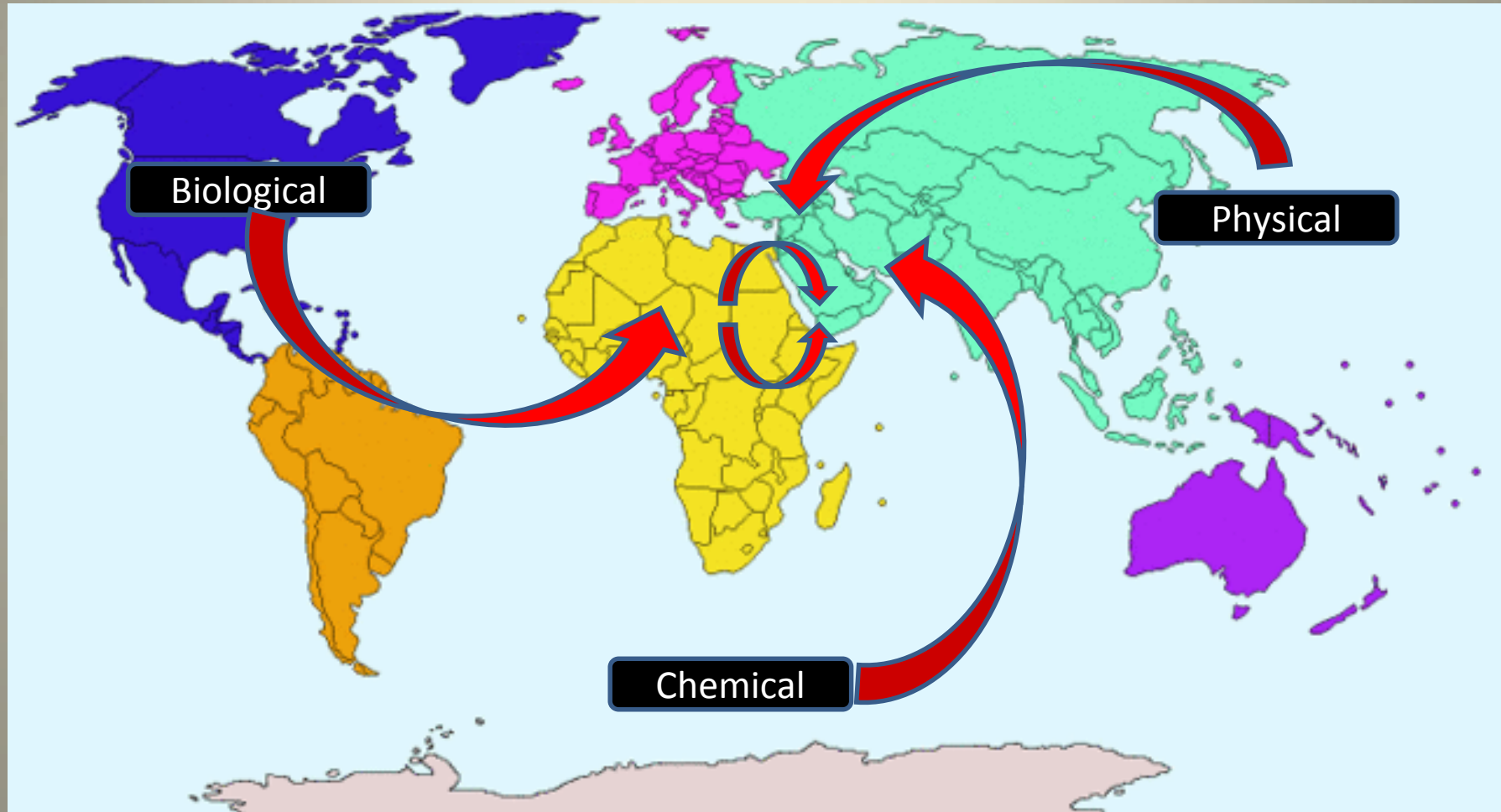


# Overview of Significance of Residues and Chemical Contaminants in Milk

*Michael Hickey*

*Dairy & Food Consultancy*

# Types of Residues and Contaminants found in Foods



# Contaminant or Residue?

For the purposes of this presentation

## **Contaminants:**

Substances that are found in food, as a result of entering at any stage of the food chain. Usually they may enter food unintentionally – but occasionally due to being intentionally added with fraudulent intent.

## **Residues:**

Substances that are found (or remain) in food as an unintended consequence of using phytosanitary products (pesticides) or veterinary drugs.

# Simple Dairy Farm to Fork Chain

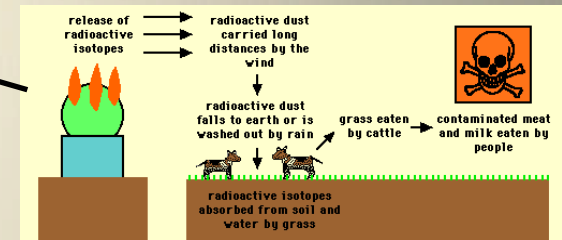
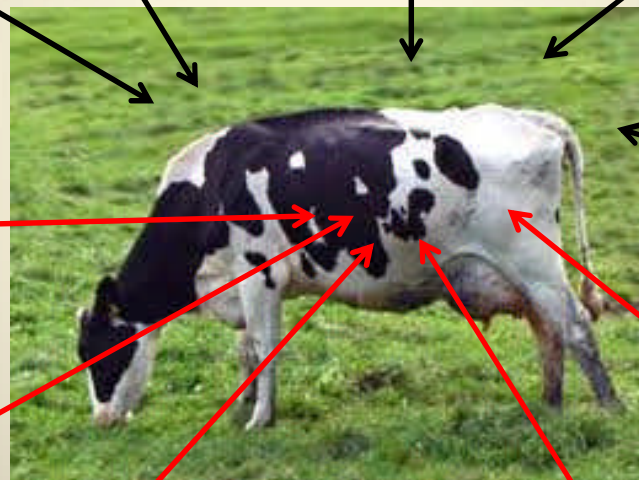


