GERMAN FEDERAL INSTITUTE FOR RISK ASSESSMENT

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RISK ASSESSMENT
SYMPOSIUM

BfR
Bundesinstitut für Risikobewertung

Veterinary drug residues and food safety

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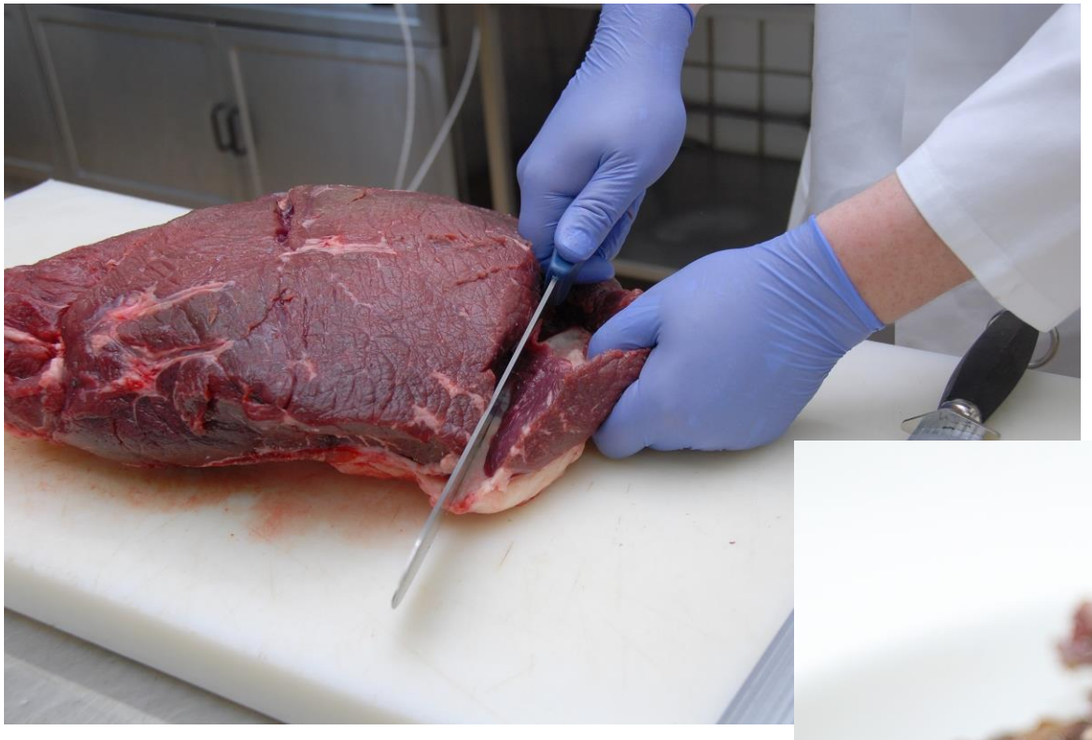
Outline

- Veterinary drugs
  - Procedures
  - Residues

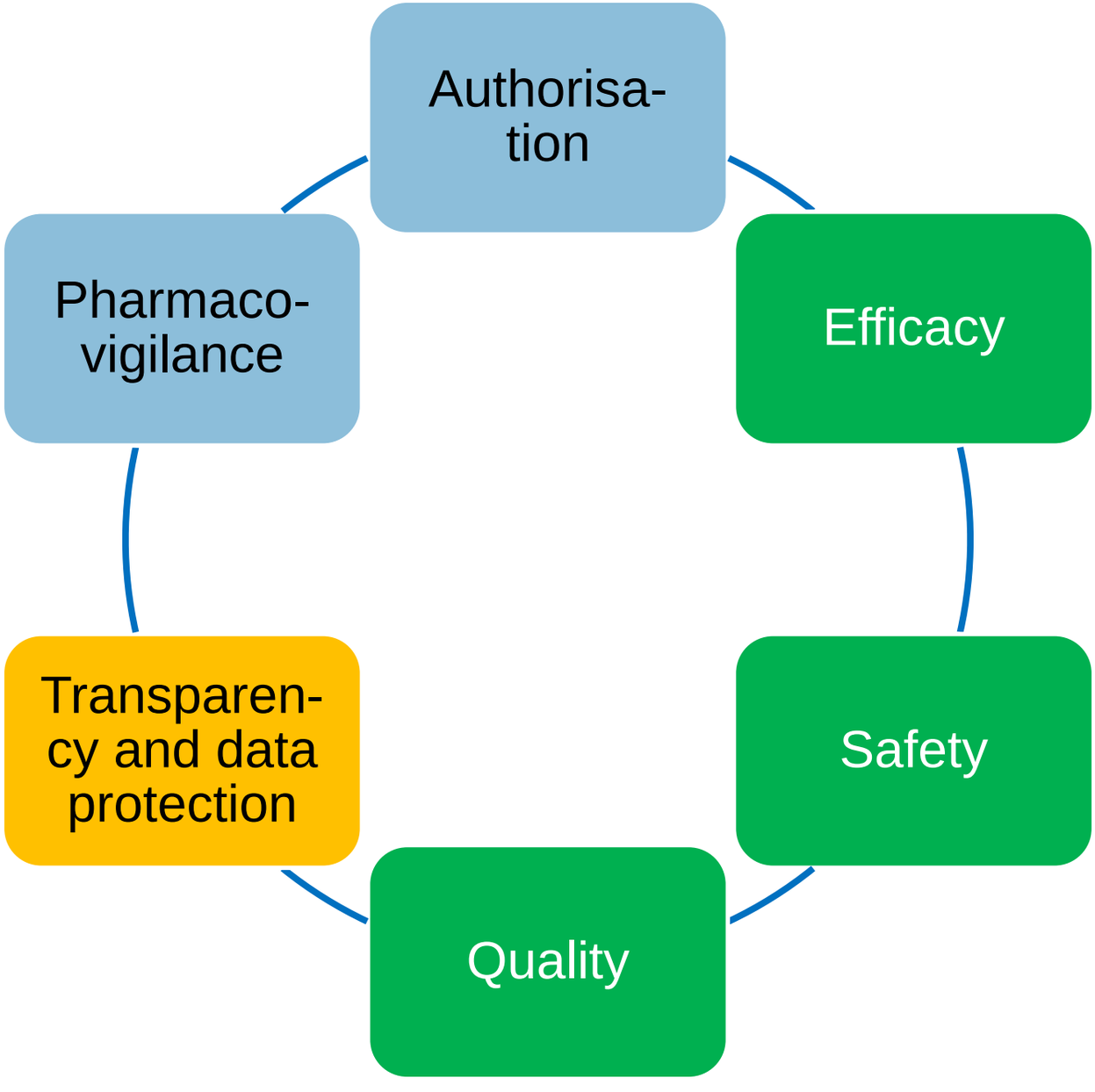
- Food safety
  - General principles
  - Information network
  - Example

