Facoltà di Scienze Agrarie, Alimentari ed Ambientali
Dipartimento di Scienze e Tecnologie Alimentari per una filiera agro-alimentare Sostenibile – DiSTAS

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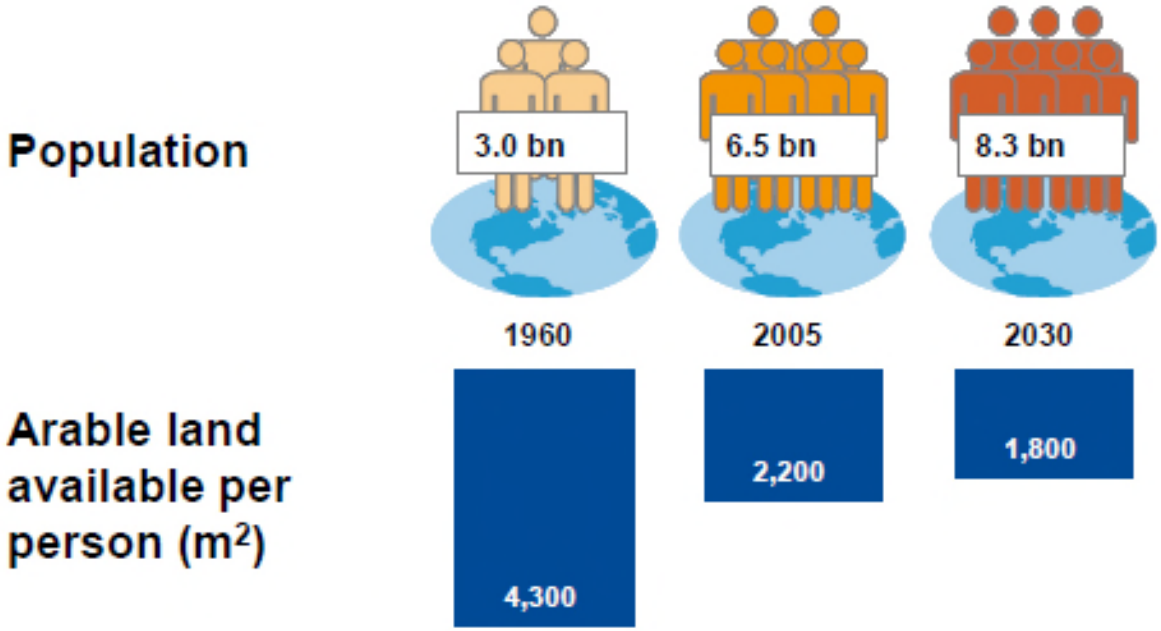
Case study: Risk-benefit of pesticides

Marco Trevisan

Parma Summer School 2019 "Risk-benefit in food safety and nutrition" 12 June 2019

The paradigma

Increasing population, decreasing agricultural area



→ Less arable land and less water for more people

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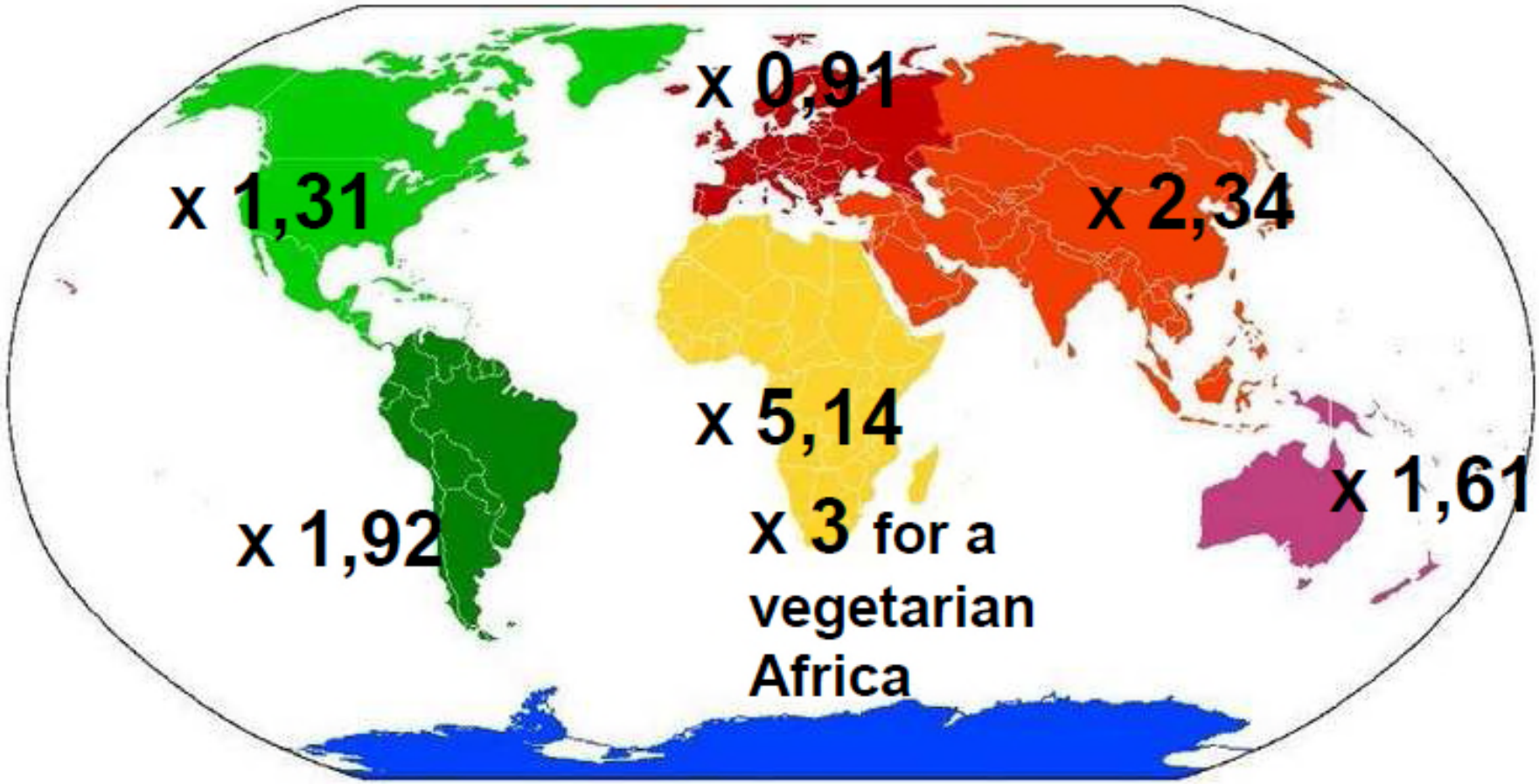
The agricultural production should be doubled if we want to feed all people in 2050



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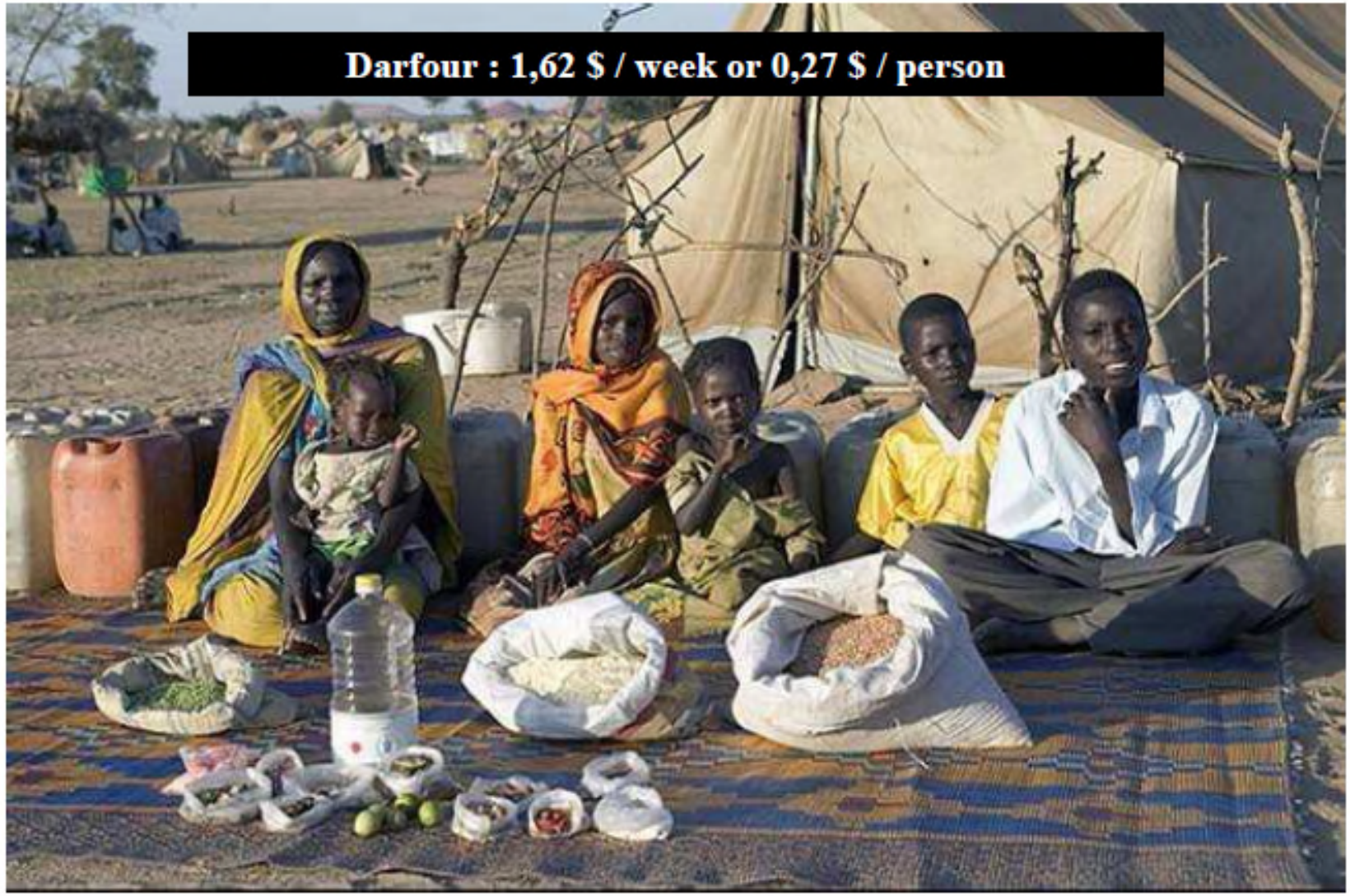
What does 1 family eat per week?



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Germany : 500,07 $ / week or 125,02 $ / person (500 times more than the family in Darfour…)

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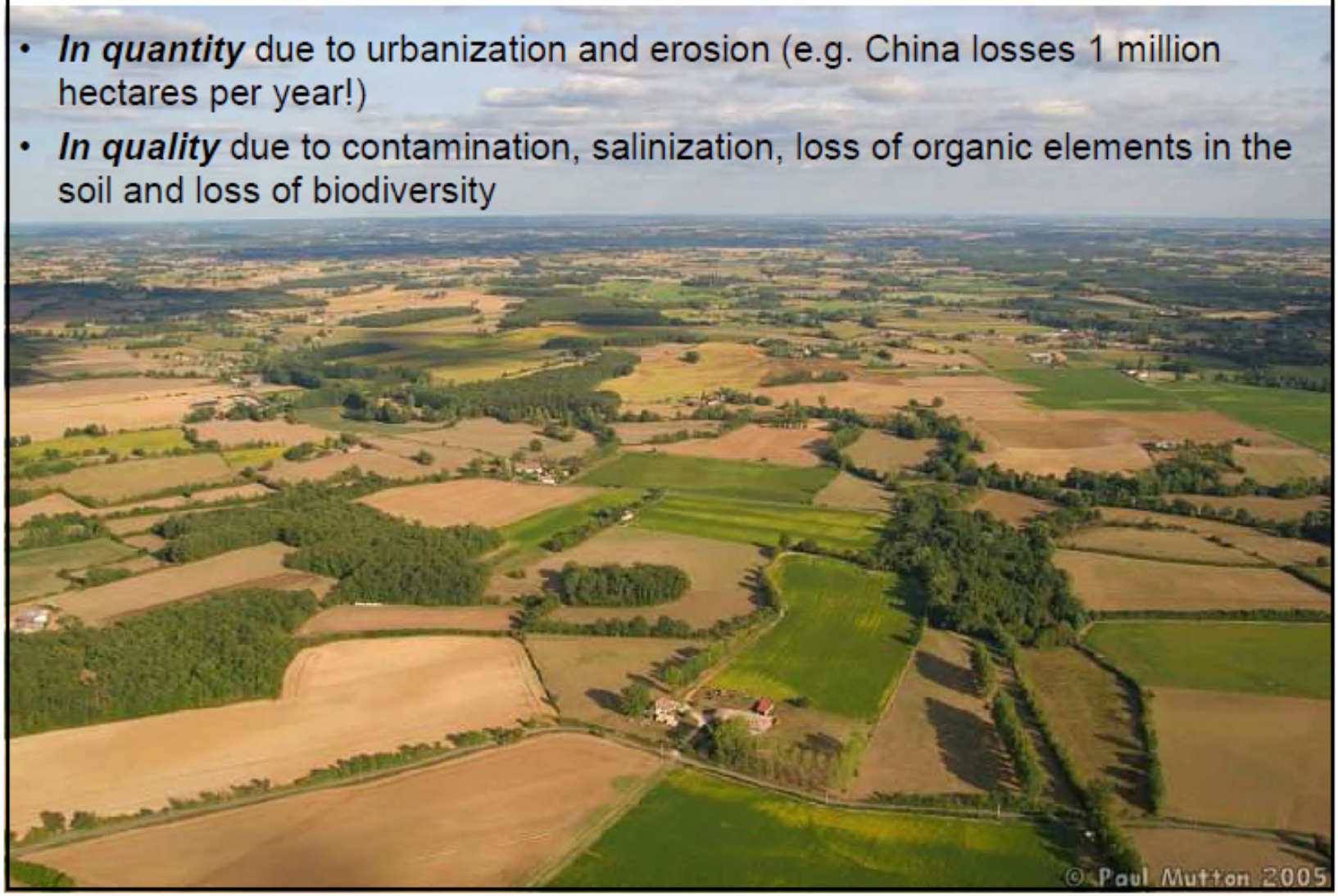
The total area of agricultural land decreases