# Potential Contamination Sources - the Raw Material Source

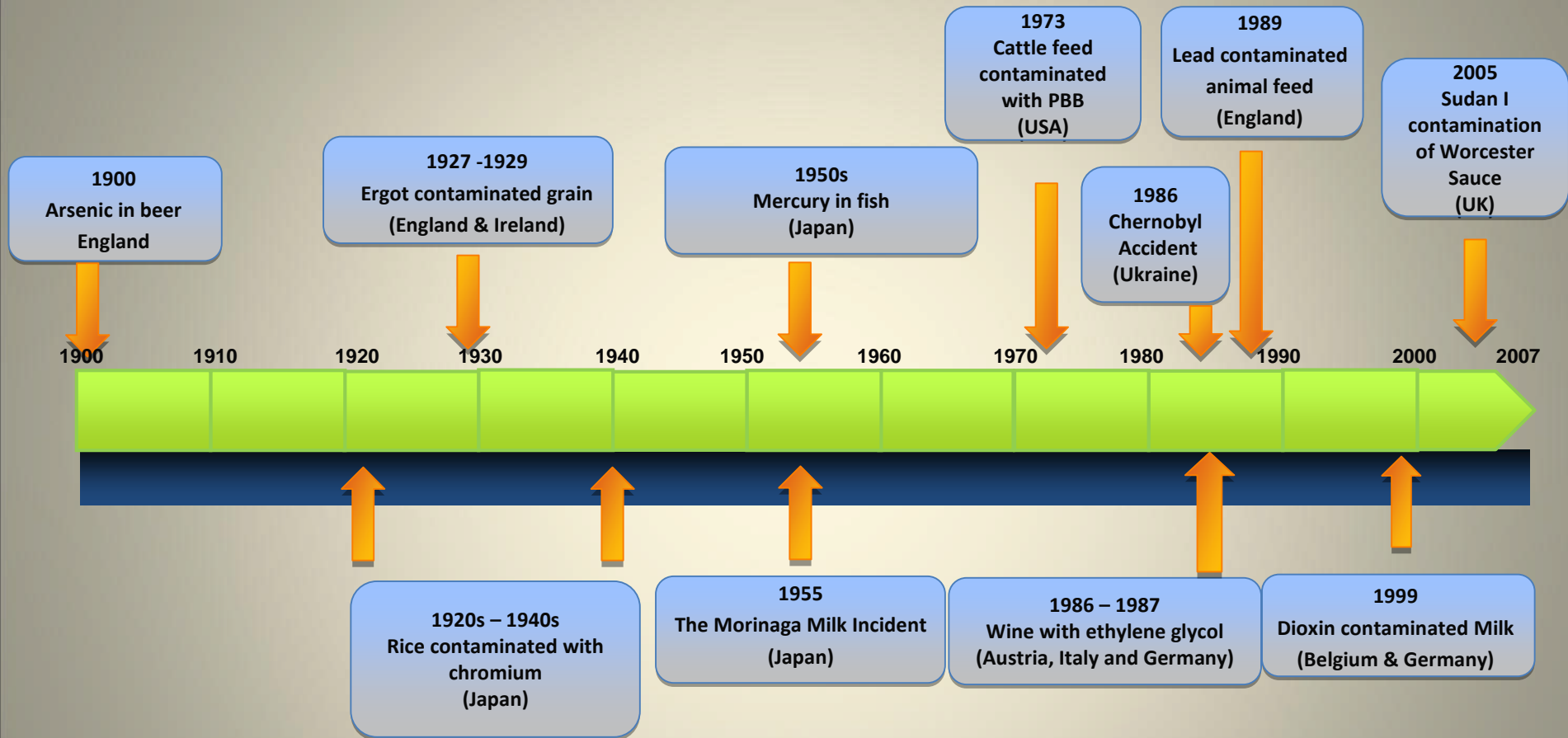


Direct →

Indirect →



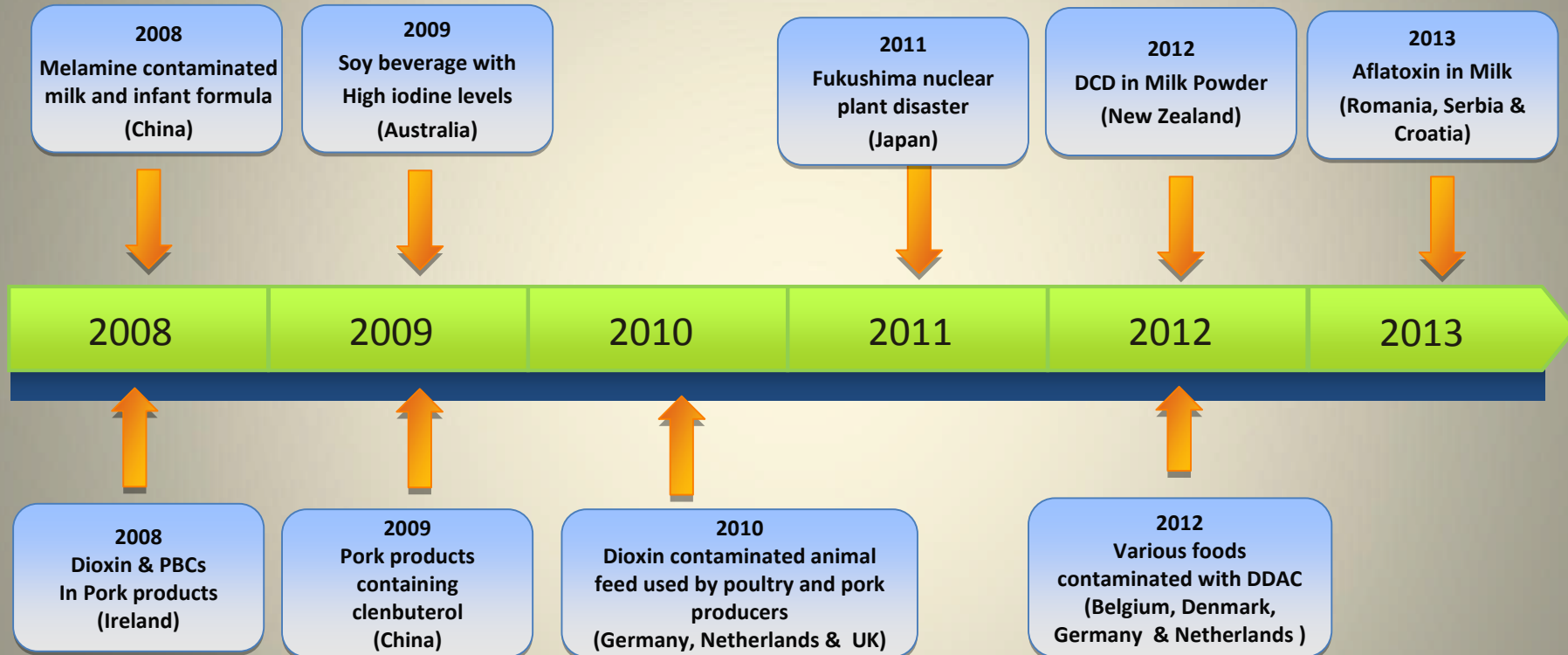
# Some examples of contamination (1900 – 2007)



