



Feed & Food Risk Assessment:

Methods in different frameworks of feed safety analysis

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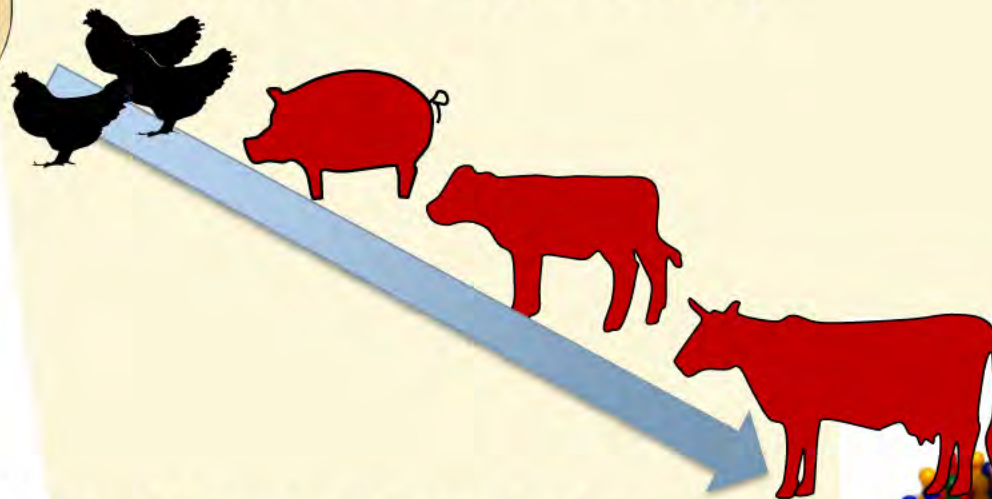
IRAS

Institute for Risk Assessment Sciences

Feed contamination: a matter of concern?