- ***In quantity*** due to urbanization and erosion (e.g. China losses 1 million hectares per year!)
- ***In quality*** due to contamination, salinization, loss of organic elements in the soil and loss of biodiversity



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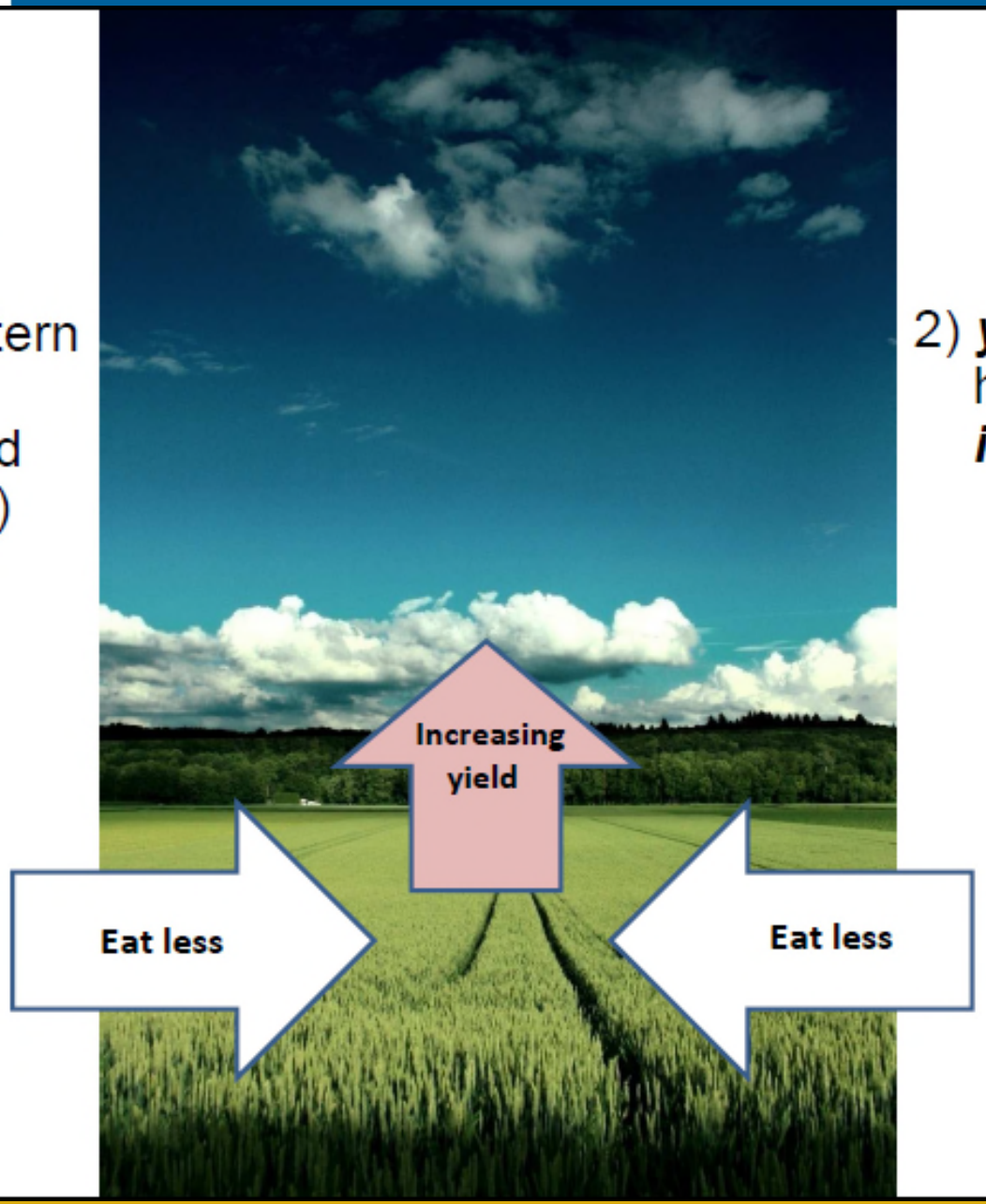
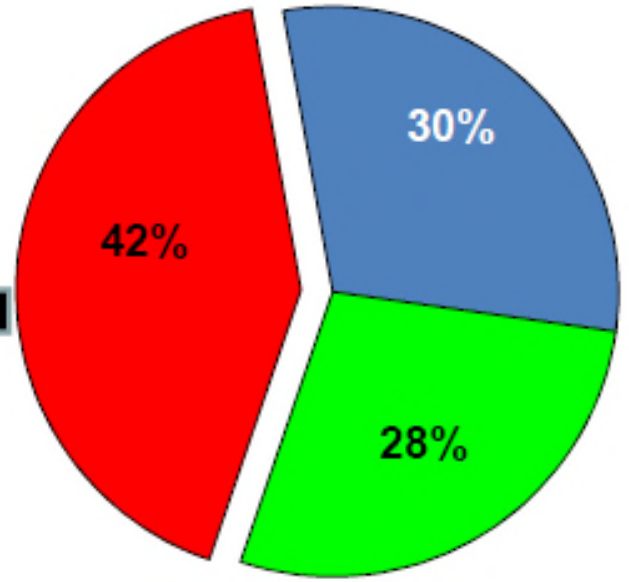
But only if:

1) we (western people / developed countries) ***eat less***



2) ***yield*** per hectare ***increases***

Global output and loss of yield: role of plant protection products



- Production without plant protection
- Avoided losses thanks to ppp
- Actual losses due to weed, damages from insects, pests and diseases

More than 40% of the yield is lost -still today!

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Pesticide is something that prevents, destroys, or controls a harmful organism ('pest') or disease, or protects plants or plant products during production, storage and transport

Some pesticides

- Acaricides
- Insecticides
- Fungicides
- Herbicides
- Growth regulators
- Nematicides
- Rodenticides
- Repellents
- Molluscicides

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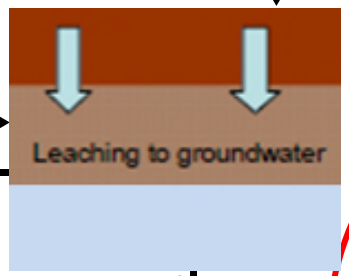
Pesticide fate

Drift

Deposition

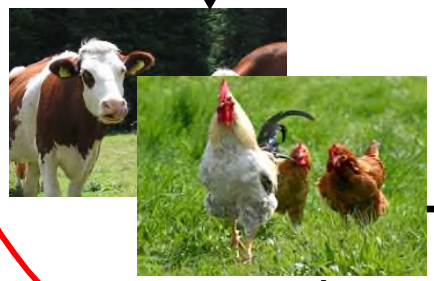
PPPs

Deposition



Crops

Runoff/
Leaching to
groundwater



Livestock

Diet

Surface waters

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Conditions for the authorization of a PPP

it shall be sufficiently effective;

it shall have no immediate or delayed harmful effect on human health, including farmer & resident

it shall not have any unacceptable effects on plants or plant products;

it shall not cause unnecessary suffering and pain to vertebrates to be controlled;

it shall have no unacceptable effects on the environment

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In force EU framework

Regulation (EC) No 1107/2009	• Regulates the placing of plant protection products on the market • Repealed Council Directives 79/117/EEC and 91/414/EEC
Regulation (EC) No 1272/2008	• is the regulation for classification, labelling, and packaging of substances and mixtures in the EU, and is referred to as the CLP Regulation.
Regulation (EU) 396/2005	• Regulates all matters related to legal limits for pesticide residues in food and feed
Directive 2009/128/EC	• a framework to achieve a sustainable use of pesticides by reducing the risks and impacts of pesticide use on human health and the environment and promoting the use of Integrated Pest Management and of alternative approaches or techniques such as non-chemical alternatives to pesticides

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Dir. 91/414/EEC

- Is a Directive so has to be adopted in each member state (MS)
- Scope: authorization, placing on the market, use and control within the Community of plant protection products → Harmonize
- Gives rules on the conditions and procedures for the authorization of plant protection products
- Introduced the ***RISK EVALUATION***: i.e. "*evaluating the foreseeable risks, whether immediate or delayed, which the substance (or PPP) may entail for humans, animals and the environment* "

Reg. (EU) 1107/2009 - Procedures

Authorization of a.s. and PPP
Procedure divided in **2 steps**

1 Active substance

Evaluation and approval at EU Level

Peer review with MSs of the same Zone and also of different Zones

Dossier requirement according to Reg.(EU) No 283/2013

Favourable opinion → a.s. is approved

2 PPP

Evaluation and authorization at zonal level

Dossier requirement according to Reg.(EU) No 284/2013

Favourable opinion → PPP is authorized

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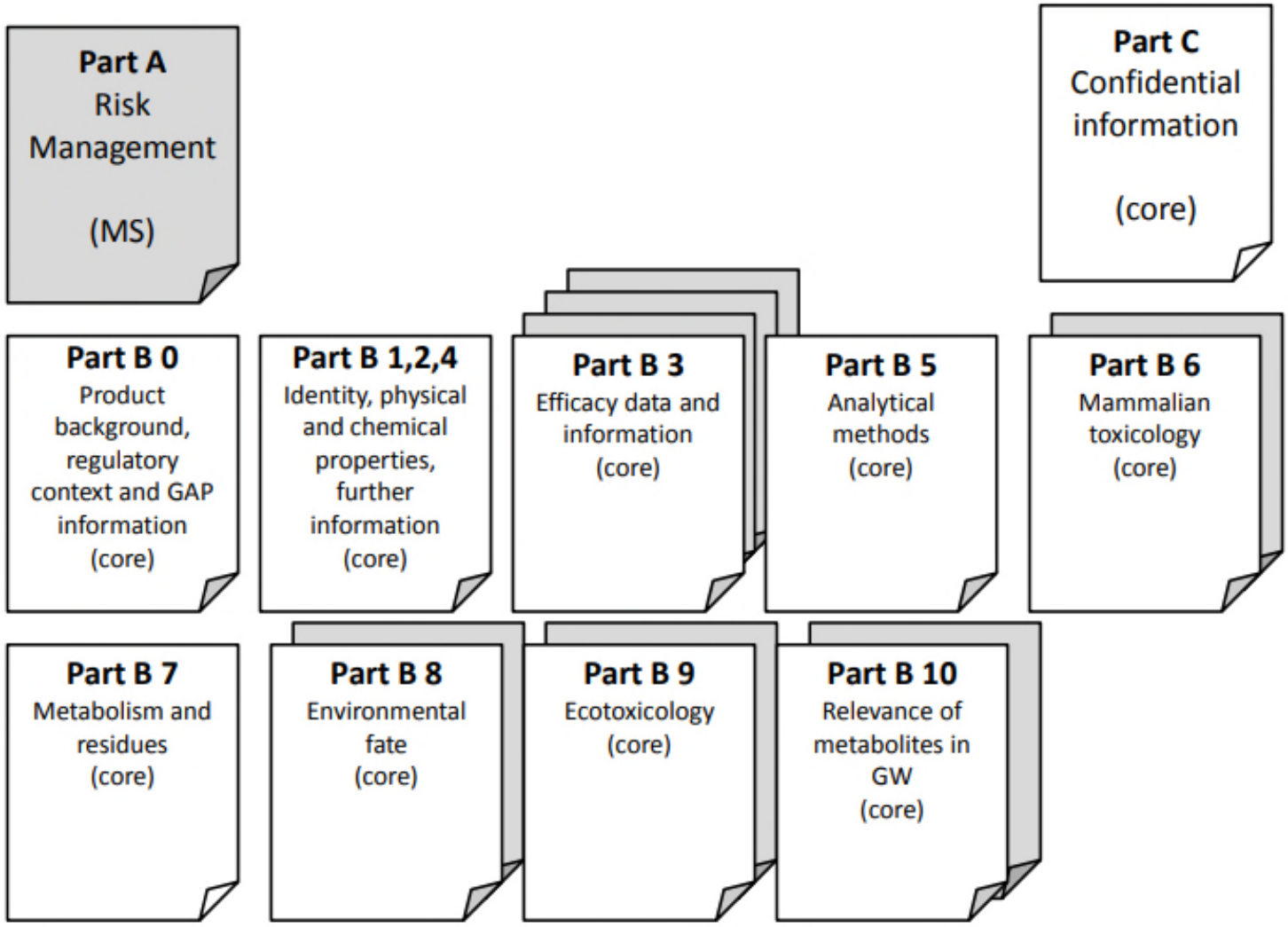
Structure of the draft Assessment Report