Morinaga Incident – recombined milk contaminated with sodium arsenate which had inadvertently contaminated a permitted food additive disodium phosphate

PBB - polybrominated biphenyl (a flame retardant)

# Some examples of contamination (2008 – 2013)

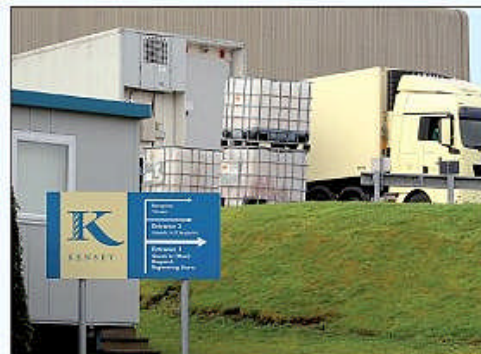
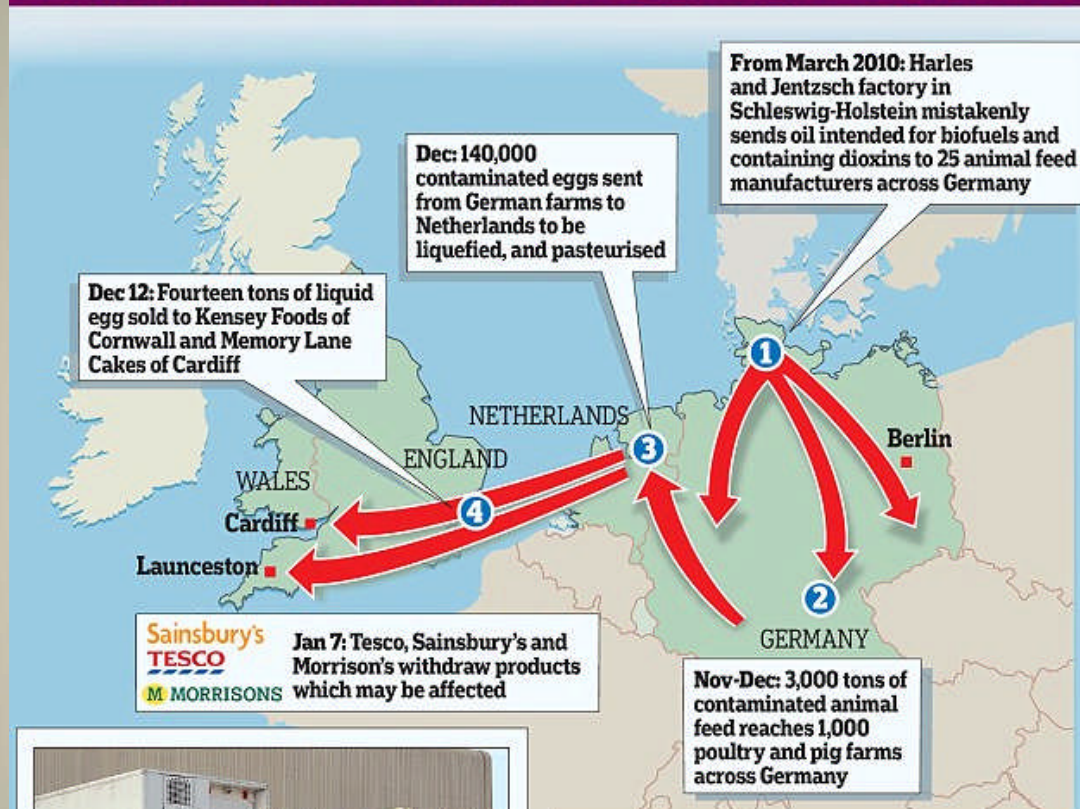


DCD – Dicyandiamide – a nitrification inhibitor that may be added to fertilizer

DDAC – Didecyldimethylammonium chloride – a Quaternary Ammonium Compound [QAC] – was authorized in EU as an active substance in plant protection products (exclusively for indoor uses for ornamental plants) – approval now withdrawn (by Implementing Reg. No 175/2013 )

# The EU Dioxin Case 2010

## HOW THE INTERNATIONAL FOOD SCARE SPREAD



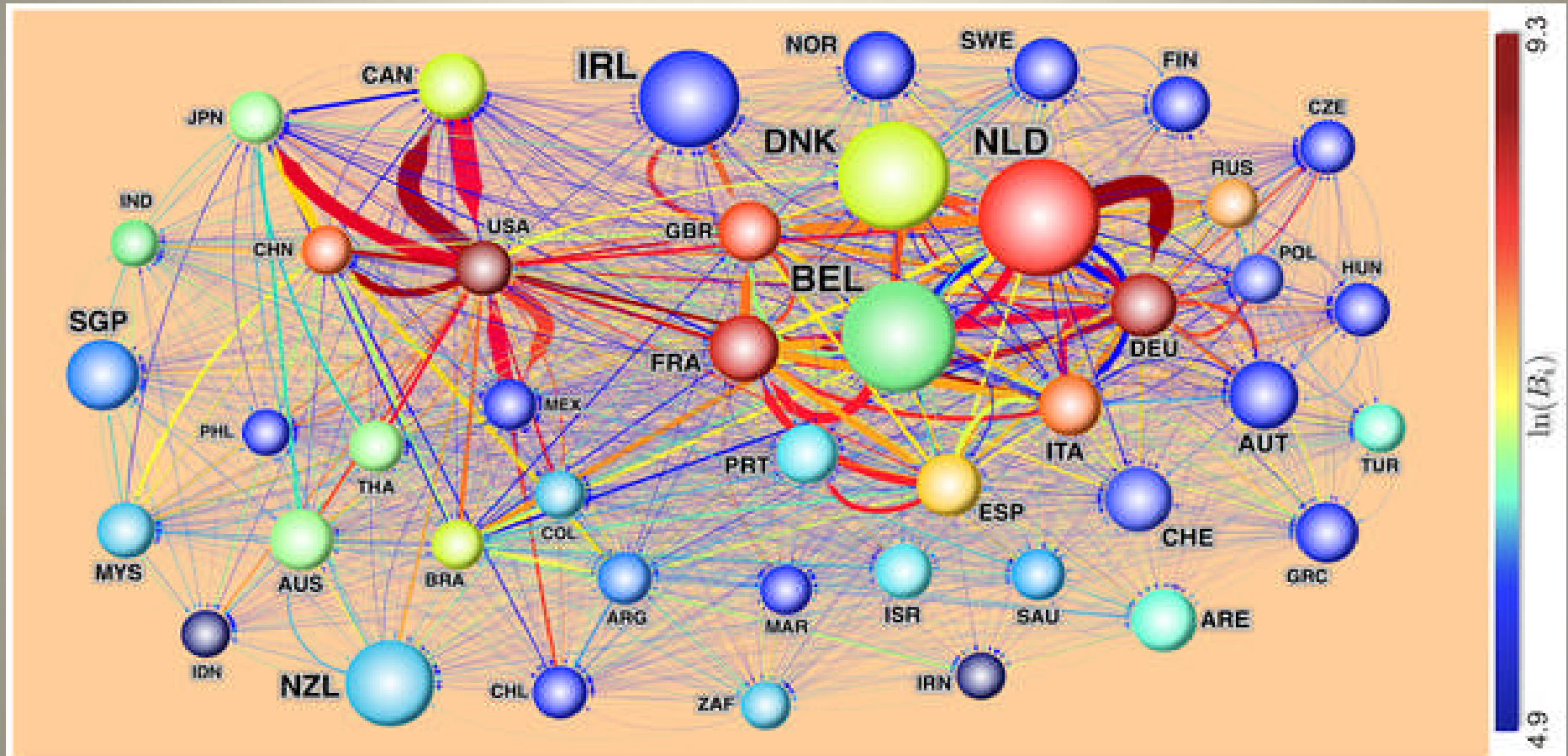
Kensey Foods, of Launceston, Cornwall, uses liquid egg to make supermarket own brand quiches.