Introduction

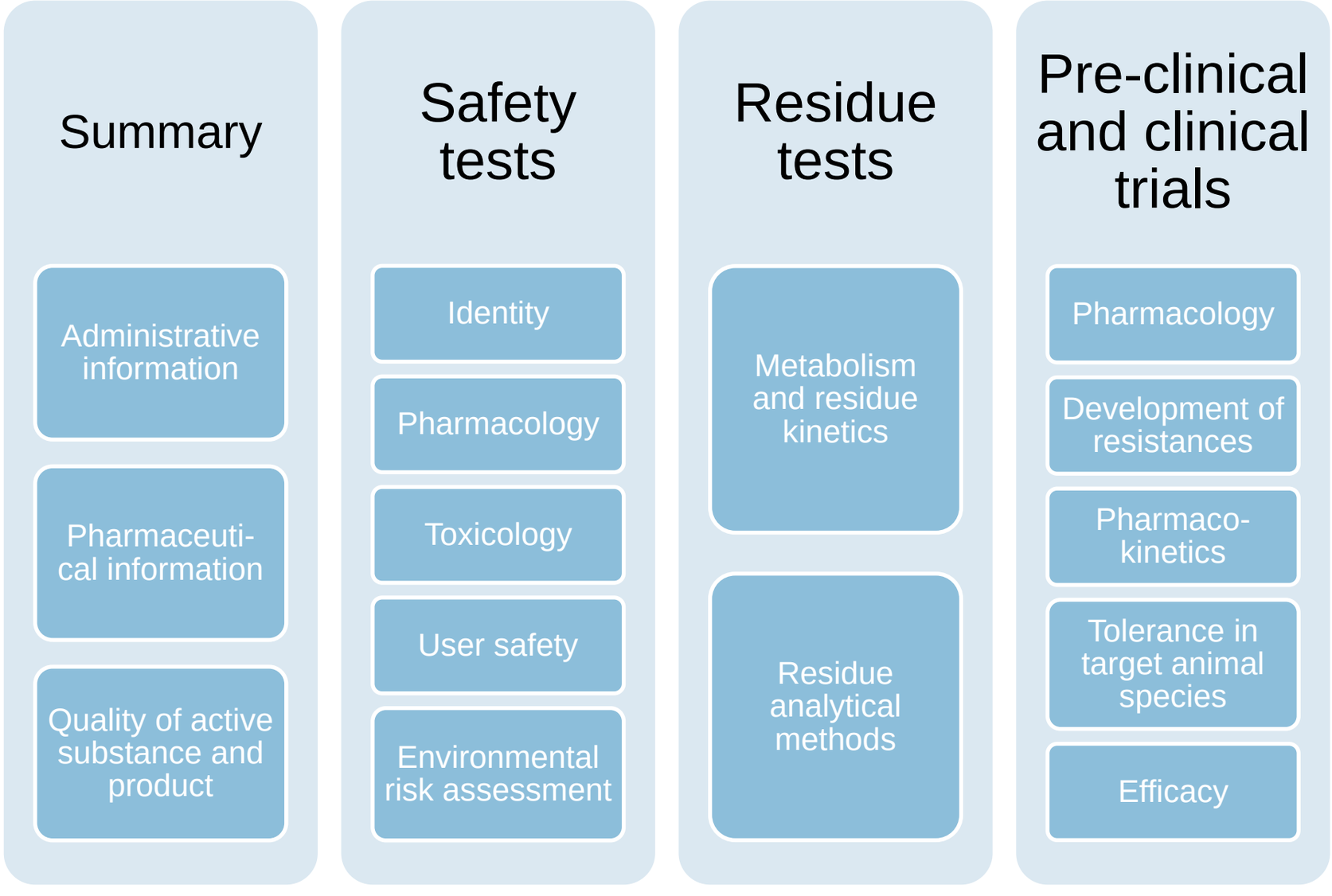
Veterinary medicinal products



Veterinary medicinal products



Selected information requirements for veterinary medicinal products



Authorisation and maximum residue limits

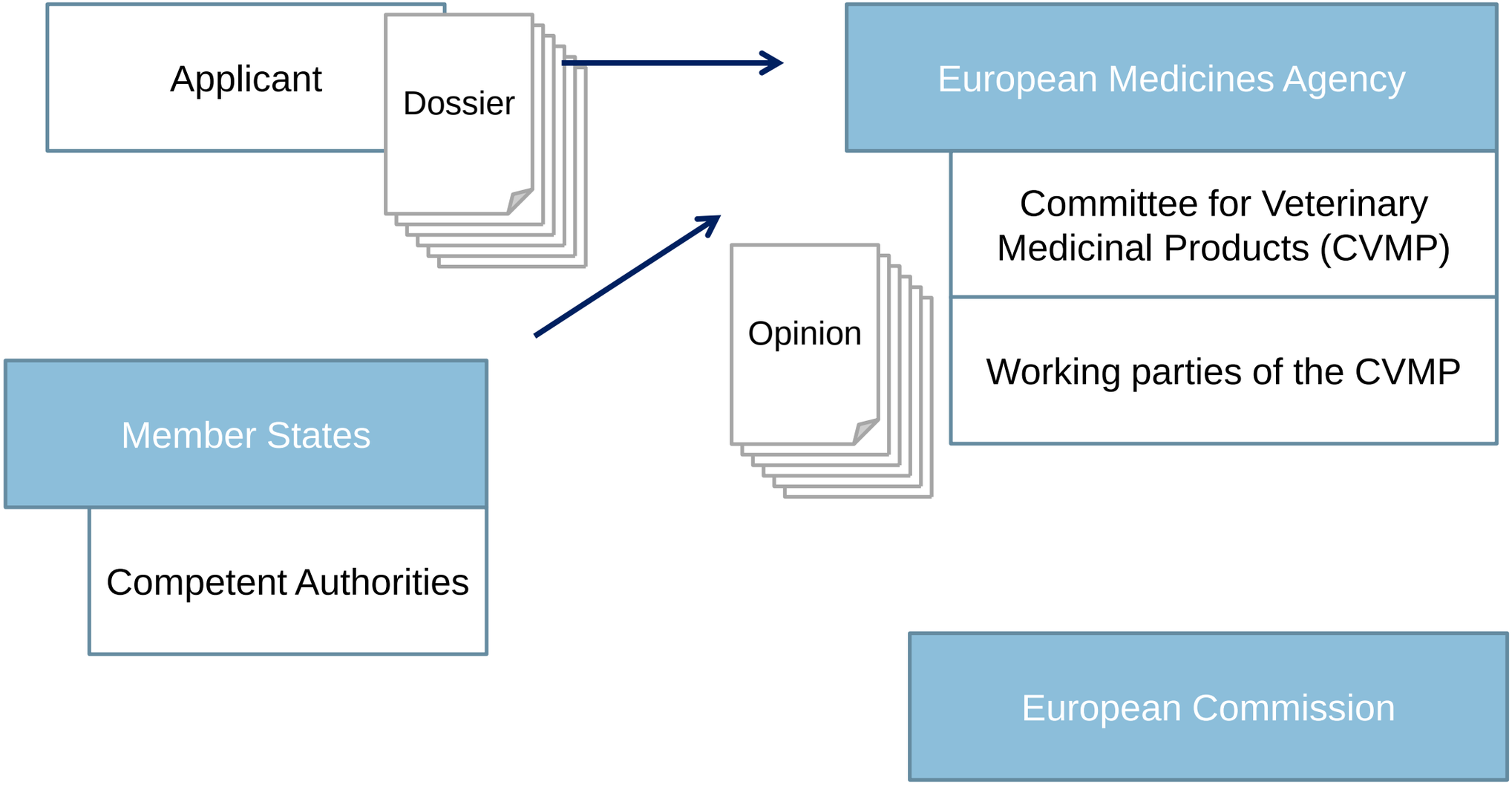
Different procedures to authorise veterinary medicinal products exist:

- Centralised procedure
- Decentralised procedure
- Mutual recognition procedure
- National procedures

To establish maximum residue limits (MRL), a respective application needs to be submitted to European Medicinal Agency (EMA). The Agency sends the Committee for veterinary medicinal Products (CVMP) opinion on the MRL application to the European Commission, which adopts a Commission Regulation confirming the classification of the substance.