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Risk evaluation

GAP/ Efficacy	• Good Agricultural Practice (GAP)
Residue in food	• Maximum residue level (MRL) set and harmonised
Human toxicology	• worker, operator, bystander, resident & consumers
Environmental Fate	• Soil, groundwater, surfacewater, plants & air
Ecotoxicological effect	• No target organism

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Efficacy Data and Information

Efficacy → To demonstrate that there is a benefit (in term of pest control and consequent yield improvement) from the application of the product

Studies to establish the Minimum Effective Dose (the dose that is the minimum necessary to achieve sufficient efficacy against a target pest across the broad range of situations in which the product will be applied)

Direct efficacy trials (compared to untreated control and to reference products)

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Information on the occurrence or possible occurrence of the development of <u>resistance</u>

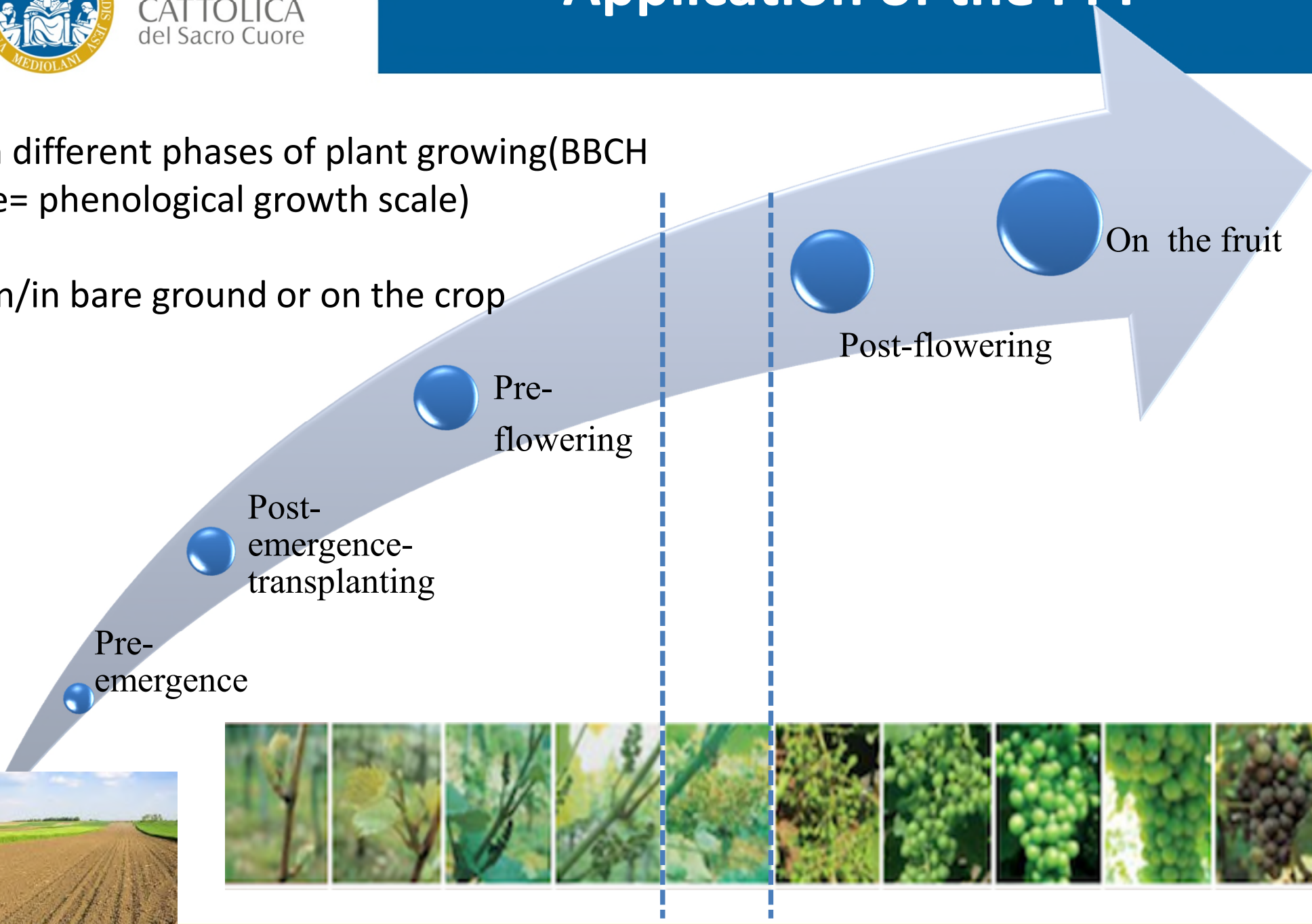
Absence of unacceptable effects

- Phytotoxicity
- Yield
- Quality (including transformation processes)
- Plants or plant parts used for propagation
- Succeeding crops
- Adjacent crops
- Pollinators and natural enemies
- Subsequently treated crops (effect of tank cleaning)

Application of the PPP

❖ in different phases of plant growing(BBCH scale= phenological growth scale)

❖ on/in bare ground or on the crop



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Good Agricultural Practice GAP

Application rate	• Maximum application rate for every single treatments. • Expressed as g or kg s.a./ha
N° of applications	• maximum number of application
Interval between applications	• Days between one application and the next one (minimum and maximum).
Water Volume	• Water volume to dilute the PPP • Expressed in L/ha
Growth stage & season	• Growth stage at last treatment
PHI=Pre-Harvest Interval	• Minimum number of days that must pass between the time of the last application of a pesticide and the harvest • It should ensure residues below the statutory legal limit (MRL)

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Fungicide GAP

1	2	3	4	5	6	7	8	9	10	11	12	13	14
					Application				Application rate				
Use No.	**Member state(s)**	**Crop and/or situation** (crop destination/ purpose of crop)	**F G or I**	**Pests or Group of pests controlled** (additionally: developmental stages of the pest or pest group)	Method/ Kind	Timing/ Growth stage of crop & season	Max. Number a) per use b) per crop/ season	Minimum interval between applications (days)	kg or L / ha a) max. rate per appl. b) max. total rate per crop/season	g or kg / ha a) max. rate per appl. b) max. total rate per crop/season	Water L/ha min/max	**PHI** (days)	**Remarks:** e.g. safener/ synergist per ha
1	Greece	Grapes, table	F	*Plasmopara viticola, Uncinula necator*	Foliar	BBCH 13-81	a) 3 b) 3	10-12	a) 1 b) 3	a) 262 b) 786	500-1200	21	
1	Italy	Grapes, table	F	*Phomopsis viticola, Uncinula necator*	Foliar	BBCH 13-81	a) 3 b) 3	10-12	a) 1 b) 3	a) 262 b) 786	500-1200	21	
1	Portugal	Grapes, table	F	*Phomopsis viticola, Plasmopara viticola, Uncinula necator*	Foliar	BBCH 13-81	a) 3 b) 3	10-12	a) 1 b) 3	a) 262 b) 786	500-1200	21	

Plasmopara viticola
causal agent of grapevine downy mildew

Uncinula necator
causal agent of grapevine downy mildew

Phomopsis viticola

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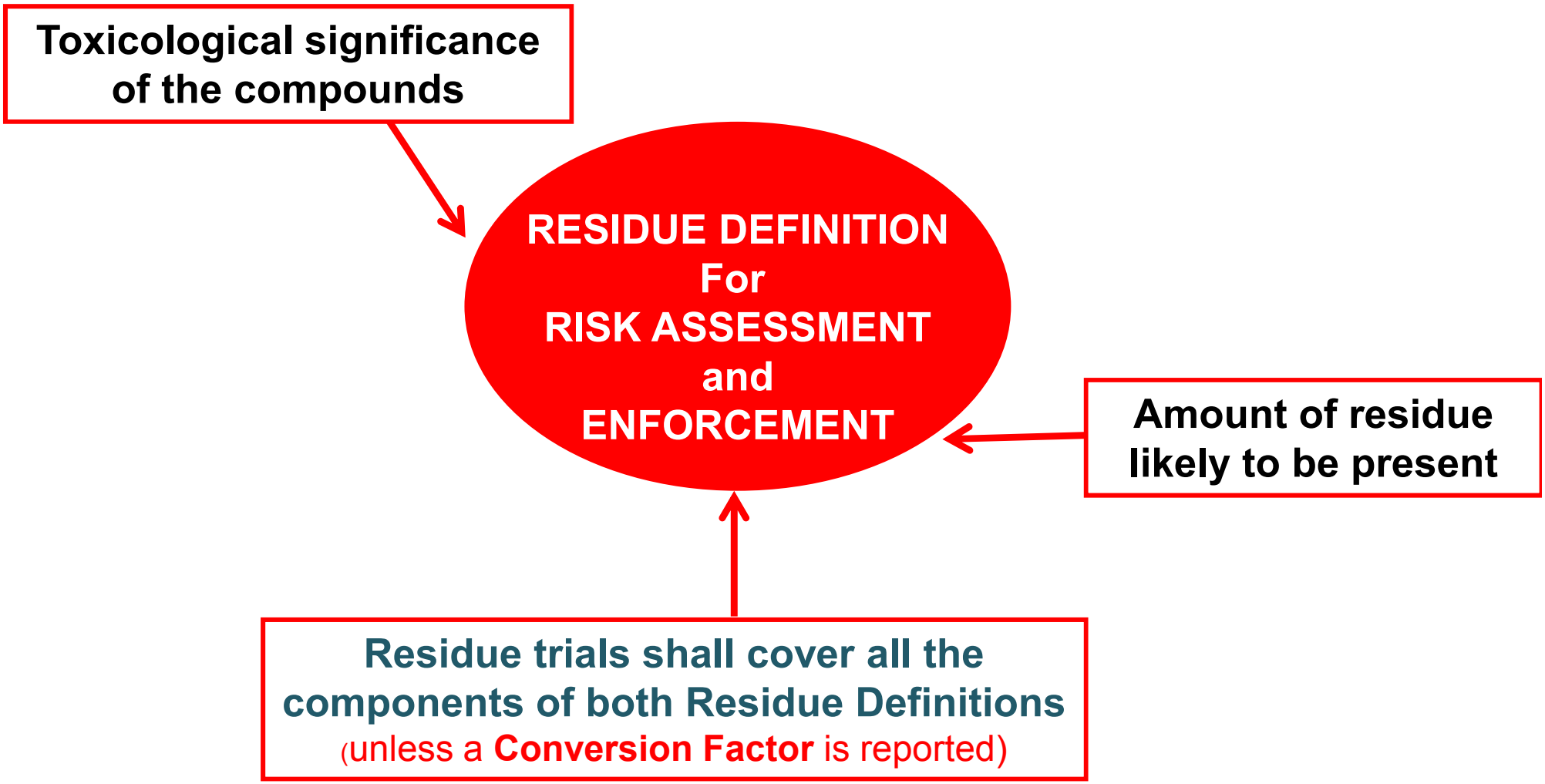
Proposed Residue Definition and Maximum Residue Levels



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BASIC REQUIREMENTS

→ Under realistic circumstances the trial conditions should be the least favourable in order to identify the highest residue (25% range tolerance admissible).