Memory Lane Cakes, of Cardiff use eggs to make cakes for supermarkets - including Sainsbury's Chocolate Caterpillar Cake



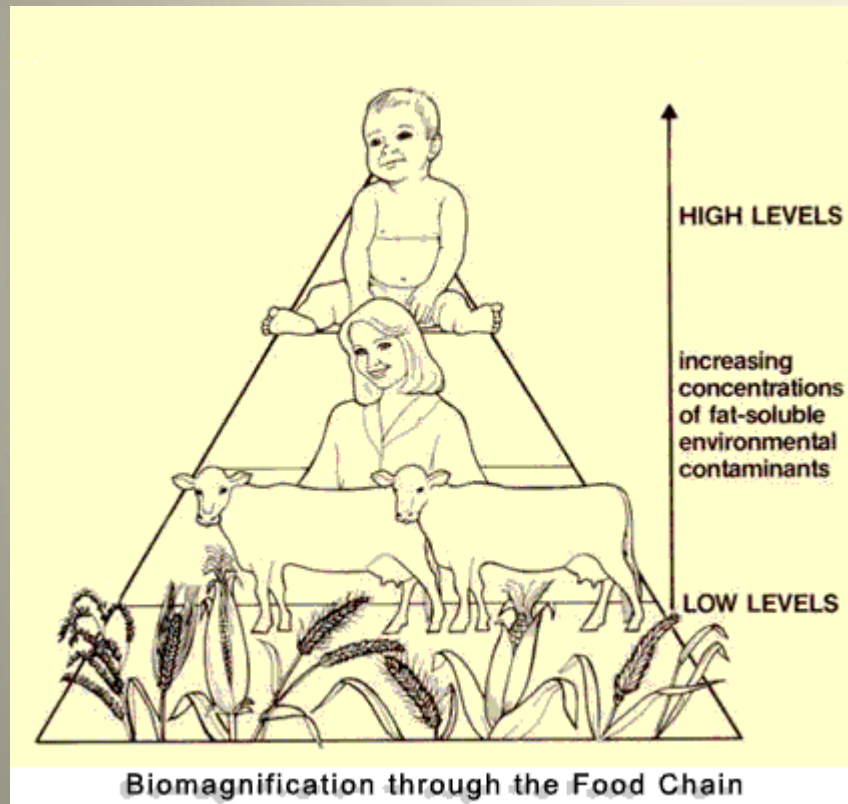
# The International Agri-Food Trade Network (IAFN Dataset 2007)



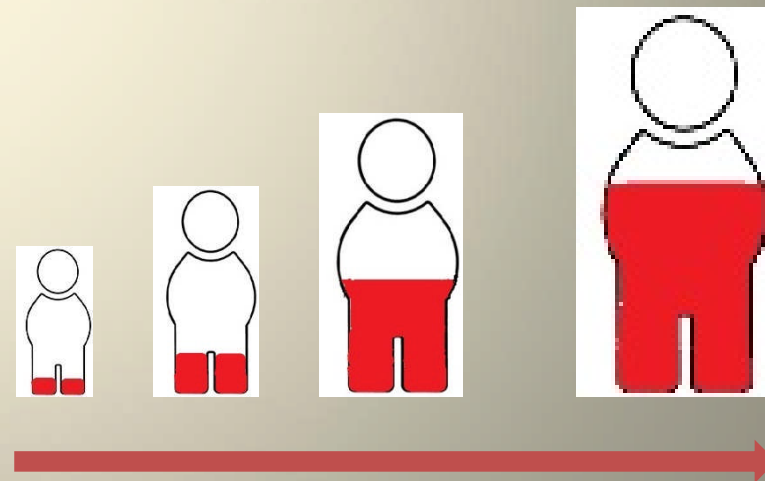
Ercsey-Ravasz M, Toroczkai Z, Lakner Z, Baranyi J (2012) Complexity of the International Agro-Food Trade Network and Its Impact on Food Safety. PLoS ONE 7(5): e37810. doi:10.1371/journal.pone.0037810  
<http://www.plosone.org/article/info:doi/10.1371/journal.pone.0037810>

# Bioconcentration Biomagnification & Bioaccumulation

## Biomagnification



## Bioaccumulation



Age

# POPS

## The Original “Dirty Dozen” (2001)<sup>1</sup>

### Pesticides

Aldrin  
Chlordane  
Dichloro-diphenyl-trichloroethane (DDT)  
Dieldrin  
Endrin  
Heptachlor  
Hexachlorobenzene (HCB)  
Mirex  
Toxaphene

### Unintended by-products

Dioxins  
Furans

### Industrial chemicals

Polychlorinated biphenyls (PCBs)

POPs = Persistent Organic Pollutants – all are polyhalogenated hydrocarbons

<sup>1</sup> Under the Stockholm Convention on Persistent Organic Pollutants - 22 May 2001

# The 10 new POPs

## Pesticide by-products

Chlordecone  
beta-Hexachlorocyclohexane (alpha-HCH)  
beta-Hexachlorocyclohexane (beta-HCH)  
Lindane (gamma-HCH)  
Endosulfan and related isomers

## Industrial Chemicals (e.g. Flame Retardants)

Hexabromobiphenyl (HBB)  
Hexabromodiphenyl ether and  
heptabromodiphenyl ether  
Pentachlorobenzene (PeCB) (also a Pesticide)  
Perfluorooctane sulfonates and  
perfluorooctane sulfonyl fluoride (PFOS)  
Tetrabromodiphenyl ether and  
pentabromodiphenyl ether