Feed shall be considered to be unsafe if it is considered

(I) to have an **adverse effect** on animal health & productivity

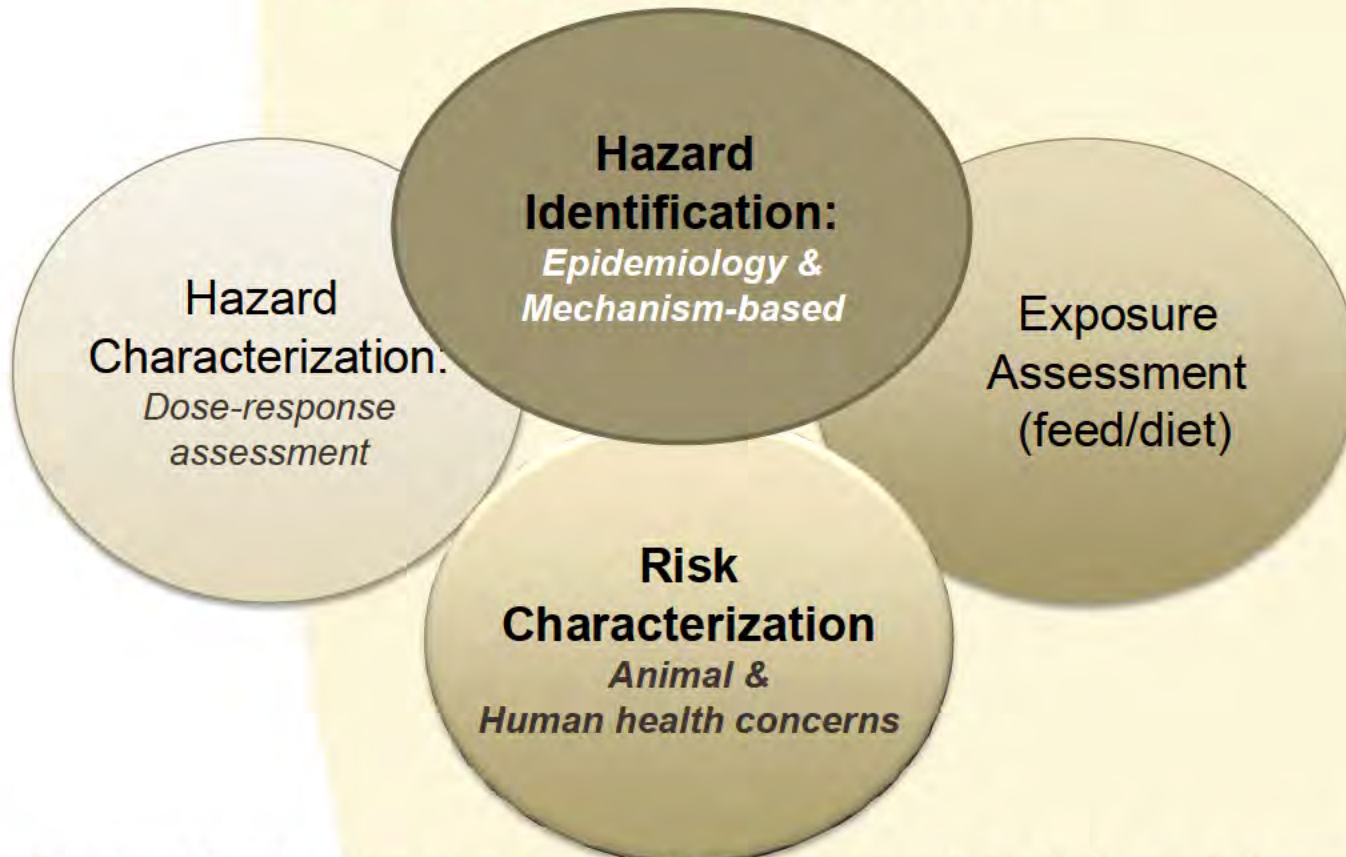


(II) to make the food derived from food producing animals (milk, meat & eggs) **unsafe for human consumption**



Animal Feed Risk Assessment

Science-based, quantitative assessment of
animal & human health concerns



Production aids: pre-marketing approval → risk avoidance
Environmental pollutants & natural occurring toxins → risk management



Hazard Identification

Pre-marketing Approval:

Based on a complete toxicological data set, including

- Toxicokinetic and toxicodynamic (mechanistic) data
- Animal Safety Data
- Environmental compliance data

Excludes substances that bio-accumulate in the food chain

Excludes carcinogenic substances

**Result in guidance for safe use
(dosages/concentrations, withholding periods)**

Health-based guidance levels
(ADI, TWI)
Maximum Levels (ML)
Statutory limits



Pre-marketing assessment

MRL – maximum residue level



Undesirable chemical substances in animal feeds

Ions and elements: As, Cd, Pb, Hg, Nitrites

Persistent organic pollutants (POP): dioxins and non-dioxin-like PCBs

Polybrominated & perfluorinated substances

Natural plant toxins (PSM – plant secondary metabolites):

saponines, glucosinolates, alkaloids, polyphenols, terpenes a.o.

Mycotoxins: AFB₁, DON, FB, ZEN, OTA, Ergot - T2-HT2, Alternaria

Botanical impurities: *Datura*, *Castor oil*, *Crotolaria*, *Madhuca*, a.o.