https://www.ema.europa.eu/en/veterinary-regulatory/research-development/maximum-residue-limits-mrl

Involved organisations (centralised procedure)



Risk assessment

Problem formulation

Hazard identification

Hazard characterisation

Exposure assessment

Risk characterisation

Communication

Hazard assessment

- Single dose toxicity
- Repeat-dose toxicity
- Tolerance in the target species
- Reproductive toxicity including developmental toxicity
- Genotoxicity
- Carcinogenicity
- (Special studies)
- Observations in humans

Illustration created with http://www.tagxedo.com

Health-based guidance values:

- ADI – Acceptable Daily Intake
- ARfD – Acute Reference Dose

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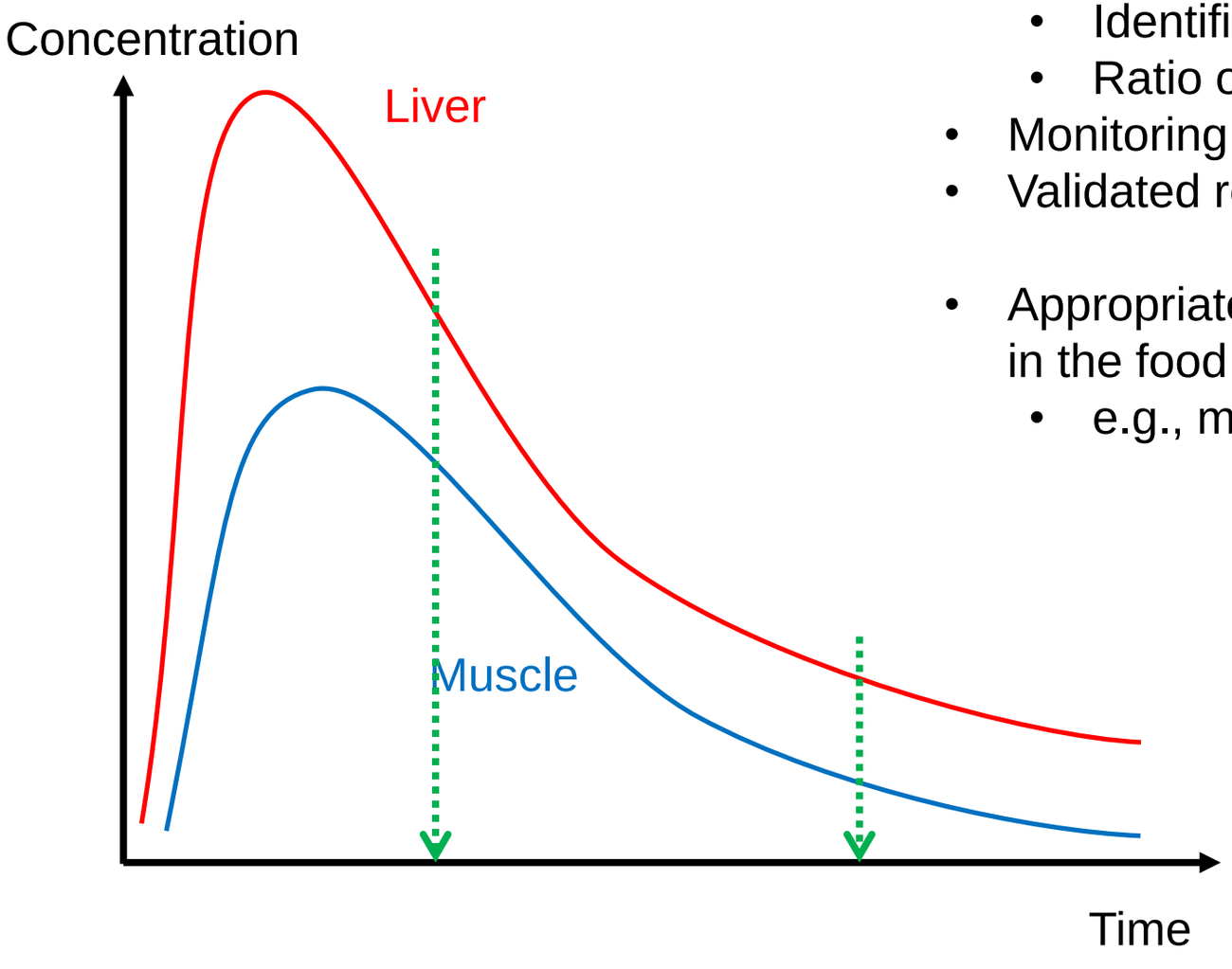
Exposure assessment