# Elements of Risk Analysis



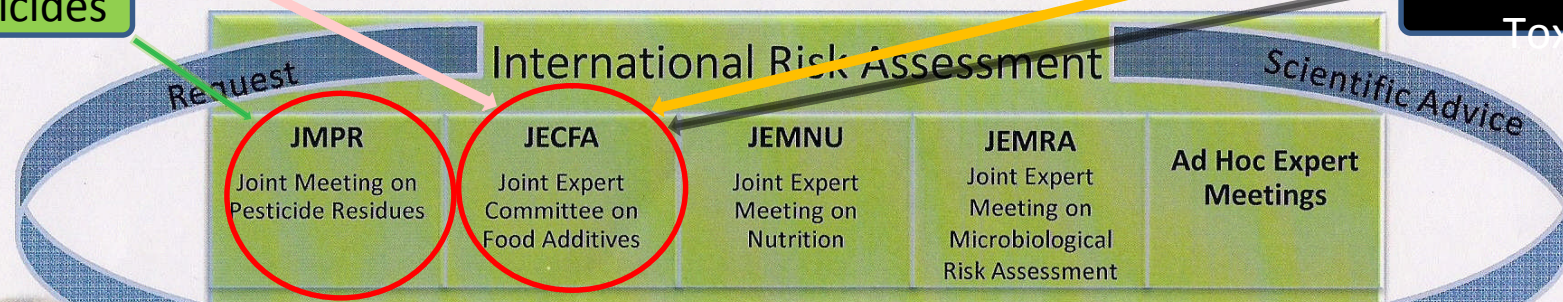
# The Scientific Basic of Codex

Vet. Drugs

Pesticides

Contaminants

Natural Toxins



Scientific Advice

## CODEX Committees

CODEX ALIMENTARIUS COMMISSION

International Food Standards

Consumer Protection and Fair Trade Practices

Output



# Chemical Contaminants in Food - EU

Nitrates

as NO<sub>3</sub>

Mycotoxins

Aflatoxins – B1, M1 and mixed B1/B2/G1/G2  
Ochratoxin A  
Patulin  
Deoxynivalenol  
Zearalenone  
Fumonisin  
T2 and H2 toxin

Metals

Lead  
Cadmium  
Mercury  
Tin (inorganic)  
[Arsenic]

