequateness/accuracy of the risk assessment
- ❖ The role of pre-marketing and post-marketing assessment
- ❖ The practical implications of food risk assessment



# The adequateness/accuracy of the risk assessment (1)

## Problems and issues of animal toxicological testing to predict toxicity in humans

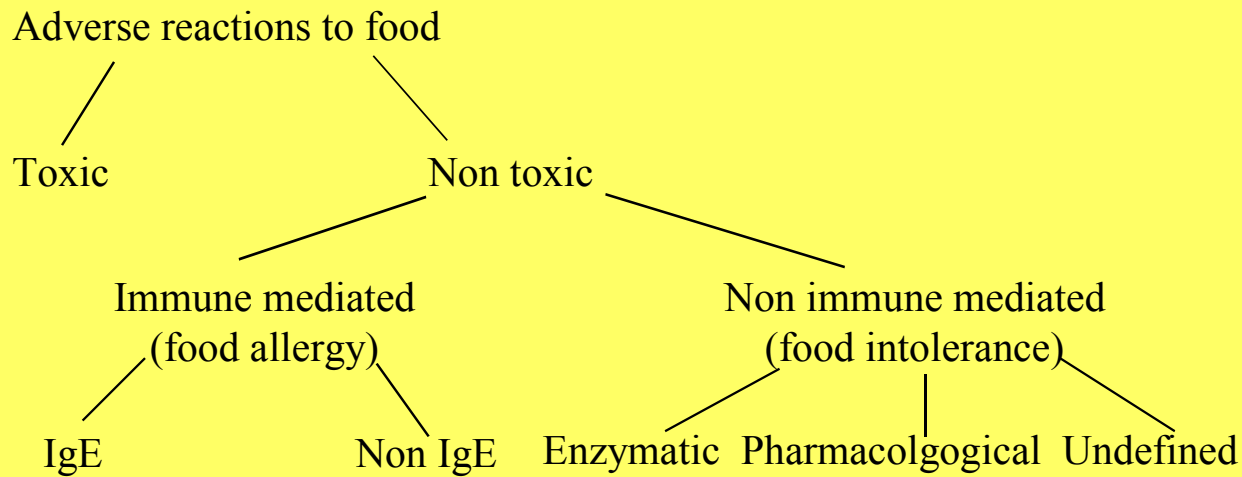
- ❖ Relevance of critical effects to man
- ❖ Limits of the animal model (behavioural and developmental effects)
- ❖ Low dose extrapolation of carcinogenicity (mechanistic data)
- ❖ Rare effects detection

Possibilities for the future: more human data, more mechanistic studies



# The adequateness/accuracy of the risk assessment (2)

## Adverse Reactions to Food



Ortolani and Vighi, 1995



# Most Common Food Allergens

- More than 170 foods cause food allergies
- Most common foods “The Big Eight”:
  - cow’s milk
  - eggs
  - fish
  - crustaceans
  - peanuts
  - soybeans
  - tree nuts
  - wheat



# Prevalence of Allergic Reactions

- IgE-mediated allergic reactions in 10-25% of the total population in developed countries
- Prevalence of hay fever and allergic asthma seems to increase
- Food-related IgE-allergies in 1-2% of the general population, in infants 5-8%
- Delayed food-induced enteropathy (coeliac disease) 1 in 300-3000



# The adequateness/accuracy of the risk assessment (3)

Table 7: Samples with residues of more than one pesticide in fresh (incl. frozen) fruit, vegetables and cereals, sum of surveillance and follow-up enforcement sampling

	No. of samples analysed	2	3	4	5	6	7	8 and more	No. of samples with multiple residues	%
<b>B</b>	1353	136	70	23	12	3	1	0	245	18.1
<b>DK</b>	1659	116	45	26	3	1	0	0	191	11.5
<b>D</b>	5478	514	193	81	27	11	1	1	828	15.1
<b>EL</b>	1472	62	16	6	1	1	0	0	86	5.8
<b>E</b>	6512	55	22	6	2	0	0	0	85	1.3
<b>F</b>	4231	539	298	129	62	18	9	4	1059	25.0
<b>IRL</b>	250	35	12	4	11	1	0	0	63	25.2
<b>I</b>	8320	550	264	104	54	24	4	6	1006	12.1
<b>L</b>	175	15	9	7	1	0	0	0	32	18.3
<b>NL</b>	2703	346	192	113	58	27	13	14	763	28.2
<b>A</b>	932	69	40	19	3	1	0	1	133	14.3
<b>P</b>	771	38	17	9	1	1	0	0	66	8.6
<b>FIN</b>	2252	327	148	62	26	4	4	0	571	25.4
<b>S</b>	3008	286	144	83	23	7	0	1	544	18.1
<b>UK</b>	1109	150	47	15	3	1	1	1	218	19.7
<b>Norway</b>	2825	263	106	39	7	2	0	0	417	14.8
<b>Iceland</b>	320	32	12	18	7	0	1	0	70	21.9
<b>Liechtenstein</b>	49	0	0	0	0	0	0	0	0	0
<b>Total</b>	<b>43419</b>	<b>3533</b>	<b>1635</b>	<b>744</b>	<b>301</b>	<b>102</b>	<b>34</b>	<b>18</b>	<b>6377</b>	
<b>%</b>		<b>8.1</b>	<b>3.8</b>	<b>1.7</b>	<b>0.69</b>	<b>0.23</b>	<b>0.078</b>	<b>0.041</b>	<b>14.7</b>	