CRITICAL GAP

- maximum number of proposed applications
- shortest interval between applications
- maximum application rate and concentration
- most critical safety intervals with regard to exposure
- agricultural production methods (i.e. outdoor versus indoor uses)
- seasons of production and types of formulations

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BASIC REQUIREMENTS

→ For the evaluation of residue behaviour and the setting of maximum residue levels (MRLs) the Union shall be divided into two zones (Regulation (EC) No 396/2005) : Northern Europe (NEU) and Southern Europe (SEU)

For the in greenhouses, post-harvest treatment and treatment of empty storage rooms, one residue zone shall apply.

→ The minimum number of trials shall vary for each residue zone between a minimum of 4 trials for a minor crop and a minimum of 8 trials for a major crop.

- ❖ Wine grape: major crop both in NEU and SEU
- ❖ Table grape: major crop in SEU and minor crop in NEU

→ The number of studies could be less if residue trials show that the residue levels in plants or plant products are lower than the LOQ.

→ If a significant part of the consumable commodity is present at the time of application, half of the supervised residue trials reported shall include data to show the effect of time on the level of residue present (residue decline studies), unless the consumable part is not exposed during application of the plant protection product under the proposed conditions of use.

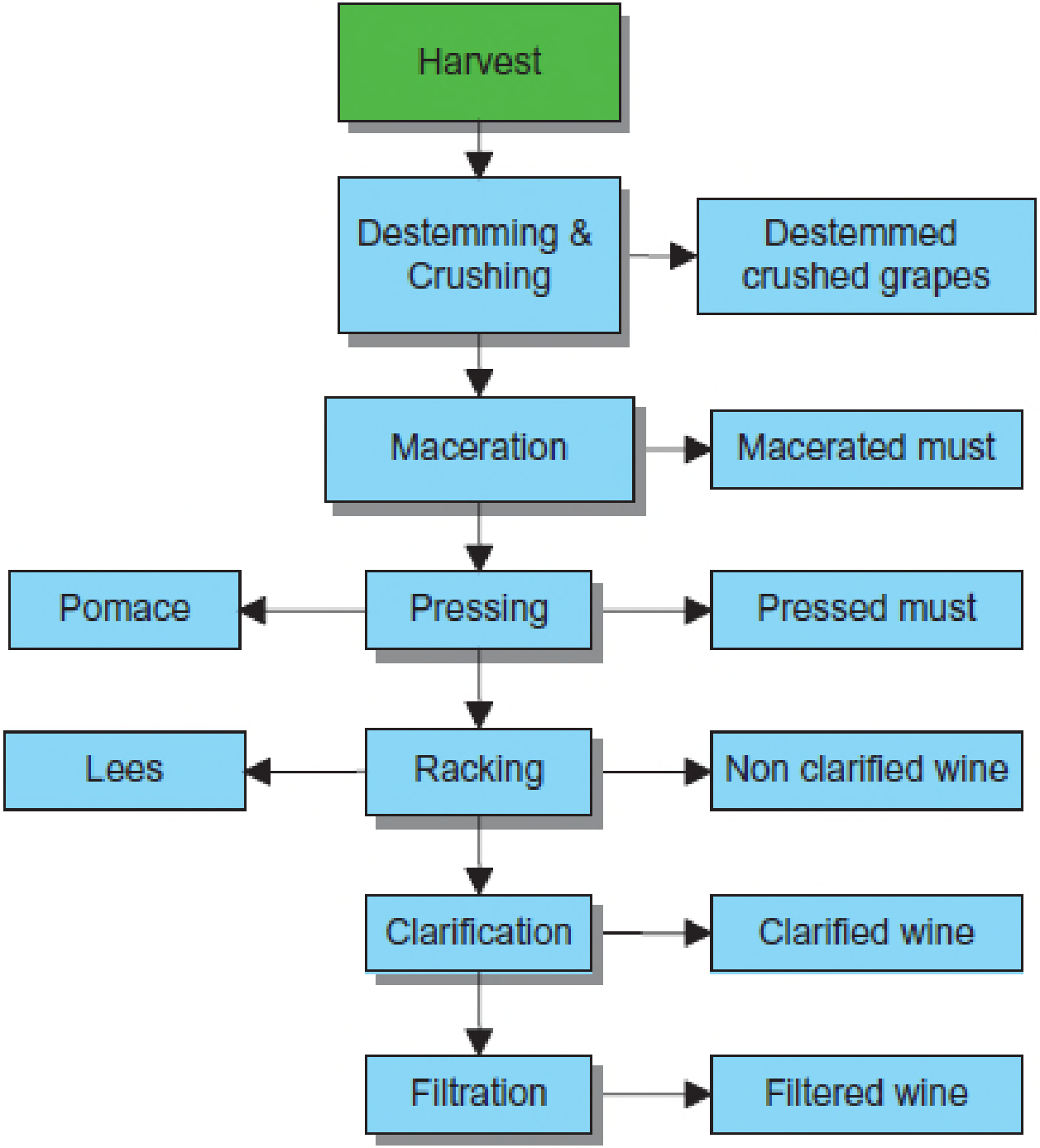

Figure 1. Scheme of the vinification process.

Studies on Industrial Processing and/or Household Preparation

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MRL calculation

Current method:

OECD calculator: uses different statistic approaches. The MRL is set at the maximum of the following three calculated results:

- **the highest residue (HR): is used as a "floor" to guarantee that the MRL proposal is always greater than or equal to the highest residue**
- **Mean + 4*SD"**
- **3*Mean*CF where CF is a correction factor**

MRL calculation

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Active substance	
Crop	
Region	
PHI	
other	
Number of values	8
mean	0,76
Dixon Test	0,40
Q10%	0,48
Result	No outlier
Rber	3,04
Rmax	4,00
Rounded EU-MRL	4,00
Highest residue	2,80
mean+ 4 SD	4,82
CF x 3 mean	2,27
Rounded MRL_{OECD}	5,00
HR	2,80
STMR	0,23
Comment	
1	0,01
2	0,02
3	0,10
4	0,11
5	0,34
6	0,98
7	1,70
8	2,80

- **MRL derives from measured data**
- **MRL is a statistical interpretation of residue trials results**

Other important values from calculation:

- **STMR: Supervised Trials Median Value**
- **HR: Highest Residue of residue data set**

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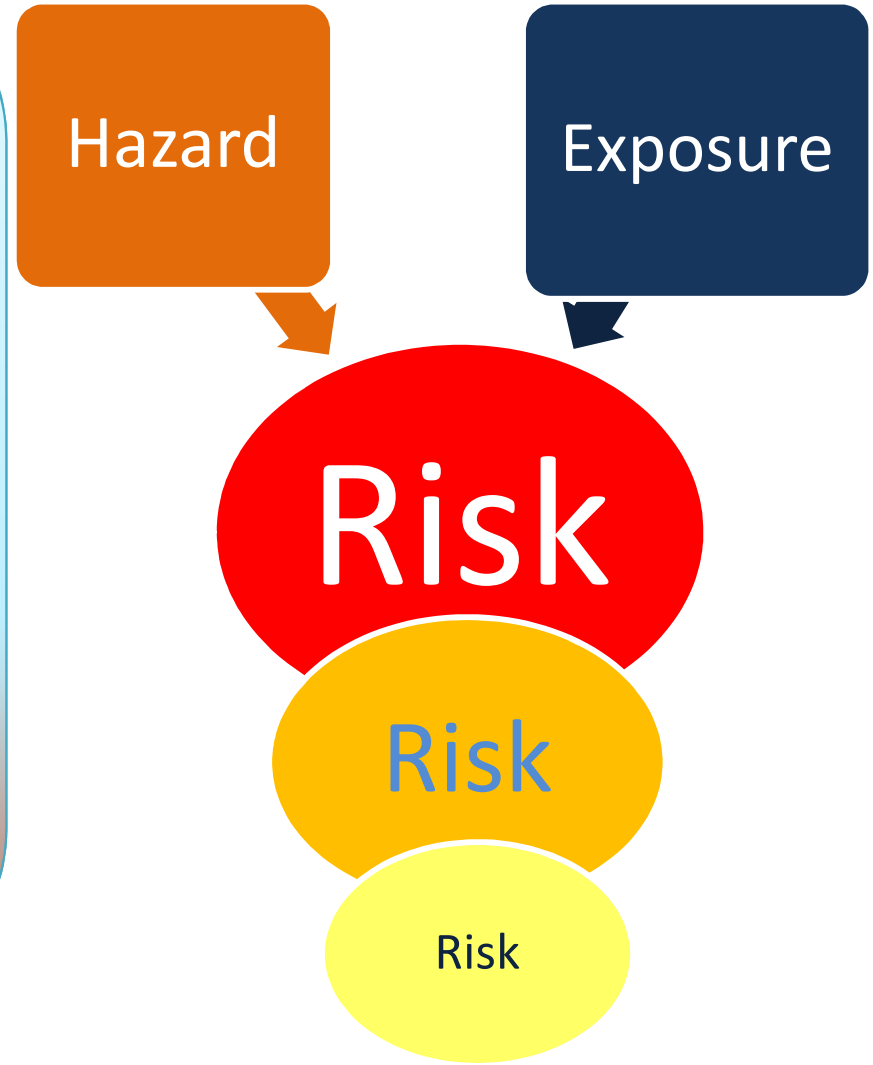
RISK ASSESSMENT

A scientifically based process consisting of the following steps:

1. Hazard identification,
2. Hazard characterization
3. Exposure assessment
4. Risk characterization

[REGULATION (EC) No 178/2002 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 28 January2002 laying down the general principles and requirements of food law, establishing the European Food Safety Authority and laying down procedures in matters of food safety]



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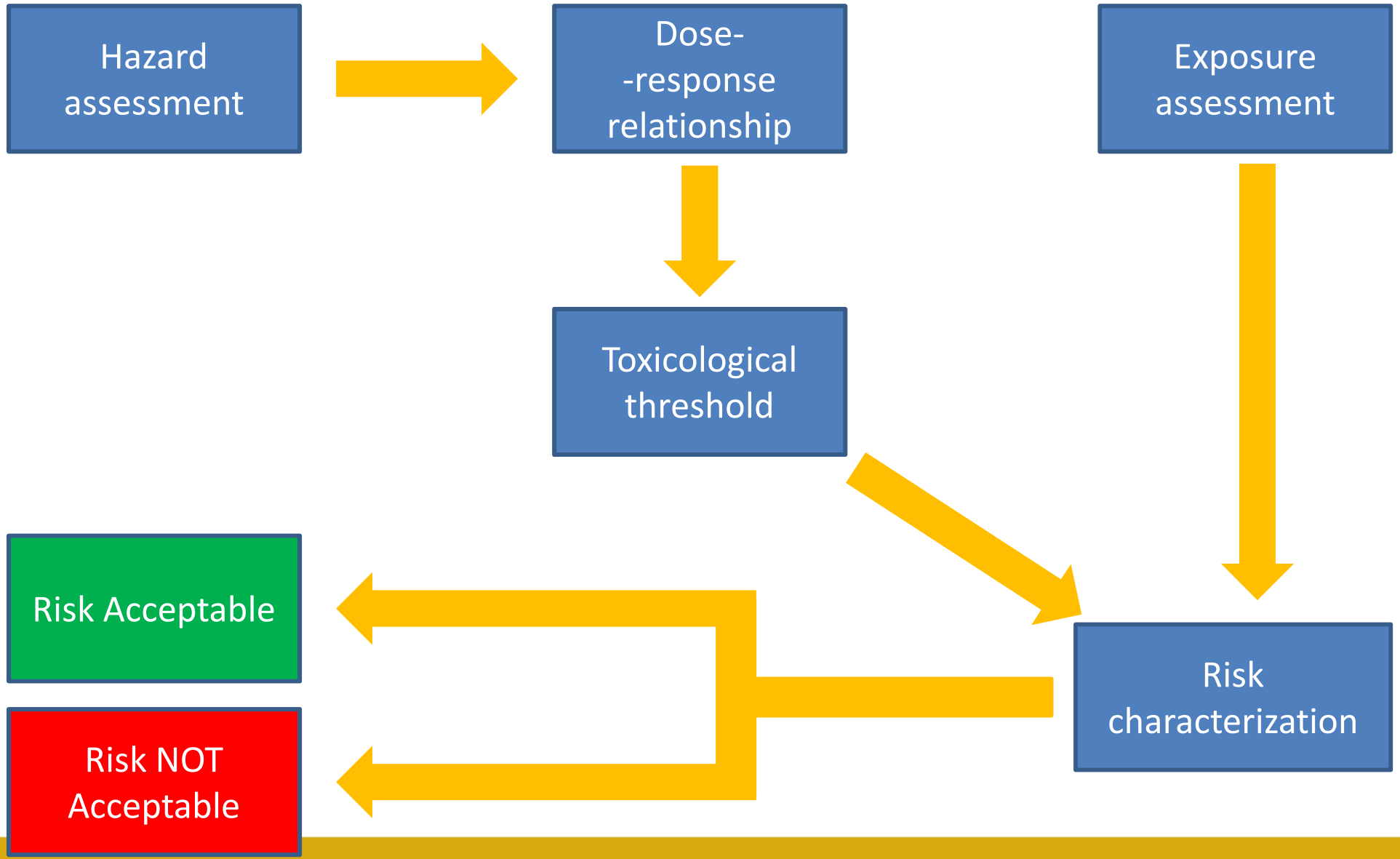
RISK ASSESSMENT