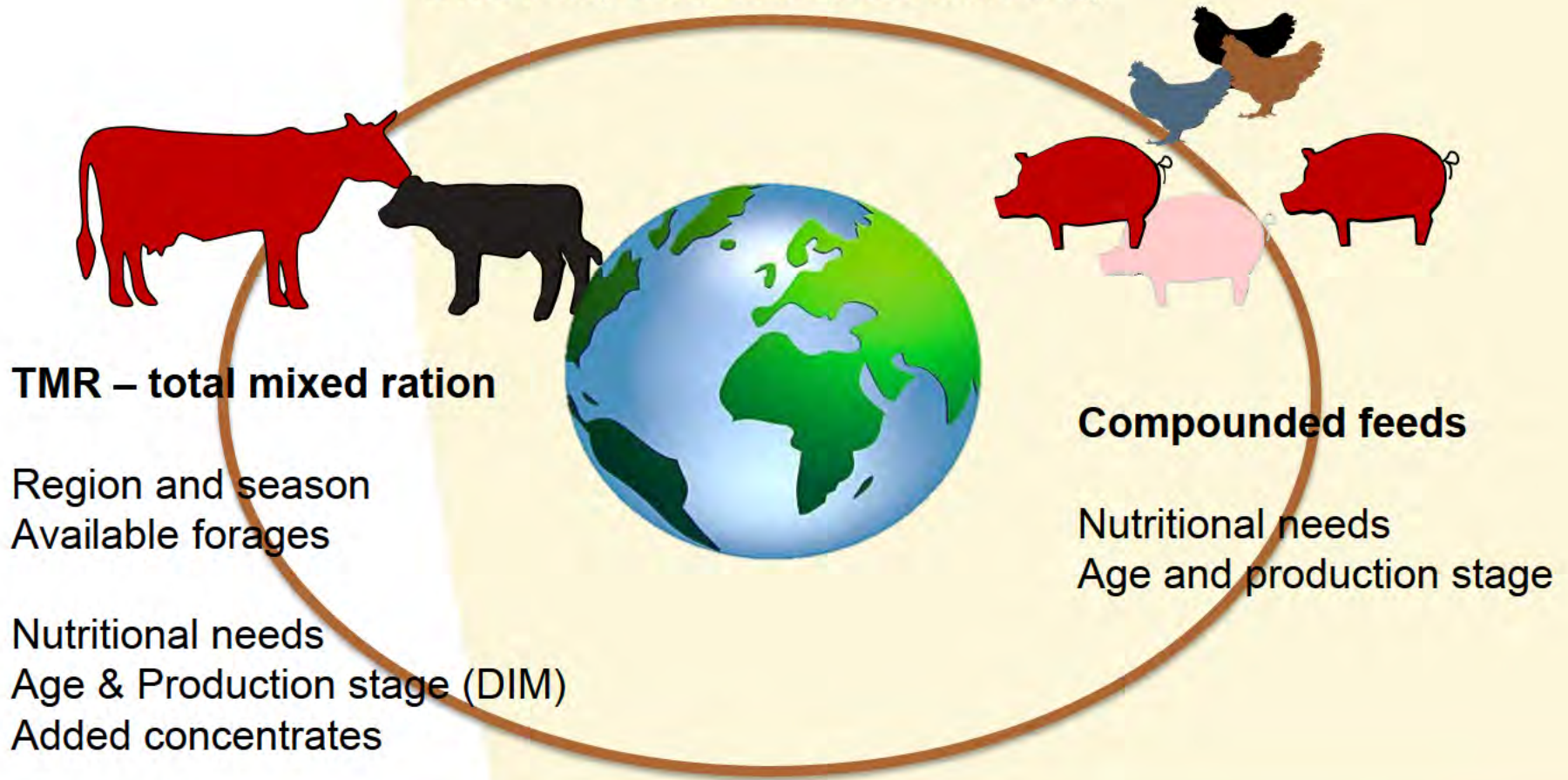
Miscellaneous: Radionuclides, Melamine, ambrosia, glycerin, a.o.,



Animal Exposure Assessment:

A major challenge in animal feed risk assessment

Diet composition is determined by



EFSA's approach to animal feed exposure assessment

Defining on the basis of nutritional needs of major ingredients
“standard diets” for all animal species

Example 1: Exposure table from the Opinion of T-2 and HT-2 Risk Assessment

Table 17: Estimated lower-bound and upper-bound exposure by lactating dairy cows to the sum of T-2 and HT-2 toxins at three levels of milk production (30, 40 and 50 kg milk/day) ($\mu\text{g/day}$, $\mu\text{g/kg b.w. per day}$ and $\mu\text{g/kg milk}$).