# Strategies to assess interactions and combined exposures

## In the risk assessment:

- ❖ Consider the mechanism of action:
  - assess potential interactions at metabolic level
  - consider additive effects on the same molecular target
- ❖ Consider frequent association profiles by crop
- ❖ Consider other environmental chemicals

## In the risk management:

- ❖ Limit formulations with multiple active substances
- ❖ Limit dietary exposure to a maximum cumulative value



# Role of pre-marketing and post-marketing assessment (1)

## Pre-marketing risk modelling versus post-marketing risk monitoring

- ❖ Current legislation provides more for pre-marketing than for post-marketing risk assessment
- ❖ Regional diets have to be considered
- ❖ Monitoring programmes on food basket are essential



# Role of pre-marketing and post-marketing assessment (2)

Table 1: Overview over the samples analysed in the EU and EEA States

A) Breakdown by fresh (incl. frozen) and processed products

<b>Total number of samples analysed in EU and EEA</b>	45213	
<b>Fresh fruit vegetables and cereals</b>	43419	96 %
<b>Processed products</b>	1794	4.0 %



# Role of pre-marketing and post-marketing assessment (3)

## 4.2. Results of the 2000 national monitoring programmes compared to the previous years

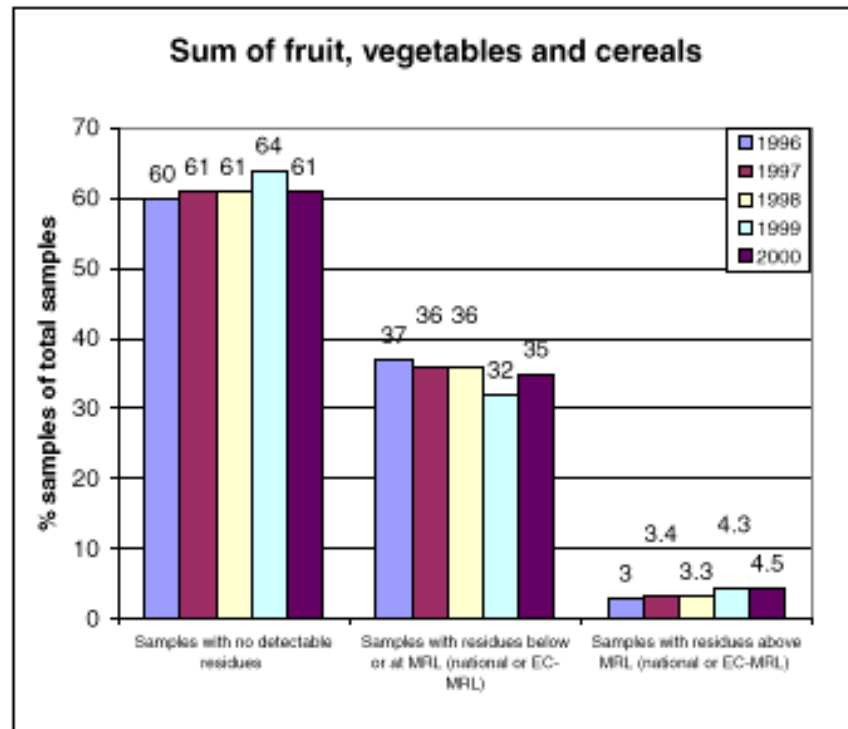


Figure 1: National monitoring results 1996 - 2000 for fruit, vegetables and cereals (sum of surveillance and follow-up enforcement sampling, fresh (incl. frozen) products only) collected in 18 participating countries



# Different techniques of risk modelling

Current models are **deterministic**: the answer is **Yes** or **No**  
Worst case assumptions in every step of the model lead to over-conservative and unrealistic final results

Alternative: **probabilistic** risk assessment

Each step has a frequency distribution. The 90<sup>th</sup>-95<sup>th</sup> upper percentile is taken into consideration.

Results are in probabilistic terms (example: 99.9% protected)

In progress applications on diet values and acute intake and on residue distribution in single food items



# Whole food chain control

**Consumer food safety to be secured “from crop to fork”**

**Role of farmers, food industry, food distribution chain, retailers**

**HACCP: hazard analysis critical control point concept**

**Food safety through food quality assurance**

**Food labelling for safety and quality**



# **The practical implications of food risk assessment**

**Who has to do what in risk assessment, risk management and risk communication?**

**The national regulatory Agencies and the forthcoming ESFA**

**Resources, cost and time in food risk assessment**

**Future trends, possibilities and gaps for research**