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RISK ASSESSMENT

Exposure assessment

Hazard Identification

Hazard Characterization

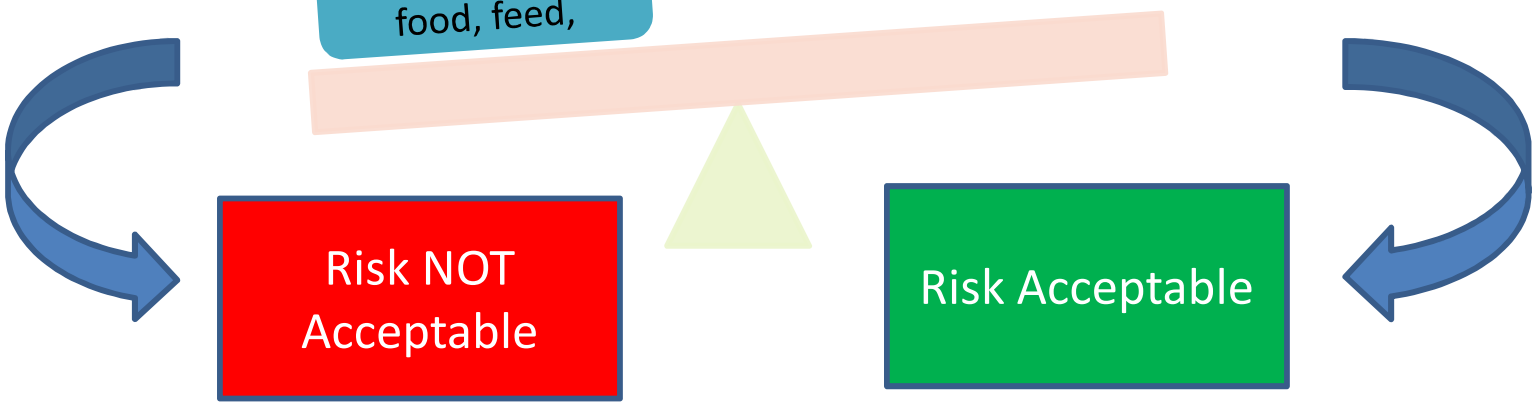
Occurrence of chemicals environment,

Occurrence of chemicals in water,

Occurrence of chemicals in food, feed,

Health based Guidance Value(ADI, TDI…)

- Toxicity: Genotox,acute/sub-chronic/chronic toxicity, NOELs, BMDL, LOAELs (animal, human) NOEC, PNEcs (Ecology..)
- Toxicokinetics (ADME)



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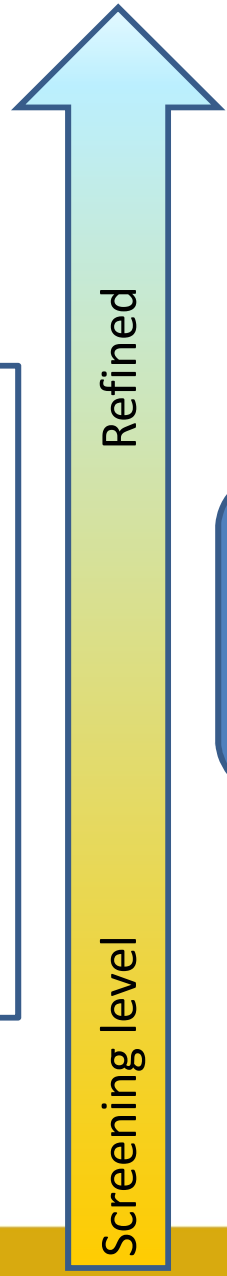
TIERED APPROACH

Increasing Complexity
Resources Requirements
Characterization of Variability and/or Uncertainty



Tier 3
- Detailed site-specific modeling
- In field data
- High cost

Evaluate and refine

Tier 2
- More realistic exposure assumptions
- More detailed modeling
- Moderate cost

Evaluate and refine

Tier 1
- Conservative exposure assumptions
- Simple modeling
- Low cost

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Data requirements

Toxicological studies

ACTIVE SUBSTANCE

- Acute toxicity
- Toxicokinetics
- Repeated dose toxicity
- Reproductive toxicity
- Genetic toxicity
- Toxicity to specific targets (e.g. neurotoxicity)

PLANT PROTECTION PRODUCT (PPP)

- Acute toxicity
- Dermal absorption

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ADI
Acceptable Daily Intake

The ADI (**mg/kg body weight**) is the acceptable daily ingestion of a particular active substance, for a **prolonged period** of time, in theory for life, which does not involve a risk to human health

ARfD
Acute Reference Dose

The ARfD (**mg/kg body weight**), is the estimate of the amount of active substance in food, or in water, that can be ingested in a **limited period of time**, generally in a meal or in a day, without appreciable risk to human health.

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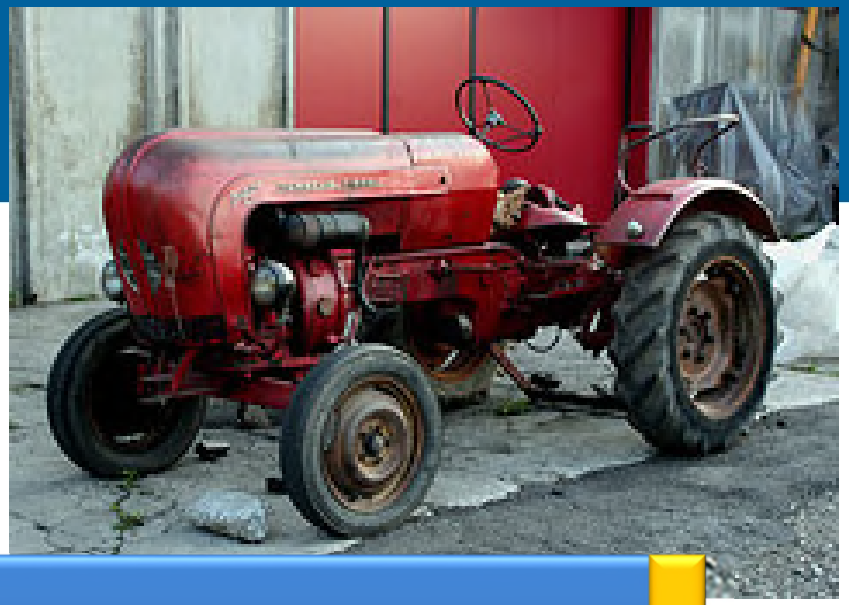
Exposure assessment – dermal and inhalation route

Exposure

- Operator → Occupational exposure during the application
- Bystander and resident → Non-occupational exposure during and/or shortly after the application
- Worker → Occupational exposure during the re-entry in field/glasshouse after the application



Many changes in 20 years….

Exposure assessment – Bystander and Resident

Acute **Chronic**

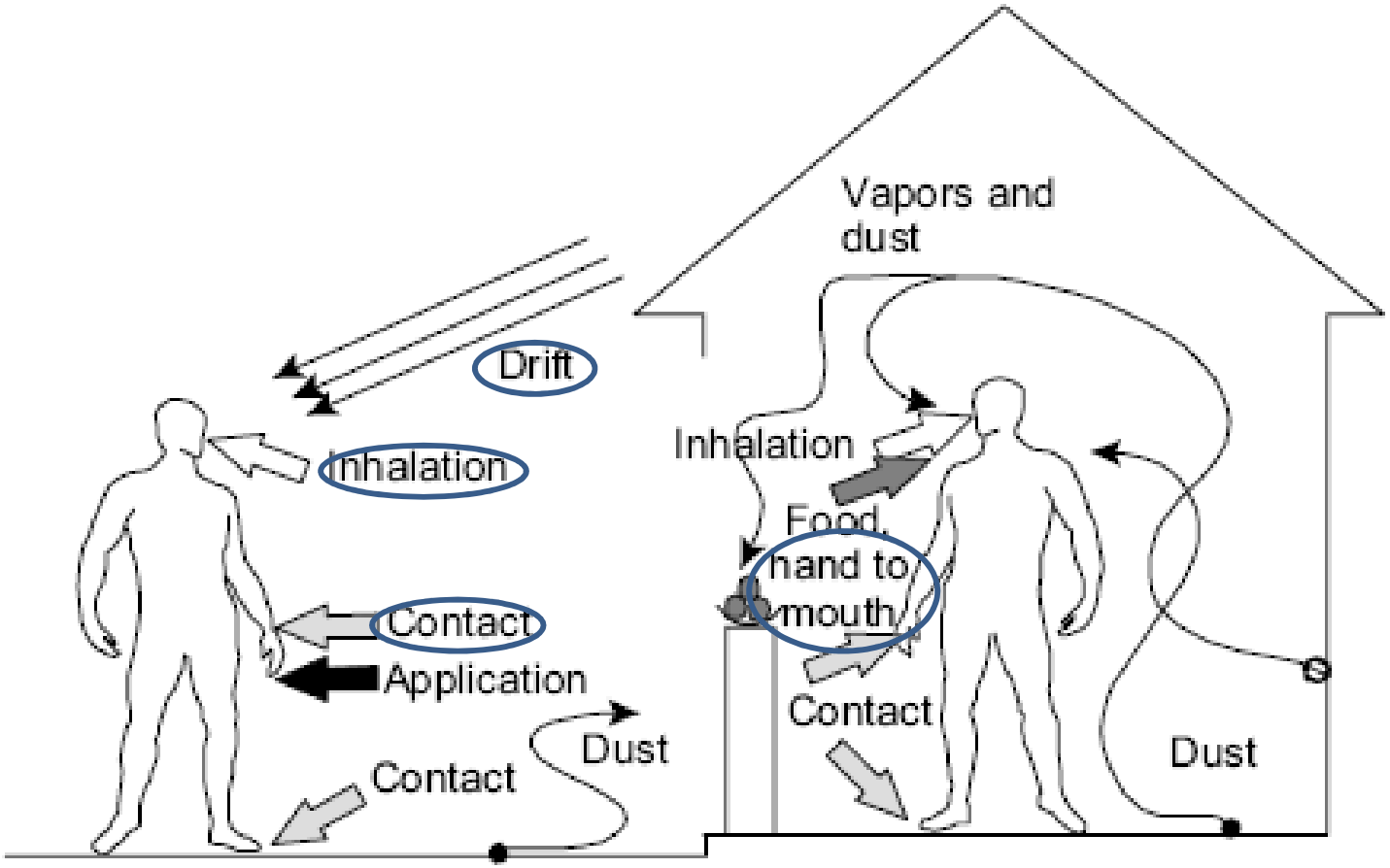


Figure 1. Potential sources of exposure in the home and landscape.