Dioxins and PCBs

PAHs

3-MCPD

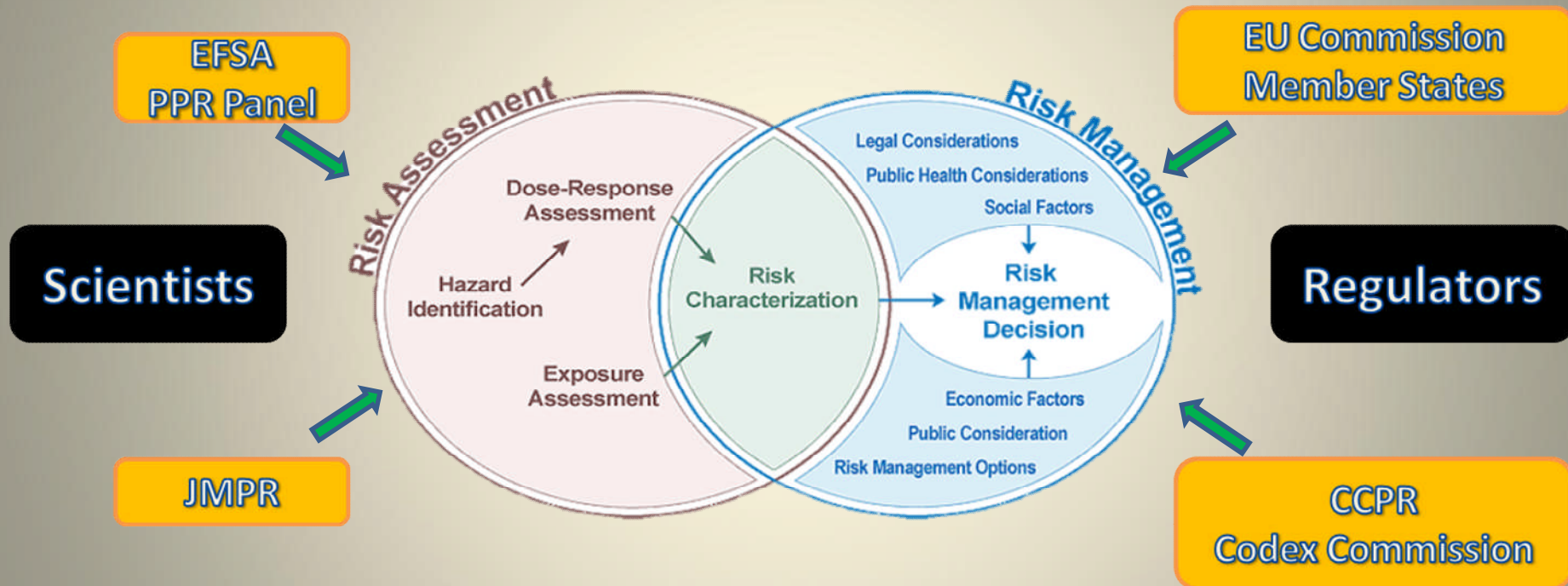
Melamine and its analogues

Milk  
MRL

Infant  
Formula  
MRL

From Regulation (EC) No 1831/2003

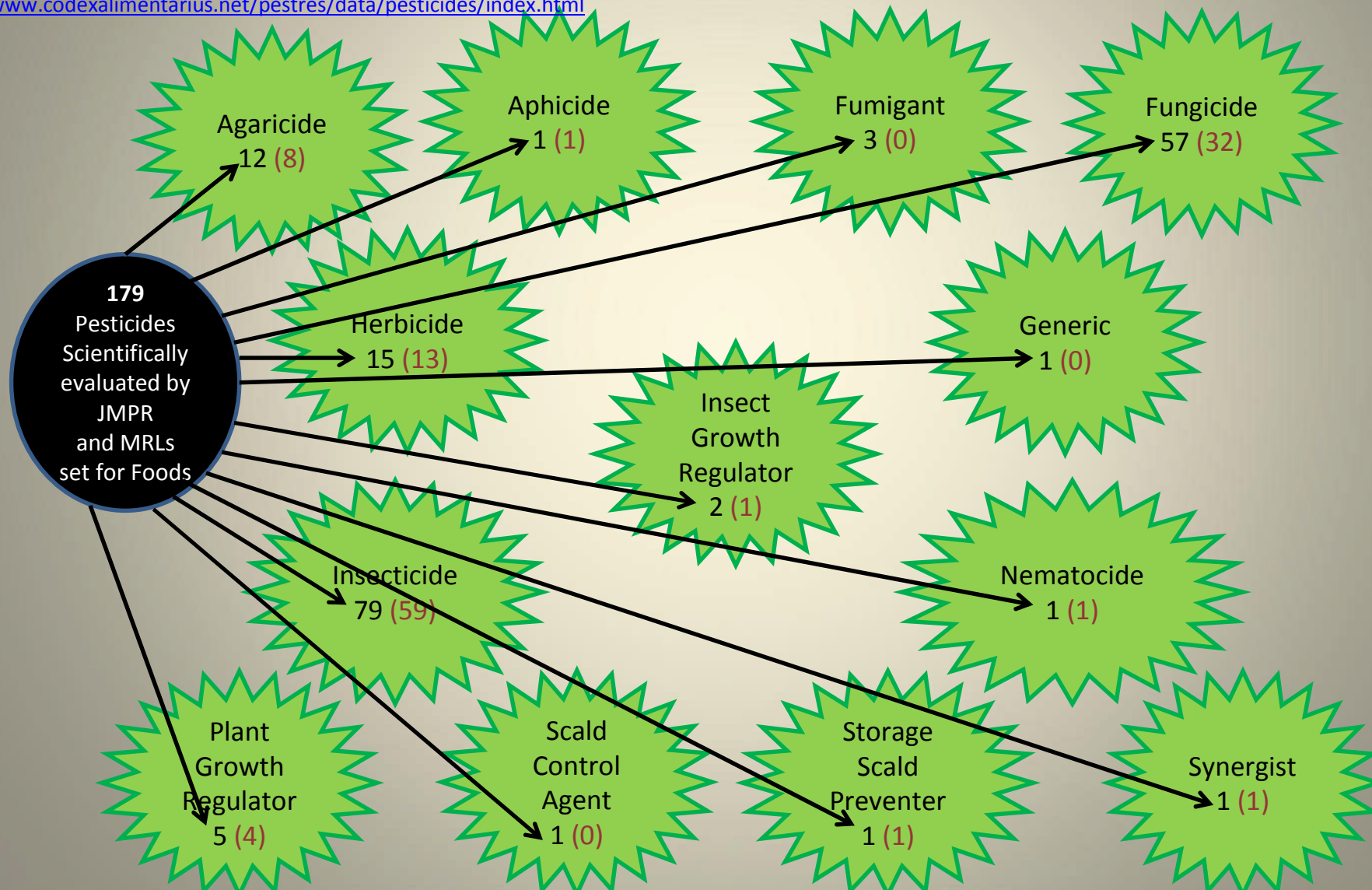
# Pesticide Residue Risk Analysis





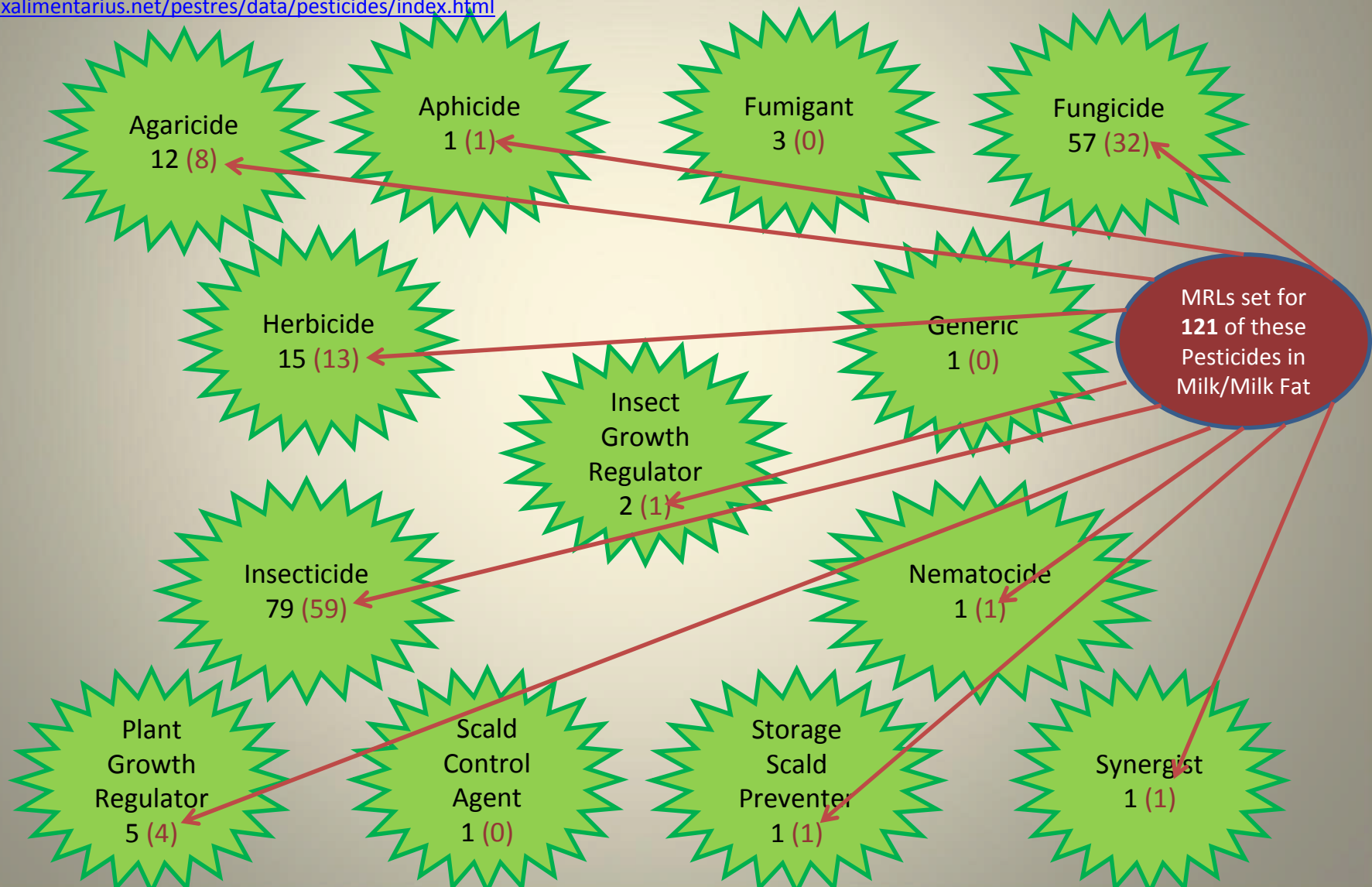
# Pesticide Functional Classes (CODEX)