Residue assessment

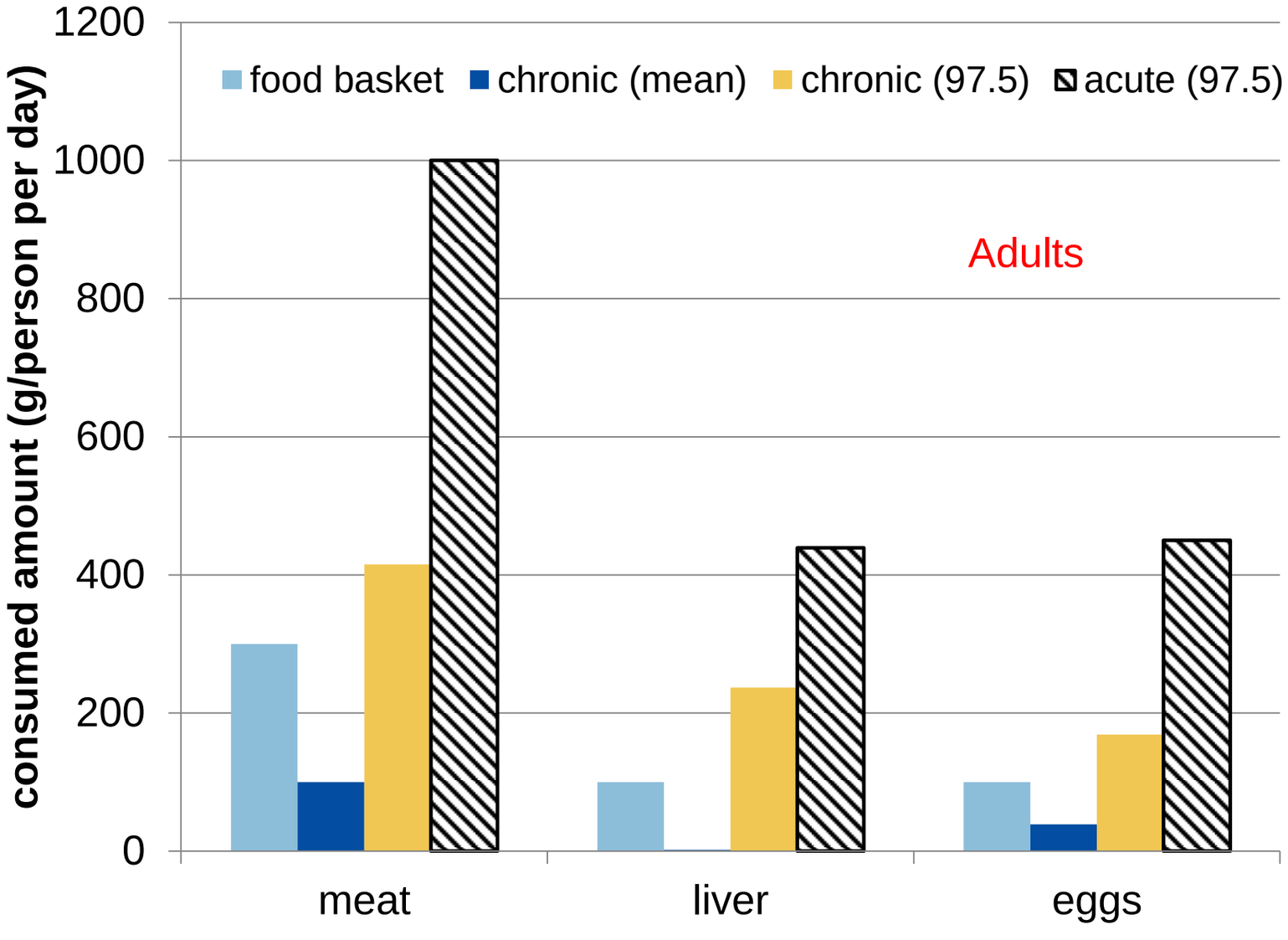
- Pharmacokinetics in food producing species
- Depletion of residues
  - Identification of marker residues
  - Ratio of marker residue to total residues
- Monitoring and exposure data
- Validated residue analytical method

- Appropriate measure for the amount of residue in the food
  - e.g., median, 95th percentile, MRL

Exposure assessment

Consumption data

- Model diet
- Consumption surveys



According to Boobis et al. (2017) *Critical Reviews in Toxicology* Vol. 47(10): 885-99. http://dx.doi.org/10.1080/10408444.2017.1340259.

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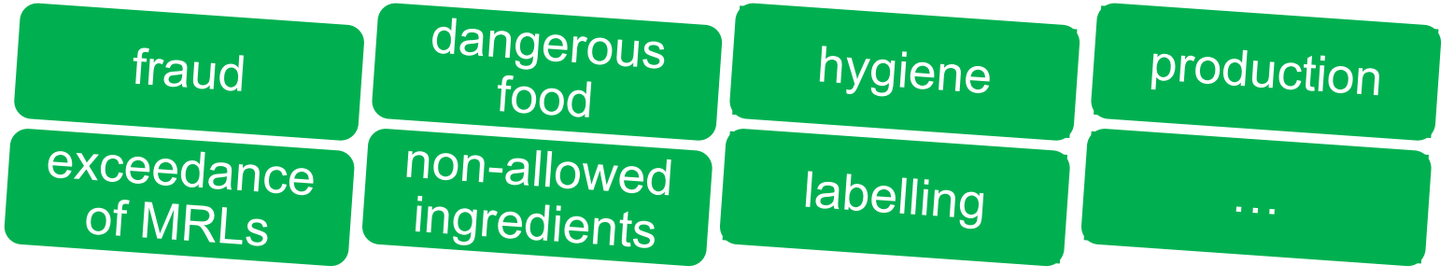
Food safety