Solomon et al, Scand J Work Environ Health 2005, vol 31, suppl 1

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Worker exposure

pruning **thinning** **harvesting**

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Worker exposure

Parameters related to the worker exposure

- Amount of dislodgeable foliar residues **(DFR)**
- Half-life of residues and day after the last treatment **(DT50 and t)**
- Activity - intensity and duration of contact with the foliage **(TC and t)**
- Use of **PPE** (gloves)

Conservative default values

OR

Measurement through field study

TC= the intensity of the workers contact with the treated crop (cm^2/h)

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Run-off

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SPRAY DRIFT

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DRIFT


FENDT

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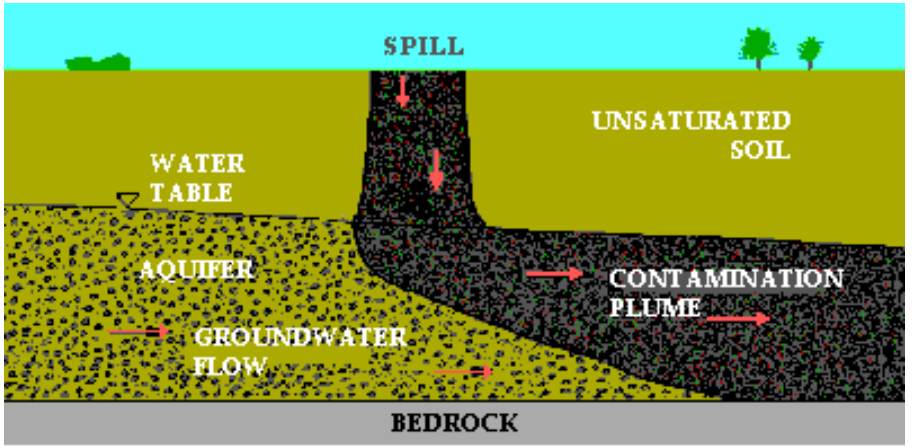
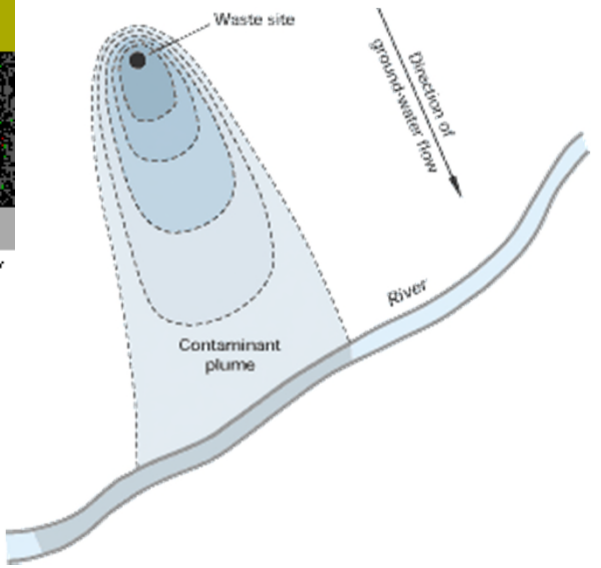
Point contamination

Point contaminations are produced by all the uncorrected practices which causes direct or indirect water bodies contamination within the life cycle of a pesticide



Source: "Variables and Technical Relationships Involved in the Contamination of Shallow Groundwaters by Agricultural Chemicals", William F. McTernan



The point contamination

The higher risk comes from:

Mixture loading (unexpected spillages)
Disposal of remaining mixture (when inappropriate)
Spray equipment washing after application





This operations, also, generate an high waste water with several problems (and costs) for a correct disposal

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The point contamination

1 drop 20%
= approx. 10 mg a.i.

Dilution to 0,1 ppb →
100000 L of water:

As a pond 100 m^2 1 m deep

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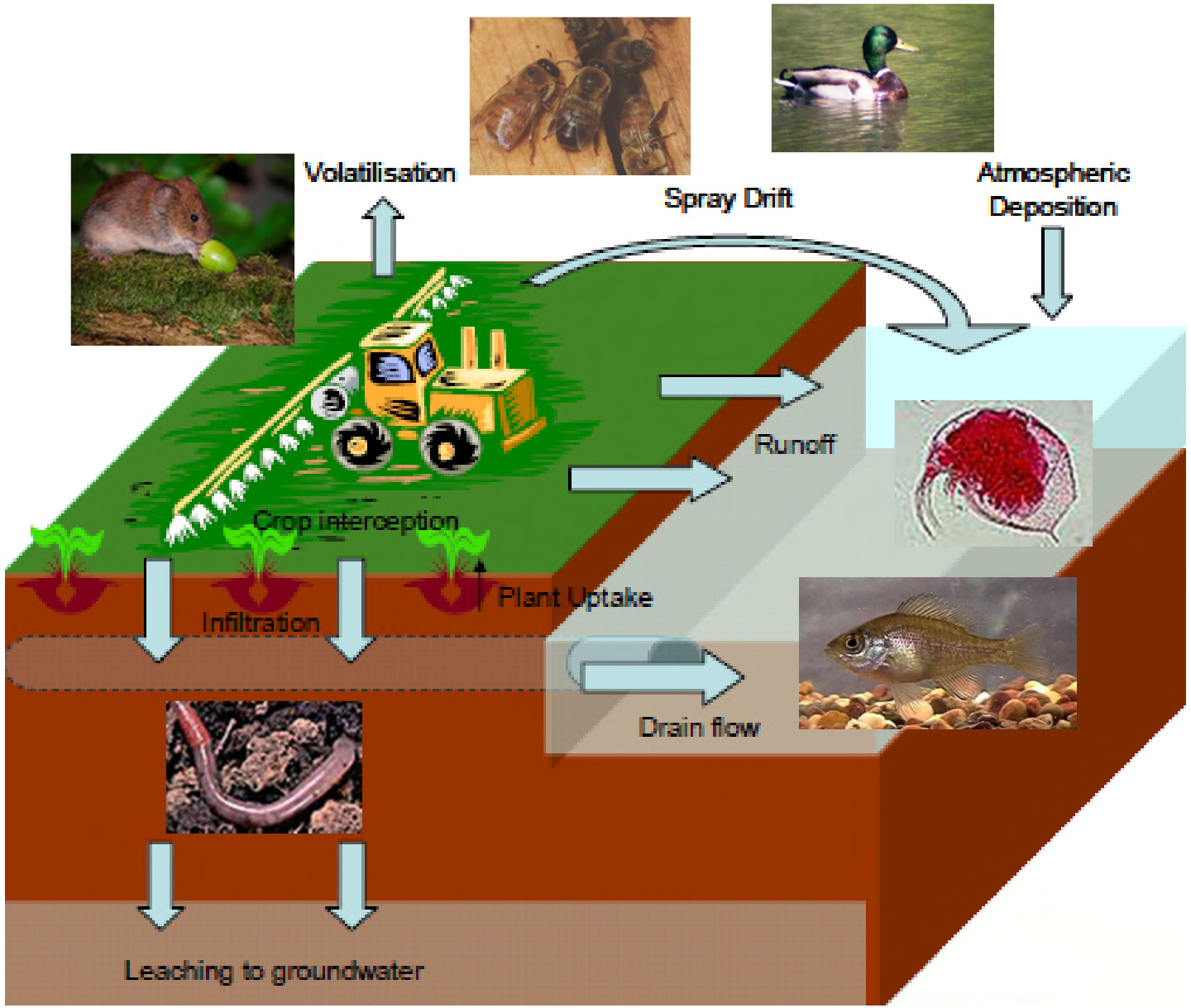
Non Target Organisms

- Birds
- Fish
- Aquatic Invertebrates
- Algae
- Aquatic plants
- Mammals
- Bees
- Other Arthropods
- Earthworms
- Soil micro-organisms
- Non Target Plants



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Ecotoxicological Risk Assessment

Endpoints (Hazard Assessment)	• Studies provided during the approval of the active substance • New studies with the formulated product
Exposure	• Based on the routes of exposure • According to the GAP proposed for the PPP
Risk Characterisation	• Quantitative approach: Toxicity/Exposure Ratio (TER) and Hazard Quotient (HQ)
Risk Assessment	• Trigger value (Reg. UE 546/2011 “Uniform principles for evaluation and authorisation of plant protection products”)

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Endpoints

LC_{50} (fish, earthworms)

Lethal Concentration (a.i.) for 50% of tested organisms

LD_{50} (birds, mammals, bees, earthworms)

Lethal Dose (a.i.) for 50% of tested organisms

EC_{50} (daphnia and aquatic invertebrates; algae; aquatic plants)

Effect concentration (a.i.) for 50% of tested organisms

NOEC No Observed Effects Concentration

(birds and mammals, fish; daphnia and aquatic invertebrates, sediments organisms, earthworms)

Max concentration (a.i.) where no effect is observed on tested organisms

BCF (fish): Bioconcentration factor

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Trigger Values

Toxicity/Exposure Ratio

$$TER_{A/LT} = \frac{\text{Toxicity endpoint}}{\text{Exposure Concentration}}$$

Hazard Quotient (for Bees and Arthropods)

$$HQ = \frac{\text{Exposure Concentration}}{\text{Toxicity endpoint}}$$

Birds & Mammals	• Acute, short-term >10 • Long-term >5
Aquatic organisms	• Acute >100 • Long-term >10
Honeybees Non target arthropods	• Oral/contact <50 • In-field/off-field <2
Earthworms Soil micro-organisms	• Acute >10, long-term >5, • 25%
Non target plants	• Long-term >5

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2016 European Union report on pesticide residues in food

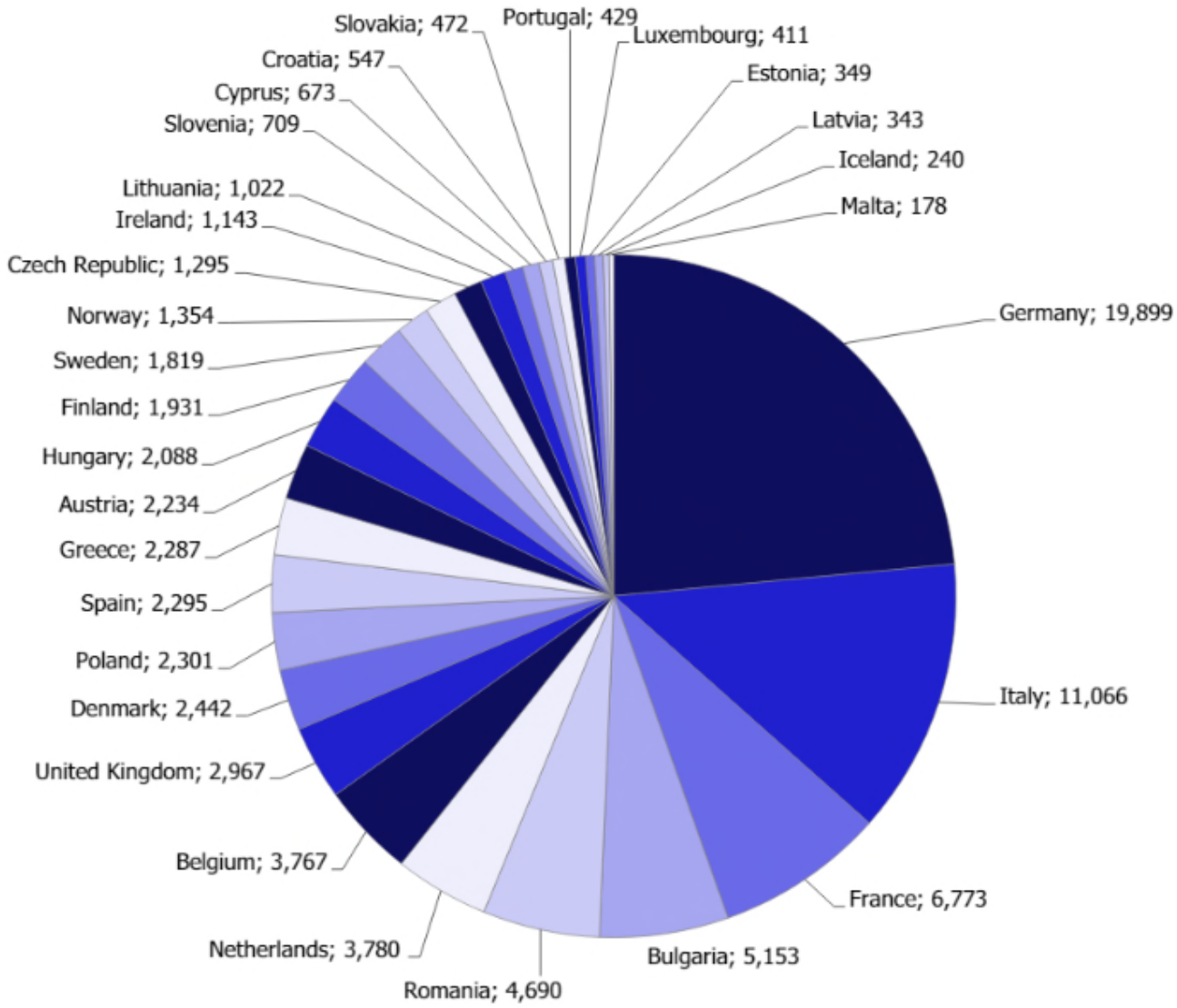

Figure 37: Number of samples analysed by each reporting country

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2016 European Union report on pesticide residues in food

- Analysed 84,657 samples for 791 different pesticides.
- The majority of the samples (56,749, 67% of the total) originated from the reporting countries (EU, Iceland and Norway);
- 22,345 samples (26.4%) concerned products imported from third countries.
- For 5,563 samples (6.6%), the origin of the products was unknown.