[www.codexalimentarius.net/pestres/data/pesticides/index.html](http://www.codexalimentarius.net/pestres/data/pesticides/index.html)

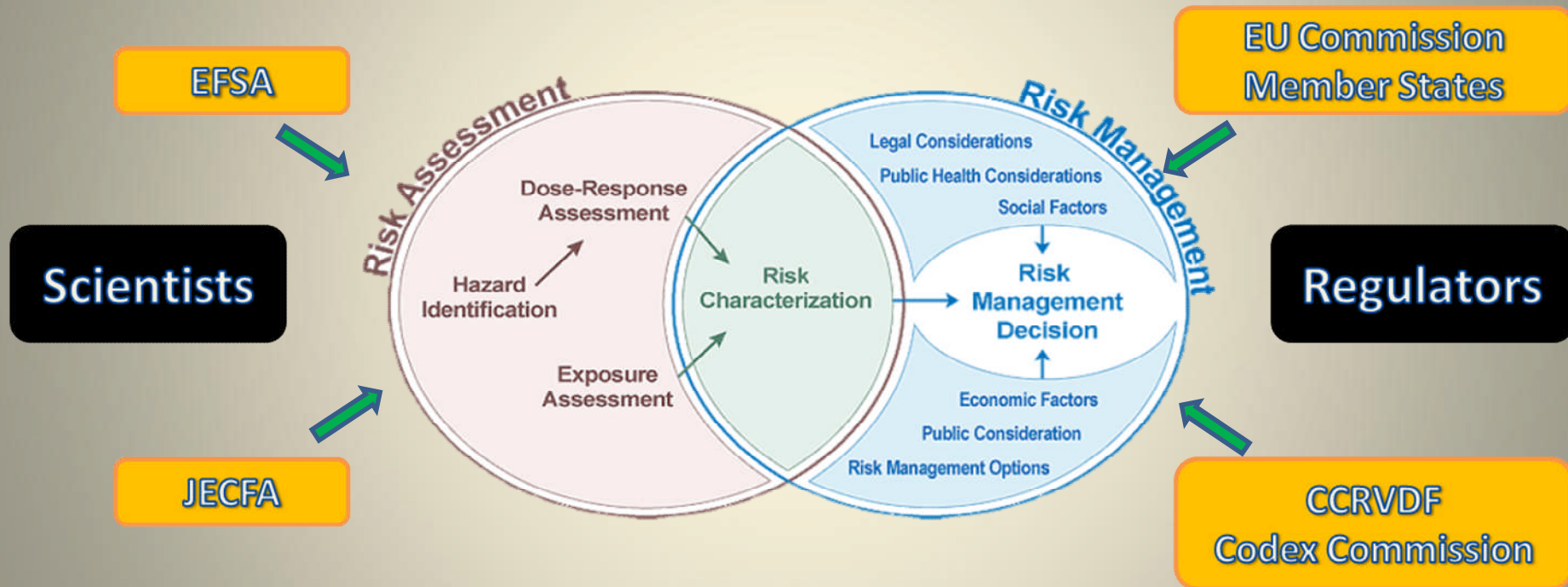


# Pesticide Functional Classes (CODEX)

[www.codexalimentarius.net/pestres/data/pesticides/index.html](http://www.codexalimentarius.net/pestres/data/pesticides/index.html)



# Veterinary Drug Residue Risk Analysis



# Functional Categories of Veterinary Drugs (CODEX)

Adrenoceptor  
Agonist  
1 (1)

Anthelmintic  
11 (6)

Antimicrobial  
22 (15)

**59 MRLs in Total  
set for Foods**

Antiprotozoal3  
(1)

$\beta$ -Adrenoceptor  
blocker  
1 (0)

**31 MRLs for set for  
Milk**

Growth  
promoter  
2 (0)

Glucocorticosteroid  
1 (1)

Insecticide  
8 (5)

Production aid  
7 (0)

Trypanocide  
2 (2)

Tranquilizer  
1 (0)

*Codex Alimentarius Commission*  
*Maximum Residue Limits for Veterinary Drugs in Foods*  
 Updated as at the 35<sup>th</sup> Session of the Codex Alimentarius Commission (July 2012)

## INDEX

| Veterinary Drug                                | Page | Veterinary Drug           | Page |
|--|------|---------------------------|------|
| Abamectin                                      | 2    | Gentamicin                | 22   |
| Albendazole                                    | 2    | Imidocarb                 | 22   |
| Amoxicillin                                    | 3    | Isometamidium             | 23   |
| Avylamycin                                     | 4    | Ivermectin                | 23   |
| Azaperone                                      | 4    | Levamisole                | 24   |
| Benzylpenicillin/Procaine benzylpenicillin     | 5    | Lincomycin                | 25   |
| Carazolol                                      | 5    | Melengestrol acetate      | 25   |
| Ceftiofur                                      | 6    | Monensin                  | 26   |
| Chlortetracycline/Oxytetracycline/Tetracycline | 7    | Moxidectin                | 27   |
| Clenbuterol                                    | 8    | Narasin                   | 28   |
| Clozantel                                      | 9    | Neomycin                  | 29   |
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| Danofloxacin                                   | 12   | Progesterone              | 32   |
| Deltamethrin                                   | 13   | Ractopamine               | 32   |
| Dexamethasone                                  | 14   | Sarafloxacin              | 33   |
| Diclaznil                                      | 14   | Spectinomycin             | 34   |
| Dicyclanil                                     | 15   | Spiramycin                | 35   |
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| Flubendazole                                   | 20   | Zeranol                   | 40   |
| Flumequine                                     | 21   |                           |      |

**Residues of ~ 90  
 Veterinary Drugs  
 evaluated by JECFA**

**59 MRLs in Total  
 set for Foods**

**31 MRLs for set for  
 Milk**

**rBST not included (yet!)**

# EU Pesticides Database

Includes Approved, Non-approved, Pending and substances that are not plant protection products