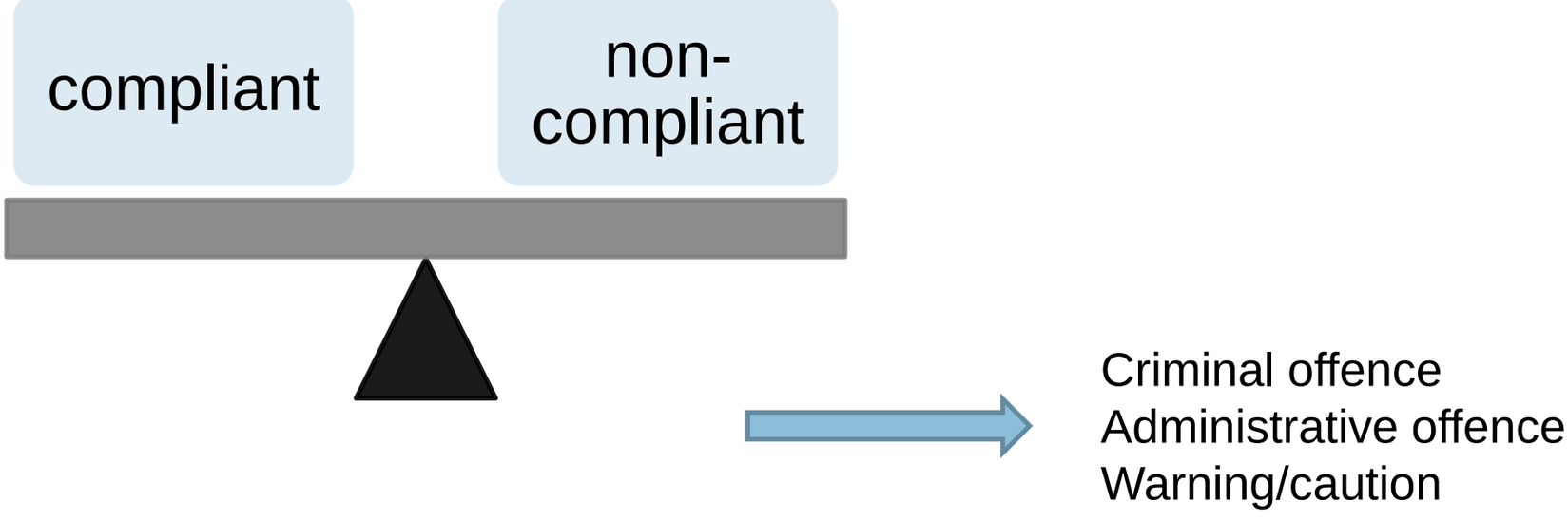
General food law (Regulation (EC) No 178/2002)

aims at a “… high level of protection of human health and consumers' interest in relation to food, taking into account in particular the diversity in the supply of food including traditional products, whilst ensuring the effective functioning of the internal market.”

“… shall apply to all stages of production, processing and distribution of food and feed. It shall not apply to primary production for private domestic use or to the domestic preparation, handling or storage of food for private domestic consumption.”

(Selected) reasons for non-compliance





General food law (Regulation (EC) No 178/2002)

Article 14

Food safety requirements

1. Food shall not be placed on the market if it is unsafe.

2. Food shall be deemed to be unsafe if it is considered to be:

(a) injurious to health;

(b) unfit for human consumption.

3. In determining whether any food is unsafe, regard shall be had:

(a) to the normal conditions of use of the food by the consumer and at each stage of production, processing and distribution, and

(b) to the information provided to the consumer, including information on the label, or other information generally available to the consumer concerning the avoidance of specific adverse health effects from a particular food or category of foods.

4. In determining whether any food is injurious to health, regard shall be had:

(a) not only to the probable immediate and/or short-term and/or long-term effects of that food on the health of a person consuming it, but also on subsequent generations;

(b) to the probable cumulative toxic effects;

(c) to the particular health sensitivities of a specific category of consumers where the food is intended for that category of consumers.

5. In determining whether any food is unfit for human consumption, regard shall be had to whether the food is unacceptable for human consumption according to its intended use, for reasons of contamination, whether by extraneous matter or otherwise, or through putrefaction, deterioration or decay.

6. Where any food which is unsafe is part of a batch, lot or consignment of food of the same class or description, it shall be presumed that all the food in that batch, lot or consignment is also unsafe, unless following a detailed assessment there is no evidence that the rest of the batch, lot or consignment is unsafe.

REGULATION (EC) No 470/2009 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

of 6 May 2009

laying down Community procedures for the establishment of residue limits of pharmacologically active substances in foodstuffs of animal origin, repealing Council Regulation (EEC) No 2377/90 and amending Directive 2001/82/EC of the European Parliament and of the Council and Regulation (EC) No 726/2004 of the European Parliament and of the Counc[1]

(Text with EEA relevance)

Article 23

Placing on the market

Food of animal origin containing residues of a pharmacologically active substance:

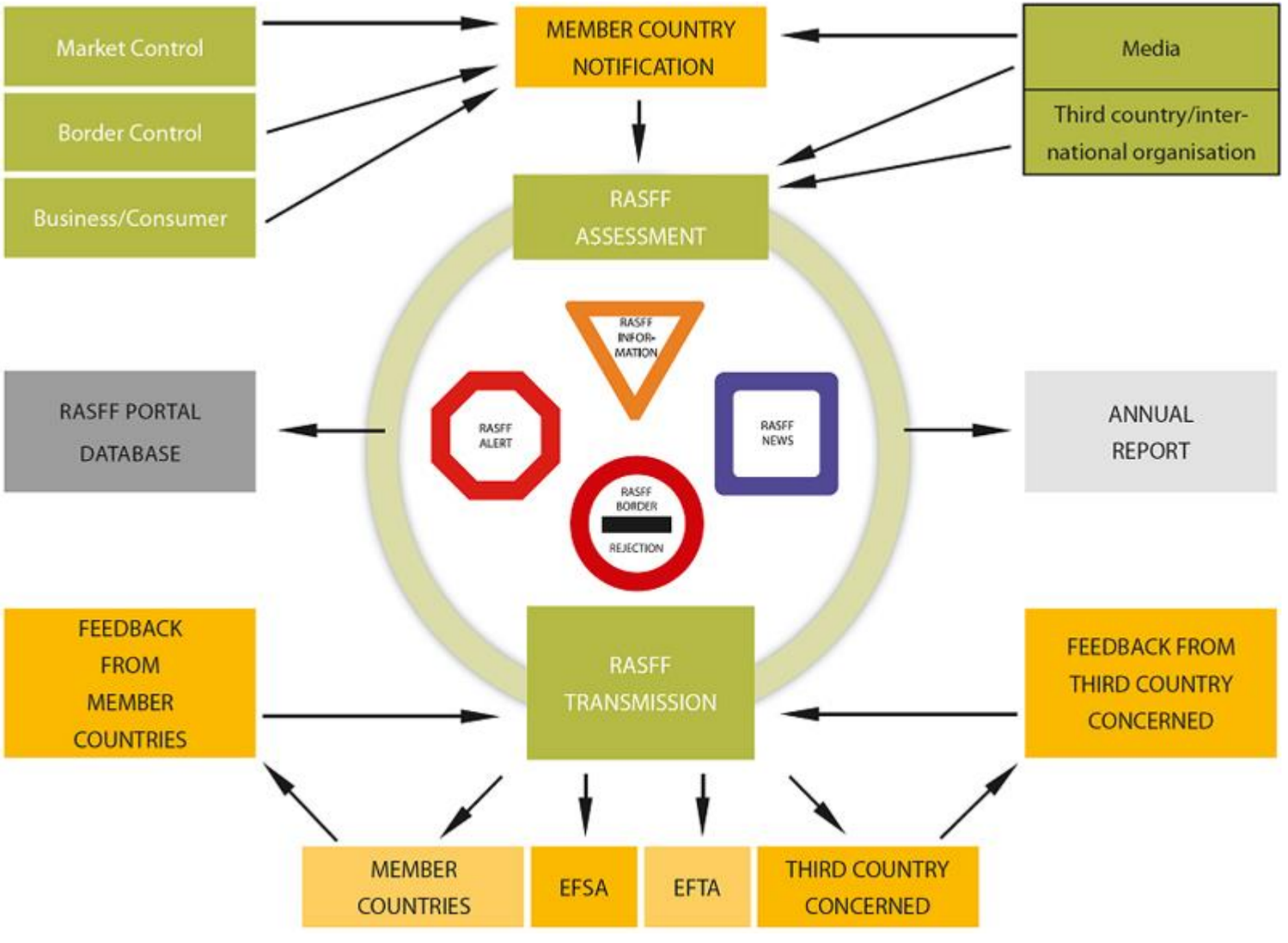
(a) classified in accordance with Article 14(2)(a), (b) or (c) at a level exceeding the maximum residue limit established pursuant to this Regulation; or

(b) not classified in accordance with Article 14(2)(a), (b) or (c), except where a reference point for action has been set for that substance pursuant to this Regulation and the level of residues does not equal or exceed that reference point for action;

shall be considered not to comply with Community legislation.

Detailed rules on the maximum residue limit to be considered for control purposes for foodstuffs derived from animals which have been treated under Article 11 of Directive 2001/82/EC shall be adopted by the Commission in accordance with the regulatory procedure referred to in Article 26(2) of this Regulation.

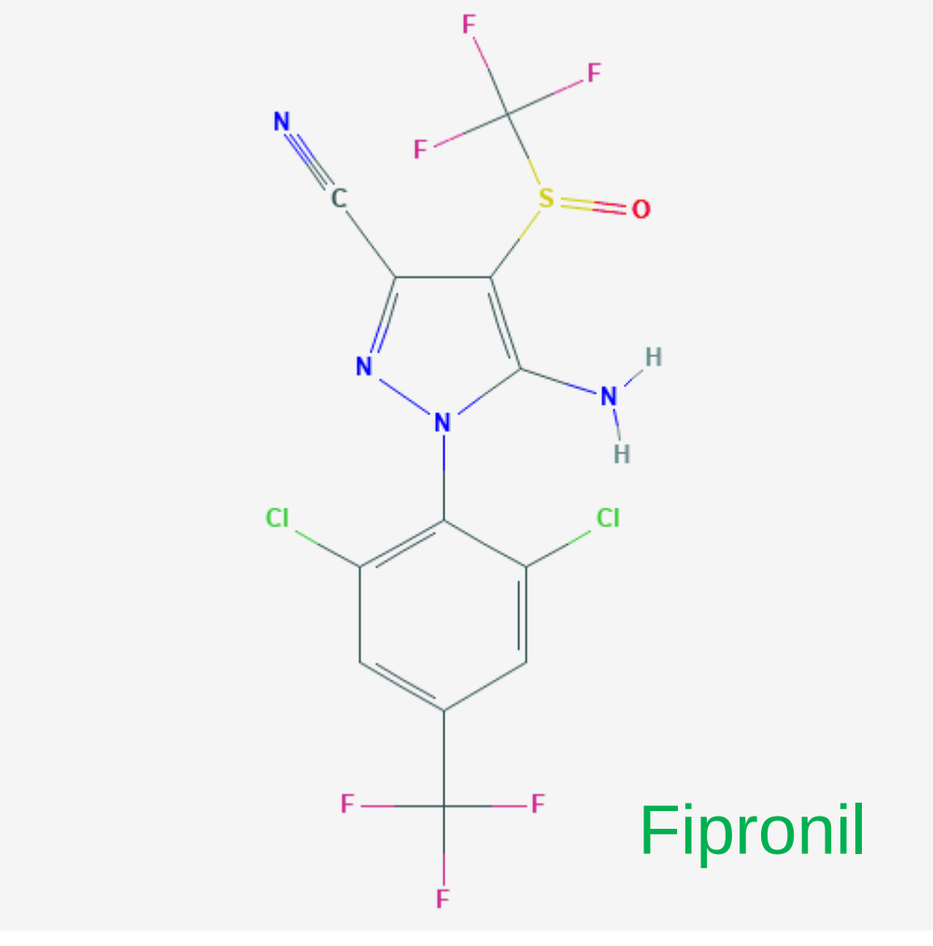
RASFF - the Rapid Alert System for Food and Feed



https://ec.europa.eu/food/safety/rasff_en

Graphics: https://ec.europa.eu/food/safety/rasff/how_does_rasff_work/notifications_process_en

A recent food incident in Europe



Fipronil

Source: PubChem
https://pubchem.ncbi.nlm.nih.gov/compound/3352#section=Structures

Reports of fipronil in hens eggs

Notification details - 2017.1065

unauthorised substance fipronil (between 0.0031 and 1.2 mg/kg - ppm) in eggs

Reference:	2017.1065	Notification type:	food - alert - official control on the market
Notification date:	20/07/2017	Action taken:	withdrawal from the market
Last update:	12/10/2018	Distribution status:	distribution to other member countries
Notification from:	Belgium (BE)	Product:	eggs
Classification	alert	Product category:	eggs and egg products
Risk decision	serious	Published in RASFF Consumers' Portal	has been published before

MRL for eggs: 0.005 mg/kg

https://webgate.ec.europa.eu/rasff-window/portal/?event=notificationDetail&NOTIF_REFERENCE=2017.1065

Risk assessment

Problem formulation

Acute dietary exposure.
All consumer groups.