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2016 European Union report on pesticide residues in food

- 96.2% of the samples analysed in 2016 (EUCP and national programmes) fell within the legal limits (81,482 samples), i.e. the measured levels did not exceed the MRLs permitted in EU legislation;
- 50.7% of the samples tested were free of quantifiable residues (residue levels below the LOQ),
- 45.5% contained quantified residues below the MRLs.
- 3.8% of the samples with residue levels exceeding the MRLs (3,175 samples).
- MRLs were exceeded in 7.2% of the samples from third countries

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2016 European Union report on pesticide residues in food

In 2016, 1,676 samples of food intended for infants and young children were analysed.
In 89.8% of the samples, no quantifiable residues were found (residues below the LOQ),
whereas 171 samples (10.2%) contained quantifiable residues at or above the LOQ.
Of these samples, 32 (1.9% of the baby food samples) exceeded the MRL of 0.01 mg/kg applicable for baby food.
The top three most frequently measured residues were copper, chlorates and fosetyl-Al.

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- In 2016, 5,495 samples of organic food (not including baby food samples) were taken;
- 4,568 samples (83.1%) were free of quantifiable residues.
- The percentage of organic samples containing residues in concentrations within the legal limits was 15.6% (856 samples);
- a significant portion of these samples contained only residues of substances that do not necessarily come from the use of pesticides (e.g. naturally occurring substances and persistent organic pollutants).
- The MRLs were exceeded in 1.3% of the organic samples analysed (71 samples)

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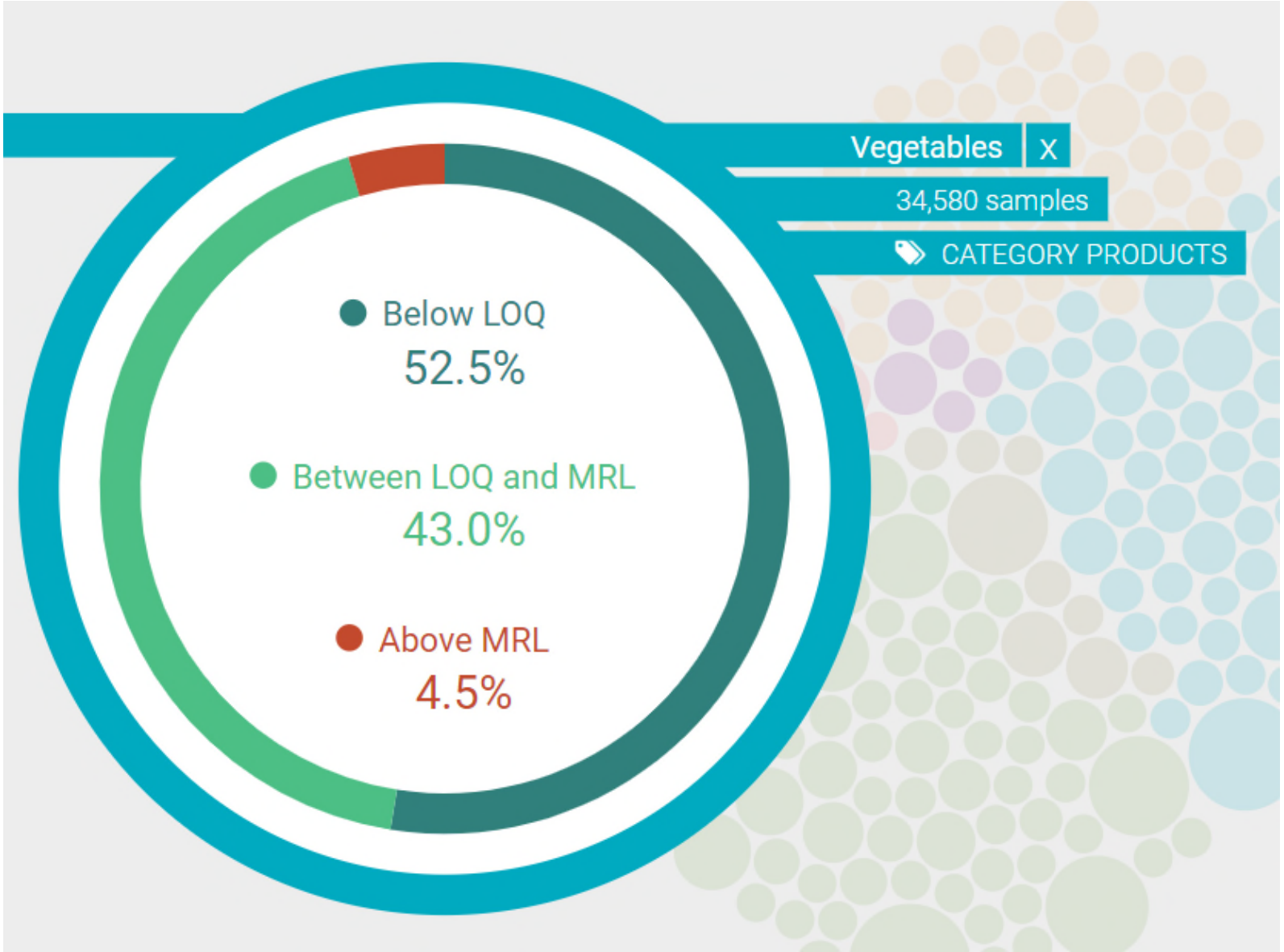

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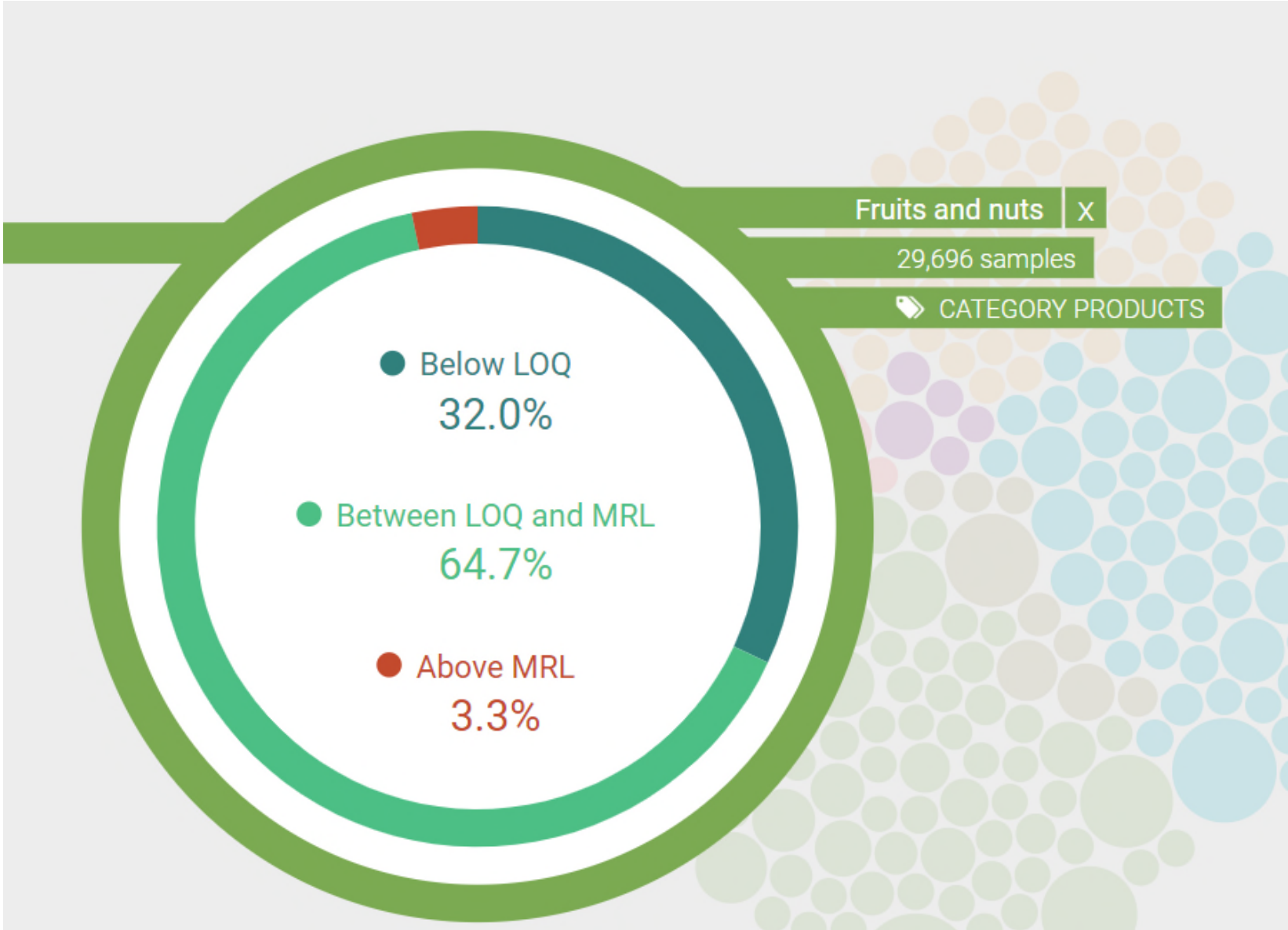

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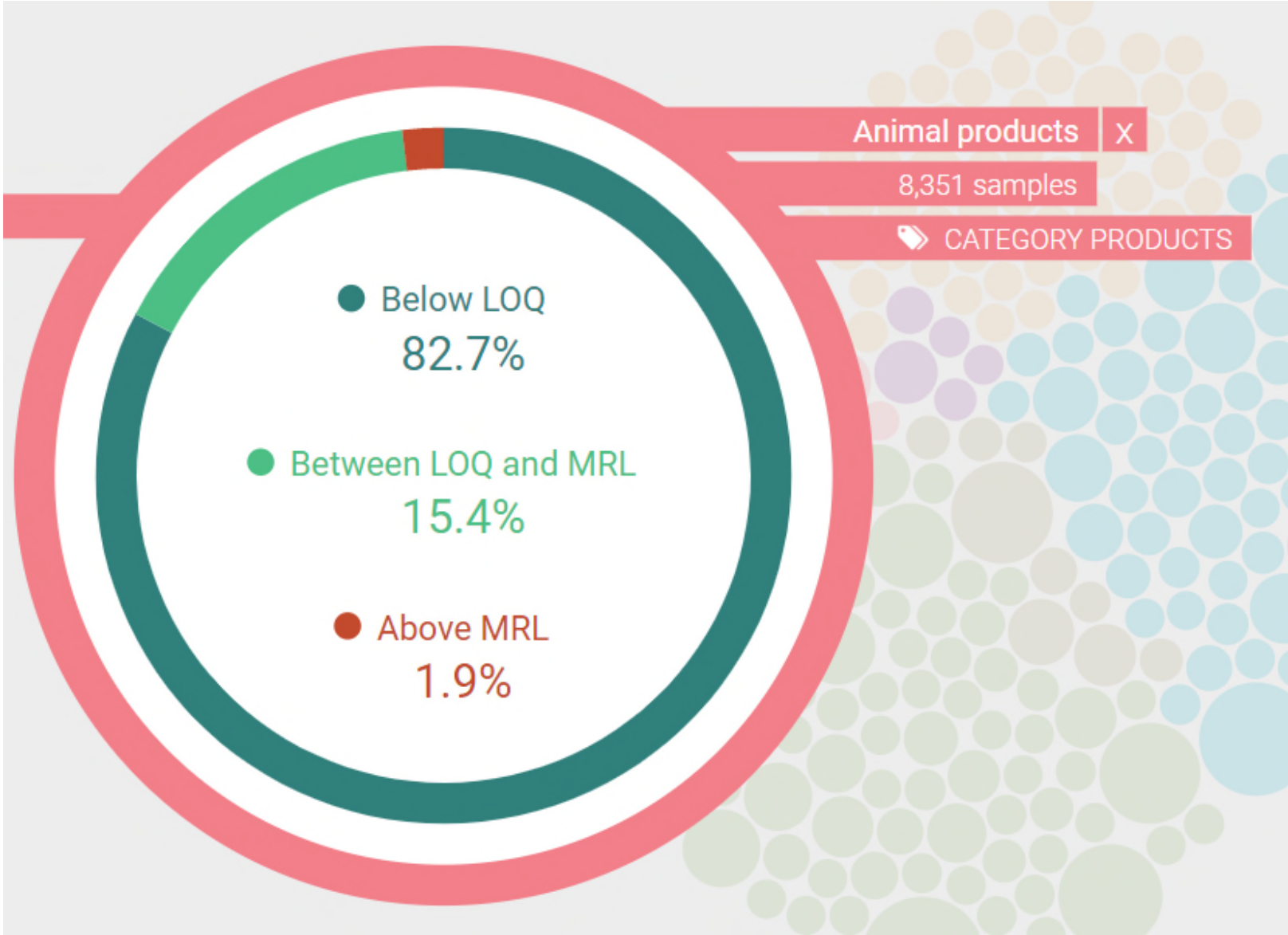