	Exposure		
	Milk yield/Non-forage feed intake (kg/day)		
	30/8.4	40/12	50/16
	$\mu\text{g/day}$		
Lower-bound	81	116	155
Upper-bound	180	257	342
	$\mu\text{g/kg b.w. per day}$		
Lower-bound	0.13	0.18	0.24
Upper bound	0.28	0.39	0.53
	$\mu\text{g/kg milk}$		
Lower-bound	2.7	2.9	3.1
Upper-bound	6.0	6.4	6.8

b.w.: body weight



Estimates of exposure – T-2 toxin as an example

Mycotoxins in forages:

	Exposure											
	Forage type											
	Maize silage			Grass silage			Hay			Pasture grass		
	Milk yield (kg/day)											
	30	40	50	30	40	50	30	40	50	30	40	50
	µg/day											
Lower-bound	262	454	428	134	351	476	304	480	421	46	274	486
Upper-bound	861	1082	1053	164	421	570	362	573	515	54	324	576
	µg/kg b.w. per day ^(a)											
Lower-bound	0.4	0.7	0.66	0.21	0.54	0.73	0.47	0.74	0.65	0.07	0.42	0.75
Upper-bound	1.3	1.7	1.6	0.25	0.65	0.88	0.56	0.88	0.79	0.08	0.50	0.89
	µg/kg milk											
Lower-bound	8.7	11	8.6	4.5	8.8	9.5	10	12	8.4	1.5	6.8	9.7
Upper-bound	29	27	21	5.5	11	11	12	14	10	2	8	12

Exposure estimates represent the external dose!



EFSA's approach to animal feed exposure assessment

Defining on the basis of nutritional needs of major ingredients
“standard diets” for all animal species

Example 2: Exposure table from the Opinion of T-2 and HT-2 Risk Assessment

Table 19: Estimated lower-bound and upper bound exposure to the sum of T-2 and HT-2 toxins by 400 kg body weight fattening beef cattle reared on grass silage plus non-forage feeds system or a cereal beef system ($\mu\text{g}/\text{day}$ and $\mu\text{g}/\text{kg}$ b.w. per day).

	Exposure	
	Grass silage + non-forage feeds Non-forage feeds consumed (kg dry matter/day) 1.9	Cereal beef 7.1
	$\mu\text{g}/\text{day}$	
Lower-bound	10	154
Upper-bound	116	303
	$\mu\text{g}/\text{kg}$ b.w. per day	
Lower-bound	0.020	0.39
Upper-bound	0.29	0.76

b.w.: body weight



EFSA's approach to animal feed exposure assessment

*Defining on the basis of nutritional needs of major ingredients
“standard diets” for all animal species*

Limitations: Assumption of diet composition based on European data
(gross average)

Advantages: Quantitative estimates → Increase in transparency
Comparison of exposure levels (Risk Ranking)

Uncertainties in Analytical Methods:
Increasingly compensated by larger community data sets



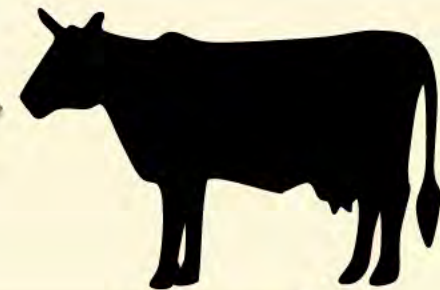
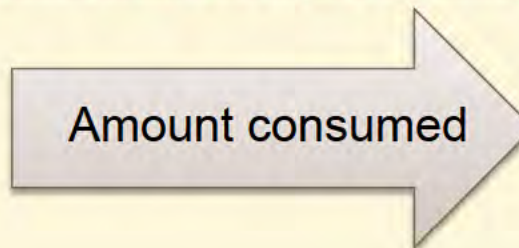
From external concentrations in feed ingredients – to the biologically active dose



Animal feed

**ppm – mg/kg
Feed / TMR**

Professional feed processing



Rate of absorption:

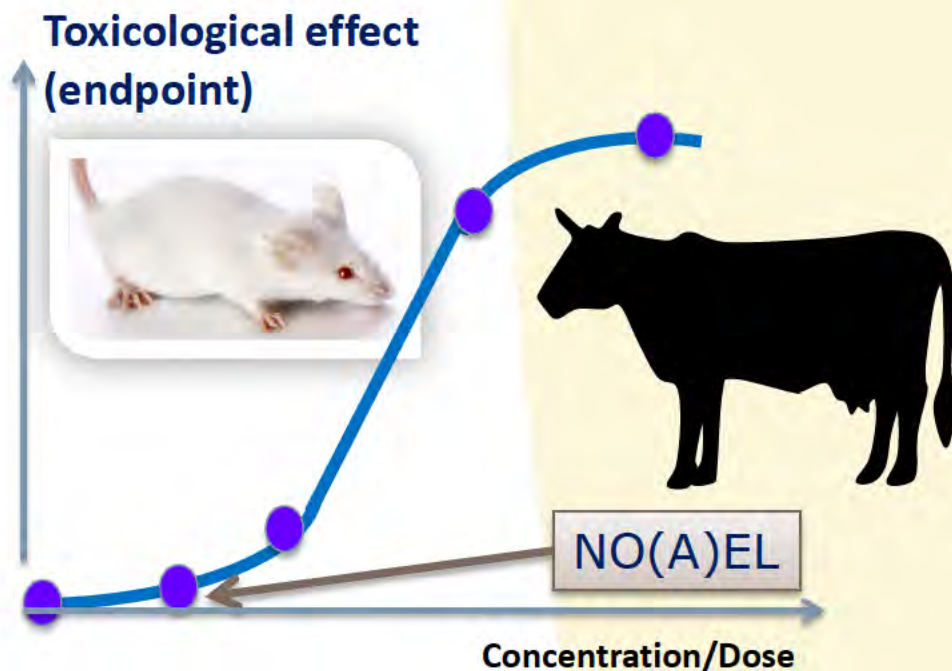
- Pre-systemic elimination (rumen)
- Monogastrics & ruminants
- Innate defense mechanisms (efflux transporters)
- Pre-systemic inactivation (biotransformation)

Significant species differences require a species-specific approach
(experimental studies in **target animal species**)



Hazard characterization: The Basic Concept

*From anecdotal (clinical) evidence of toxicity
to a professional dose-response assessment*



**Dose response characteristics are
often missing in target animals**

Endpoints in animal health risk assessment differ from common human endpoints:

Adverse effects on

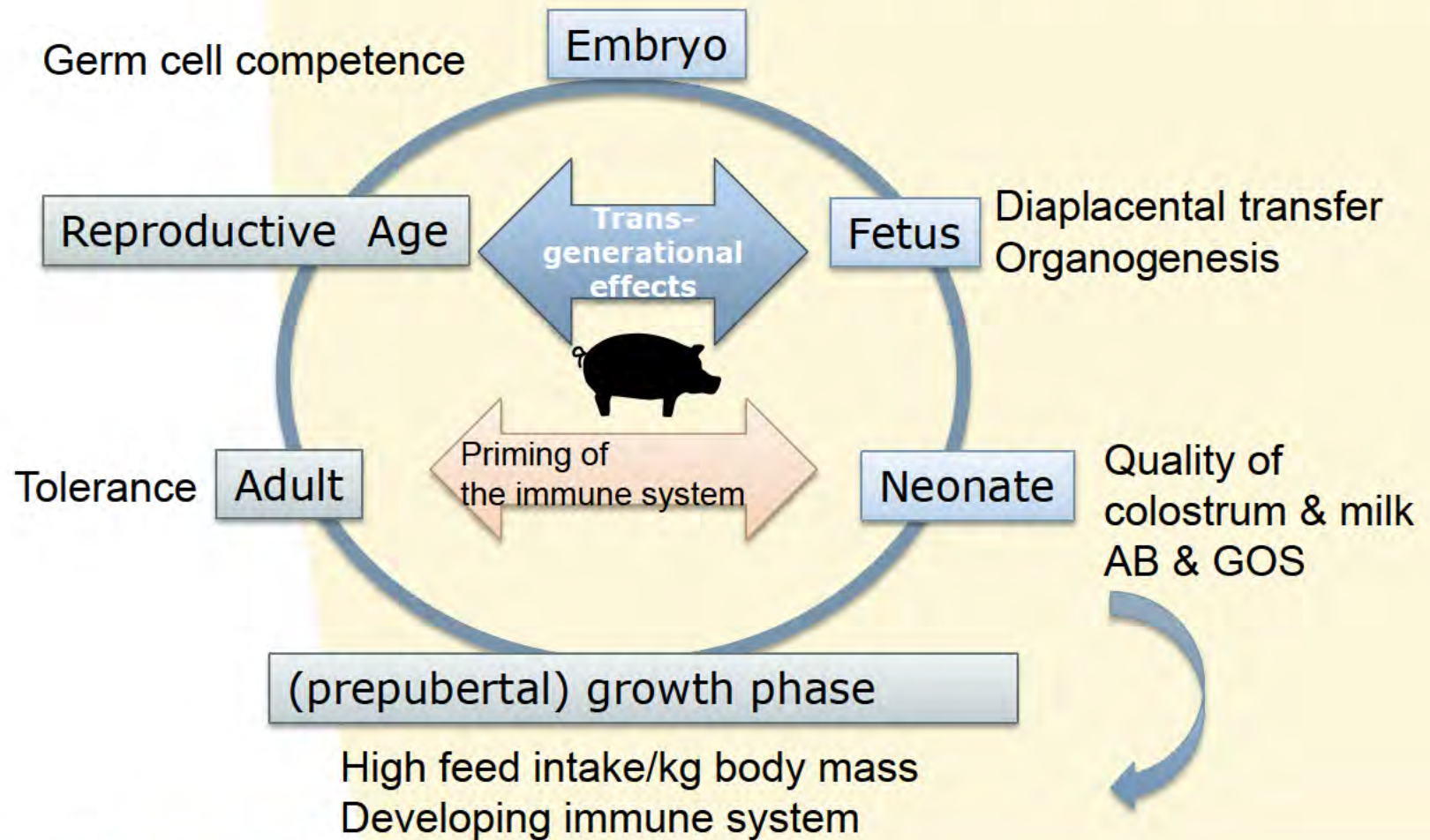
- Feed intake & efficiency
- Growth rate
- Productivity
- Fertility
- Immune competence