Hazard identification

ADI: 0.0002 mg/kg bw
ARfD: 0.009 mg/kg bw
(EFSA, 2006)

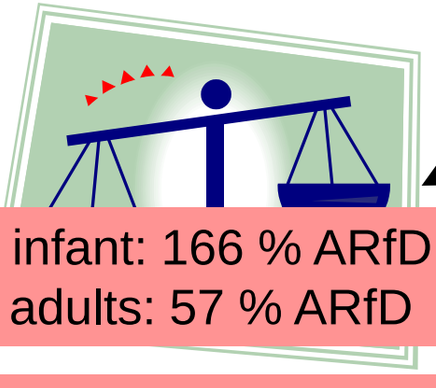
Hazard characterisation

Exposure ass

Eggs: 1.2 mg/kg

*

Amount eaten



EFSA PRIMO (version 3.1), acute
UK infant: 108 g / 8.7 kg bw
FR adults: 282.2 g / 66.4 kg bw

UK infant: 166 % ARfD
FR adults: 57 % ARfD

Serious risk for infants/children
Medium-severity symptoms
Concentration of 0.72 mg/kg is the threshold

Communication

BfR

Follow-up

fup720	France	28/06/2018	additional information
fup721	Denmark	06/07/2018	outcome of investigations

Hazards

Substance / Hazard	Category	Analytical result	Units	Sampling date
unauthorised substance fipronil	pesticide residues	between 0.0031 and 1.2	mg/kg - ppm	15/05/2017

Countries/organisations concerned (D = distribution, O = origin)

Afghanistan (D) | Angola (D) | Austria (D) | Belgium (D) | Bulgaria (D) | Canada (D) | Cape Verde (D) | Commission Services | Congo (Brazzaville) (D) | Cyprus (D) | Czech Republic (D) | Denmark (D) | Equatorial Guinea (D) | Estonia (D) | Finland | France (D) | Germany (D) | Greece (D) | Hong Kong (D) | Hungary (D) | INFOSAN | India (D) | Iraq (D) | Ireland (D) | Isle of Man | Israel (D) | Italy (D) | Latvia (D) | Lebanon (D) | Liberia | Liechtenstein (D) | Lithuania (D) | Luxembourg (D) | Maldives (D) | Malta (D) | Montenegro (D) | Netherlands (D) | Norway | Philippines (D) | Poland (D) | Portugal | Qatar (D) | Romania | Russia (D) | Saudi Arabia (D) | Singapore (D) | Sint Maarten (D) | Slovakia (D) | Slovenia (D) | South Africa (D) | Spain (D) | Sweden (D) | Switzerland (D) | Turkey (D) | Ukraine | United Arab Emirates (D) | United Kingdom (D) | United States (D)

https://webgate.ec.europa.eu/rasff-window/portal/?event=notificationDetail&NOTIF_REFERENCE=2017.1065

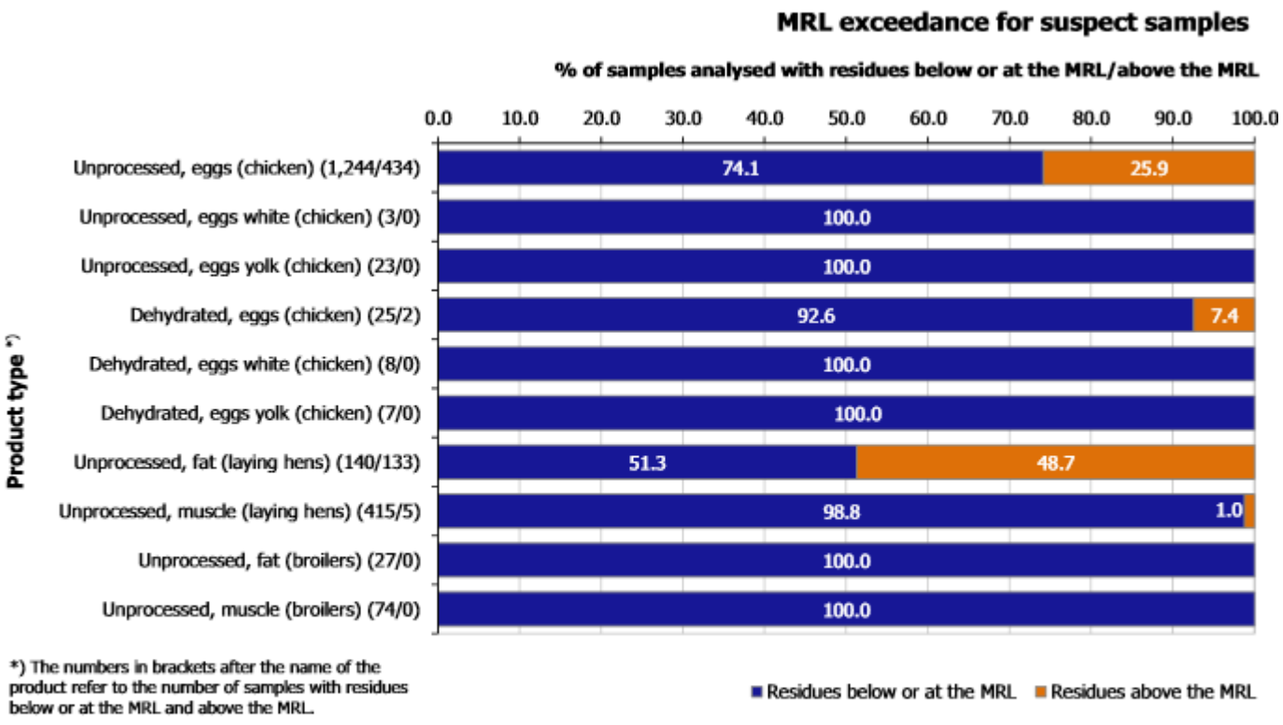


Figure 8: Number and percentage of samples with residues below or at the EU MRL and residues above the EU MRL by product type – suspect samples o

Follow-up: ad-hoc monitoring program

5,439 samples taken between 1 September 2017 and 30 November 2017 (thereof 2,899 randomly taken) were analysed for up to 66 substances.