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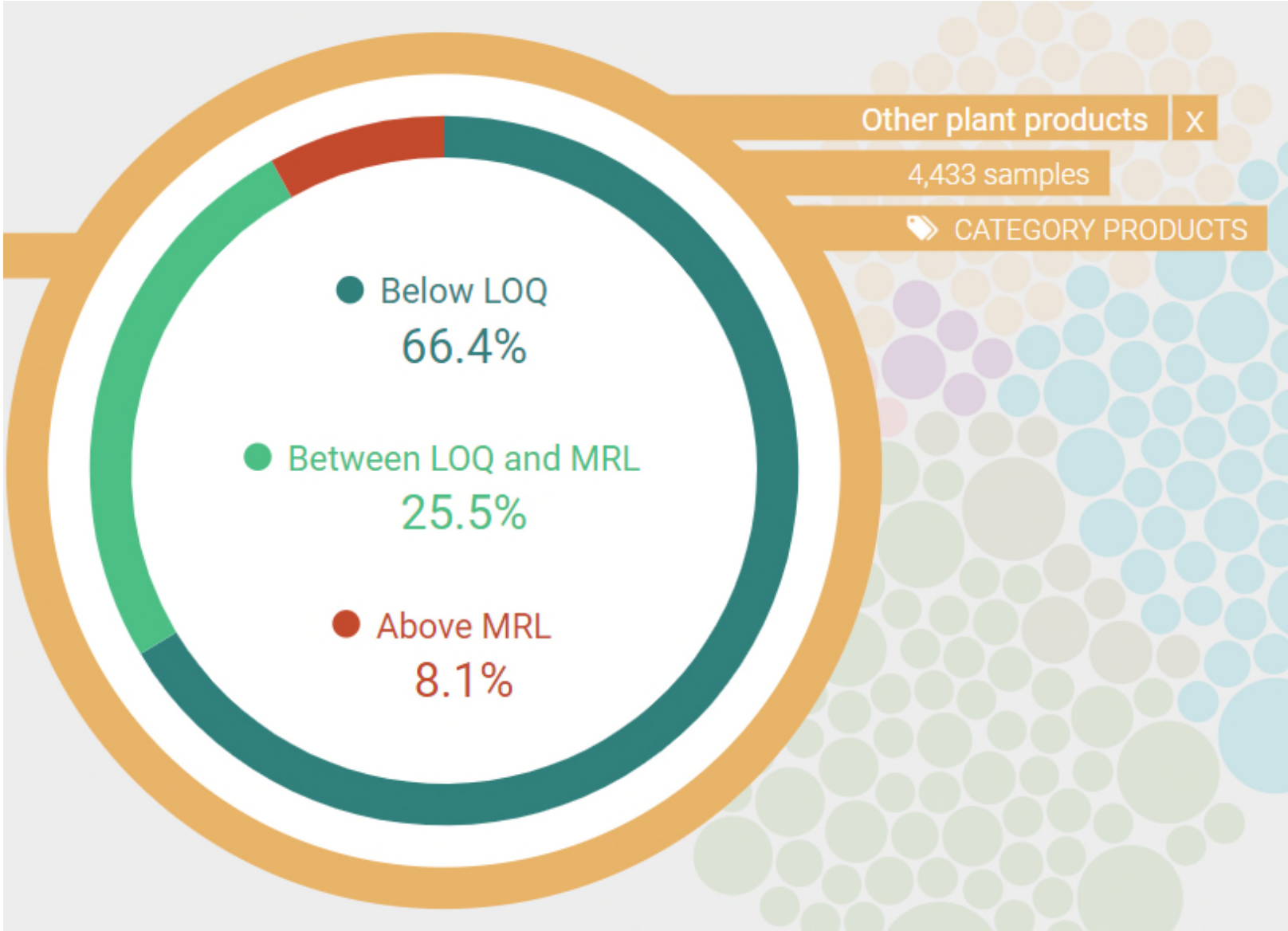

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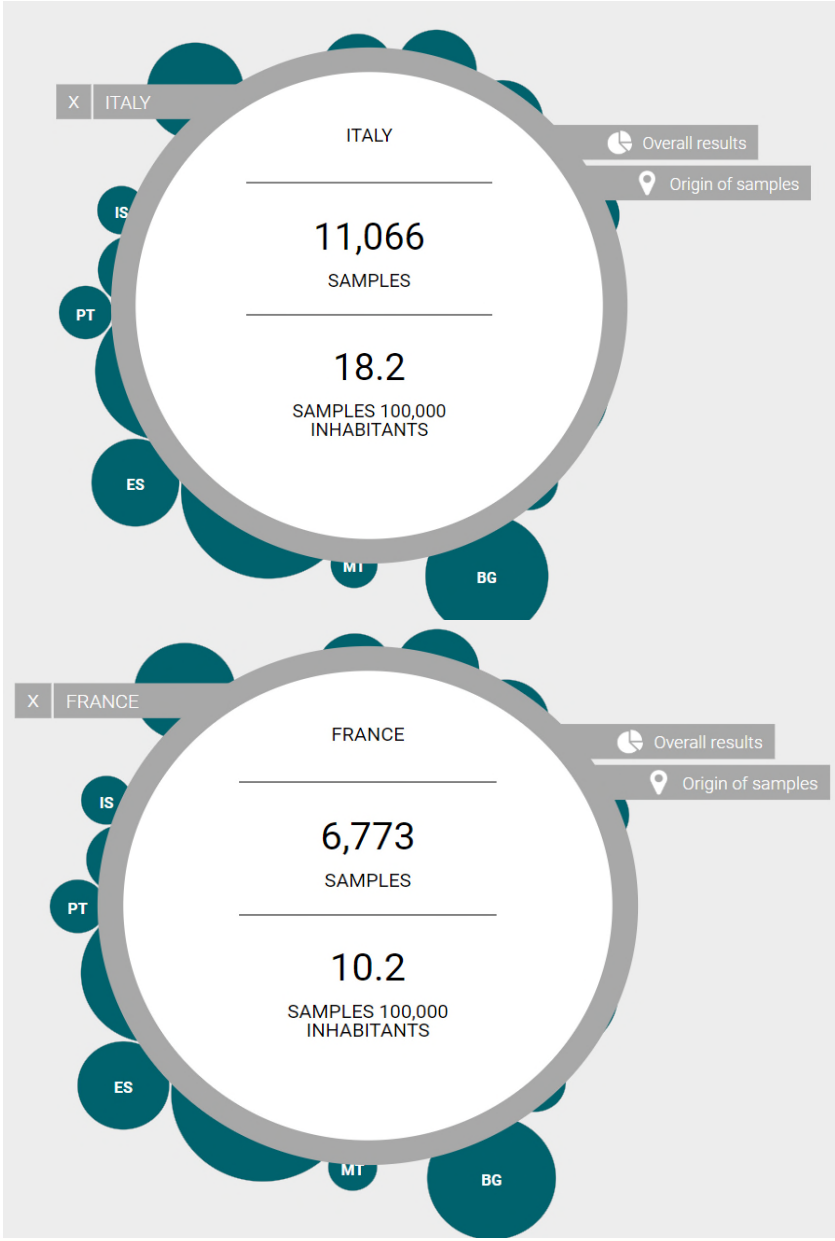

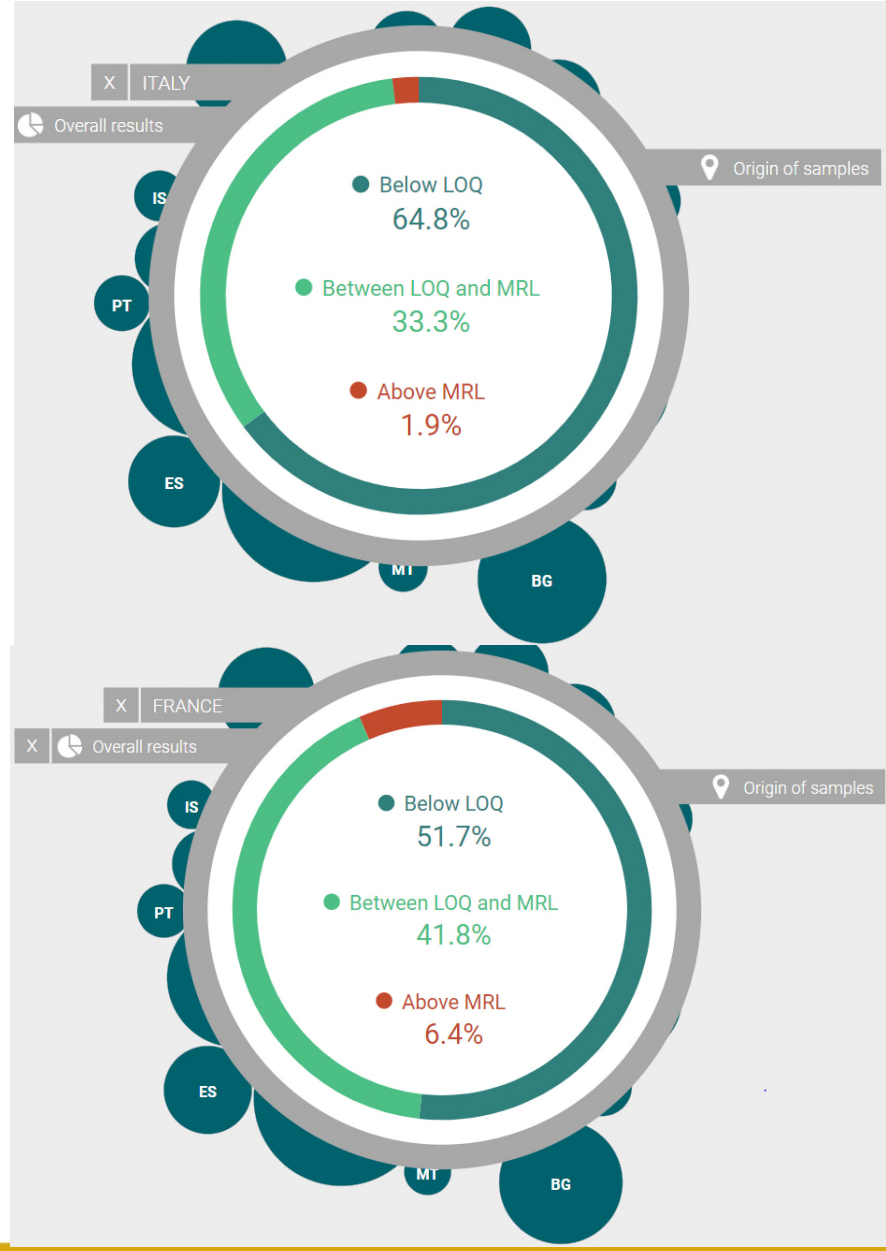

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2016 European Union report on pesticide residues in food

Short-term dietary exposure assessment

- The European Food Safety Authority (EFSA) performed the acute (short-term) dietary risk assessment for the pesticide/food product combinations covered by the EUCP.
- Overall, 122 pesticides were assessed.
- For 89 of those pesticides, the exposure was below the acute reference dose (ARfD).
- For the other 33 pesticides, the exposure assessment exceeded the ARfD in 209 samples (1.0% of the samples tested).
- The products with the highest number of exceedances of the ARfD were apples (76 samples), lettuce (46), peaches (39) and tomatoes (29).
- The pesticides which most frequently exceeded the ARfD were chlorpyrifos, iprodione and lambda-cyhalothrin.
- Considering these findings, EFSA concluded that the probability of being exposed to pesticide residues exceeding concentrations that may lead to negative health effects is low.

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2016 European Union report on pesticide residues in food

Long-term dietary exposure assessment

- The long-term (chronic) exposure was calculated for all pesticides covered by the EUCP.
- For the first time, the calculations took into account results for all types of food products which are covered by the dietary intake model used for consumer risk assessment.
- The exposure amounted to less than 100% of the ADI for all pesticides except for dieldrin, dichlorvos, dimethoate (omethoate scenario) and the dithiocarbamates (ziram scenario).
- For 142 pesticides out of the 165 covered by the EUCP, the estimated long-term exposure was less than 10% of the ADI;
- for 73 of these, exposure was lower than 1% of the ADI.
- EFSA concluded that according to the current scientific knowledge, the long-term dietary exposure to pesticides covered by the 2016 EUCP was unlikely to pose a health risk to consumers.

«Omnia venenum sunt: nec sine veneno quicquam existit. Dosis sola facit, ut venenum non fit.»