Are generally more relevant than

- Organ-specific acute effects

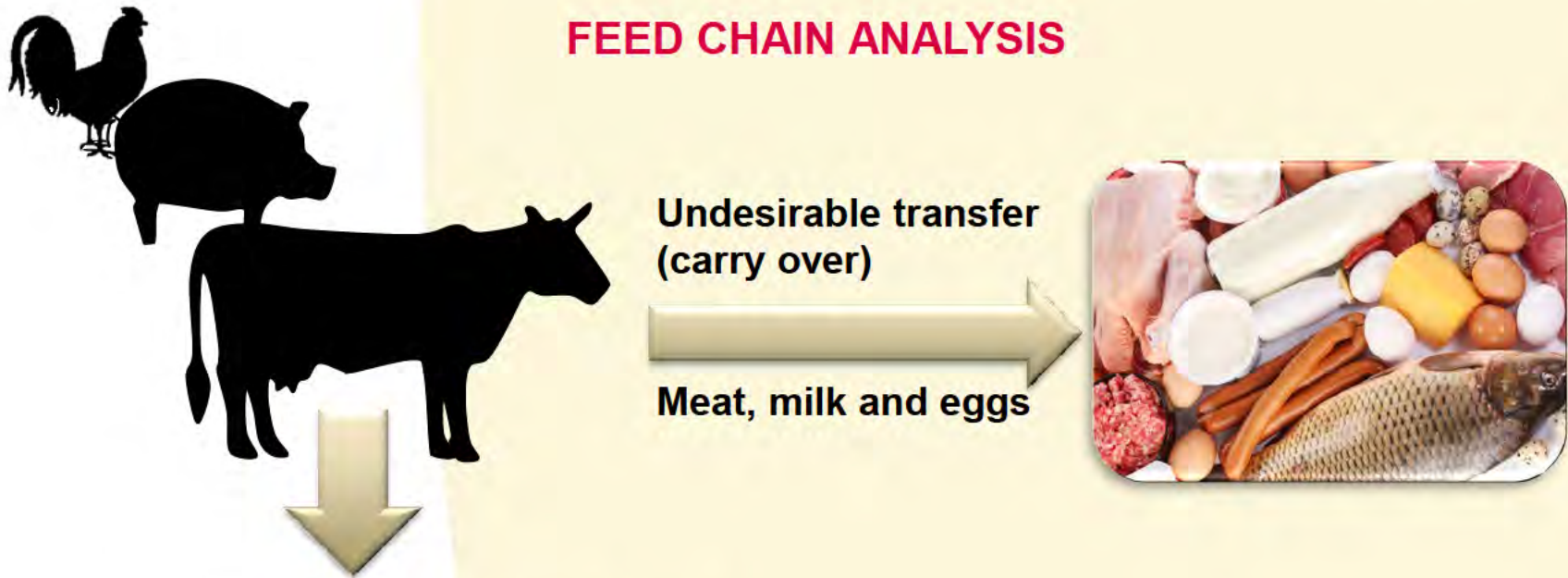


Risk Characterization at Different Stages of Life



Risk Characterization of Feed Contamination

FEED CHAIN ANALYSIS



Adverse animal health effects

- Animal health, welfare and productivity
- Animal health maintenance (undesirables use of extensive medication) (example: undesirable drug residues and antimicrobial resistance)
- Environmental impact of animal husbandry



Risk Characterization:

Physiological factors determining the transfer of contaminants into foods from animal origin



Short production time of broilers

vs

Persistence of lipophilic substances in egg yolk!

Typical examples: low prevalence of non-compliant residues of heavy metals in broilers
vs

Residues of dioxins (and other lipophilic organic pollutants) & coccidiostats in eggs

Outcome of EU survey 2005-2010 NRCP (96/23 EC): **0.27%** non-compliant



Risk Characterization:

Physiological factors determining the transfer of contaminants into foods from animal origin



Short production period (fattening pigs)
Accumulate lipophilic substances
(some dioxin contamination incidents)
Sensitive to infectious diseases (drug residues)

EU survey 2005-2010 NRCP (96/23 EC):

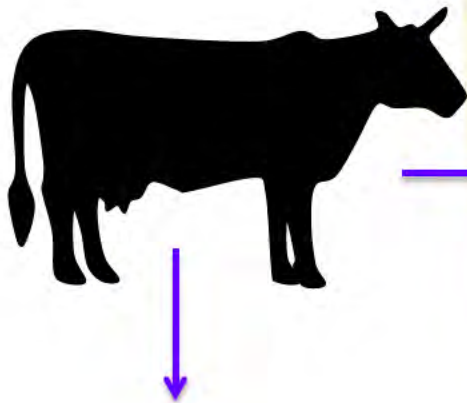
Total non-compliant **0.21-0.23 %** (residues of VMPs)

Total non-compliant heavy metals: 1.26% (predominantly kidneys)



Risk Characterization:

Physiological factors determining the transfer of contaminants into foods from animal origin