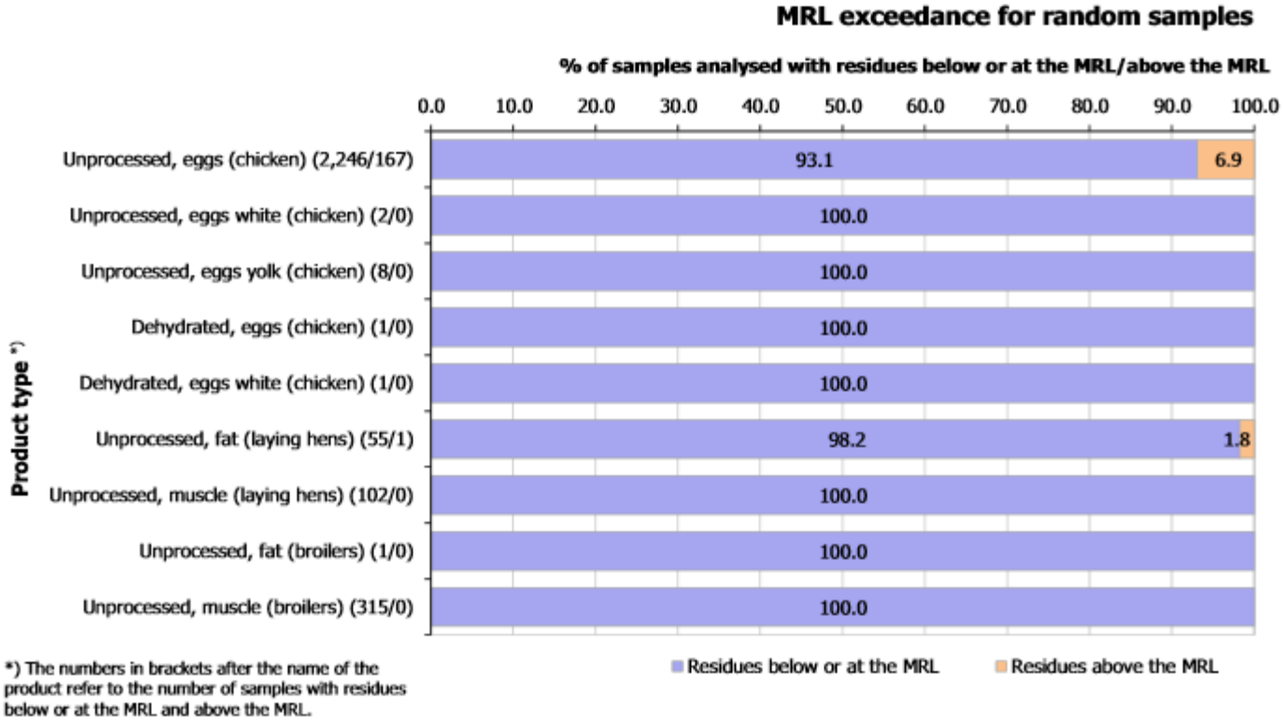


Figure 9: Number and percentage of samples with residues below or at the EU MRL and residues above the EU MRL by product type – samples taken by random sampling

EFSA (2018): Occurrence of residues of fipronil and other acaricides in chicken eggs and poultry muscle/fat
http://www.efsa.europa.eu/en/efsajournal/pub/5164

Conclusion

- ✓ The food law aims at safe food while maintaining traditional products. The effective functioning of the market should also be ensured.
- ✓ There are specific rules for the different stages of production, processing and distribution. (E.g., authorisation of veterinary medicinal products; maximum residue limits)
- ✓ Food surveillance should ensure that the rules are complied with.
- ✓ Depending on the reason for non-compliance, different follow-up actions can be prudent.

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Thank you for your attention

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Further reading

Legislation on authorization of veterinary medicinal products

- Directive 2001/82/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to veterinary medicinal products https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:32001L0082 (needed to be translated into national legislation by all EU member states)
- Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:32004R0726
- Regulation (EU) 2019/6 of the European Parliament and of the Council of 11 December 2018 on veterinary medicinal products and repealing Directive 2001/82/EC https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:32019R0006 (does not yet apply)

Further reading

Legislation on maximum residue limits of pharmacologically active substances

- Regulation (EC) No 470/2009 of the European Parliament and of the Council of 6 May 2009 laying down Community procedures for the establishment of residue limits of pharmacologically active substances in foodstuffs of animal origin, repealing Council Regulation (EEC) No 2377/90 and amending Directive 2001/82/EC of the European Parliament and of the Council and Regulation (EC) No 726/2004 of the European Parliament and of the Council https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:32009R0470
- Commission Regulation (EU) No 37/2010 of 22 December 2009 on pharmacologically active substances and their classification regarding maximum residue limits in foodstuffs of animal origin https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:32010R0037
- Commission Implementing Regulation (EU) 2018/470 of 21 March 2018 on detailed rules on the maximum residue limit to be considered for control purposes for foodstuffs derived from animals which have been treated in the EU under Article 11 of Directive 2001/82/EC https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:32018R0470
- Commission Regulation (EU) 2018/782 of 29 May 2018 establishing the methodological principles for the risk assessment and risk management recommendations referred to in Regulation (EC) No 470/2009 https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:32018R0782

Further reading

Guidance documents

European Medicines Agency (EMA) https://www.ema.europa.eu/en/veterinary-regulatory/marketing-authorisation/guidance-documents

International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Medicinal Products (VICH) https://www.vichsec.org/en/guidelines.html

Further reading

General food law

- Regulation (EC) No 178/2002 of the European Parliament and of the Council of 28 January 2002 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 https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:32002R0178
- Rapid alert system on food and feed https://ec.europa.eu/food/safety/rasff_en