Long life-span (accumulation of heavy metals, environmental pollutants (fat, kidney))

EU survey 2005-2010 NRCP (96/23 EC):
0.25% non-compliant samples

Milk:

Transfer rates higher in high producing animals and buffalo's

Active excretion of selected toxins (AFM₁ → ABCG1)

Active secretion of some VMPs

Active excretion of basic plant metabolites

Drug residues (mastitis treatment) at non-compliance with withdrawal periods



The future challenge: Integrated analysis of the food chain

Recent surveys report a comparable low number of non-compliant samples found in the prescribed routine analyses of slaughter animals.

These surveys are, however, based on control plans (NRCP), which are based on previous hazard analyses. An amendment of NRCPs, taking into account recent risk assessment of (new) contaminants in the food chain has been recommended.

Many of the recently reported food safety concerns originate from feed contamination



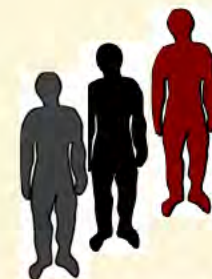
Stimulating the information transfer from feed quality programs to food controls is considered as an opportunity to further reduce the occurrence of undesirable residues in animal derived foods



Future Challenges - implementing



Food Chain Information



Feed analyses (compound feeds – fattening pigs, poultry - indoor)

Compliance
with statutory limits

Reporting
(certificate of analysis)

Reduction
of (need for)
residue testing

Feed analyses (on farm mixing, pasture)

Hazard identification

Reporting
(Surveillance programs)

Targeted sampling
Risk reduction

IMPROVING FEED & FOOD SAFETY – RISK-based controls!