Active substances

Select your criteria

Category All

Status All

Class. (Dir. 67/548/EEC) - -

Class. (Reg. 1272/2008) - -

Authorisations - -

Legislation -

ADI from All to/untill All

ARfD from All to/untill All

AOEL from All to/untill All

Approval date All

Expiration date All

Search Reset

Find substance

Show details

Export list

alphabetically

(4Z-9Z)-7,9-Dodecadien-1-ol  
(E)-10-Dodecen-1-yl acetate  
(E)-11-Tetradecen-1-yl acetate  
(E)-2-Methyl-6-methylene-2,7-octadien-1-ol (myrcenol)  
(E)-2-Methyl-6-methylene-3,7-octadien-2-ol (isomyrcenol)  
(E)-5-Decen-1-ol  
(E)-5-Decen-1-yl acetate  
(E)-8-Dodecen-1-yl acetate  
(E)-9-Dodecen-1-yl acetate  
(E,E)-7,9-Dodecadien-1-yl acetate  
(E,E)-8,10-Dodecadien-1-ol  
(E,E)-8,10-Dodecadien-1-yl acetate  
(E,Z)-2,13-Octadecadien-1-yl acetate  
(E,Z)-4,7-Tridecadien-1-yl acetate  
(E,Z)-7,9-Dodecadien-1-yl acetate  
(E,Z)-8,10-Tetradecadien-1-yl  
(E,Z)-8-Dodecen-1-yl acetate  
(E,Z)-9-dodecen-1-yl acetate; (E,Z)-9-Dodecen-1-ol; (Z)-11-Tetradecen-1-yl acetate  
(IR)-1,3,3-Trimethyl-4,6-dioxatricyclo[3.3.1.0<sup>2,7</sup>]nonane (lineatin)  
(Z)-11-Hexadecen-1-ol  
(Z)-11-Hexadecen-1-yl acetate  
(Z)-11-Hexadecenal  
(Z)-11-Tetradecen-1-yl acetate  
(Z)-13-Hexadecen-11-yn-1-yl acetate  
(Z)-13-Octadecenal  
(Z)-3-Methyl-6-isopropenyl-3,4-decadien-1-yl acetate  
(Z)-3-Methyl-6-isopropenyl-9-decen-1-yl acetate

1297 entries found

Total of 1297 Substances

[http://ec.europa.eu/sanco\\_pesticides/public/?event=activesubstance.selection](http://ec.europa.eu/sanco_pesticides/public/?event=activesubstance.selection)

# EU Pesticides Database

Active substances

Select your criteria

Category All

Status **Approved**

Class. (Dir. 67/548/EEC) -

Class. (Reg. 1272/2008) -

Authorisations -

Legislation -

ADI from All to/until All

ARfD All All

AOEL All All

Approval date All All

Expiration date All All

Search Reset

Find substance

Show details

Export list

alphabetically

(E)-11-Tetradecen-1-yl acetate  
(E)-5-Decen-1-ol  
(E)-5-Decen-1-yl acetate  
(E)-8-Dodecen-1-yl acetate  
(E,E)-7,9-Dodecadien-1-yl acetate  
(E,E)-8,10-Dodecadien-1-ol  
(E,Z)-2,13-Octadecadien-1-yl acetate  
(E,Z)-7,9-Dodecadien-1-yl acetate  
(E,Z)-8-Dodecen-1-yl acetate  
(Z)-11-Hexadecen-1-ol  
(Z)-11-Hexadecen-1-yl acetate  
(Z)-11-Hexadecenal  
(Z)-11-Tetradecen-1-yl acetate  
(Z)-13-Hexadecen-11-yn-1-yl acetate  
(Z)-13-Octadecenal  
(Z)-7-Tetradecenal  
(Z)-8-Dodecen-1-ol  
(Z)-8-Dodecen-1-yl acetate  
(Z)-9-Dodecen-1-yl acetate  
(Z)-9-Hexadecenal  
(Z)-9-Tetradecen-1-yl acetate  
(Z,E)-7,11-Hexadecadien-1-yl acetate  
(Z,E)-9,12-Tetradecadien-1-yl acetate  
(Z,Z)-7,11-Hexadecadien-1-yl acetate  
(Z,Z,Z,Z)-7,13,16,19-Docosatetraen-1-yl isobutyrate  
1-Decanol  
Methyl-cyclopropene

440 entries found

Total of just 440 APPROVED Substances

# EU Pesticides Database

## Active substances

Select your criteria

Category: HB - Herbicide

Status: Approved

Class. (Dir. 67/548/EEC): -

Class. (Reg. 1272/2008): -

Authorisations: -

Legislation: -

ADI: All

ARfD: All

AOEL: All

Approval date: All

Expiration date: All

Search    Reset

Find substance

Show details

Export list

alphabetically

2,4-D  
2,4-DB  
Acetic acid  
Aclonifen  
Amidosulfuron  
Amitrole (aminotriazole)  
Azimsulfuron  
Beflubutamid  
Benfluralin  
Bensulfuron  
Bentazone  
Bifenox  
Bispyribac  
Bromoxynil  
Capric acid (CAS 334-48-5)  
Caprylic acid (CAS 124-07-2)  
Carbetamide  
Carfentrazone-ethyl  
Chloridazon (aka pyrazone)  
Chlorotoluron  
Chlorpropham  
Chlorsulfuron  
Clethodim  
Clodinafop  
Clomazone  
Clopyralid  
Cycloxydim

128 entries found

128 APPROVED Herbicide Substances



# Targeted Sampling Approach

## The National Residue Plan



### **Aimed at:-**

Detecting of the illegal use of prohibited substances.

Monitoring compliance with the specified MRLs for veterinary drugs, pesticides, mycotoxins, heavy metals etc.

Monitoring levels of environmental contaminants.

### **Sampling focus:-**

Most samples (c. 80%) are taken in accordance with criteria designed to target animals or products, which are more likely to contain illegal residues

However sampling may also be conducted in specific cases where the presence of illegal residues was suspected

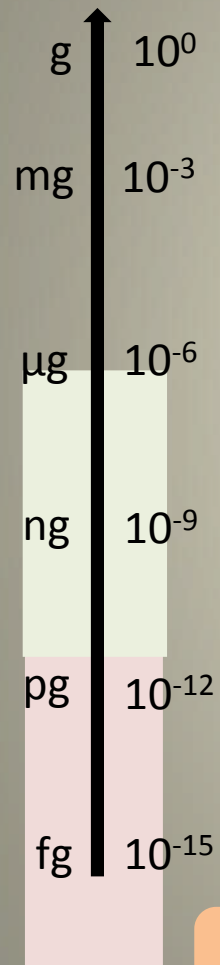
# National Residue Plan (Ireland) for Milk

| <b>GROUP A – Substances having anabolic effect and unauthorised substances</b> |  | <b>Milk</b> |
|--|--|-------------|
| A1   | Stilbenes and derivatives  |             |
| A2   | Antithyroid agents   |             |
| A3   | Steroids (natural and synthetic)   |             |
| A4   | Resorcylic acid lactones (incl. zeranol)                                       |             |
| A5   | Beta-agonists  |             |
| A6   | Compounds in Annex IV of Reg. 2377/90 (e.g. chloramphenicol, nitrofurans etc.) | ✓           |
| <b>GROUP B – Veterinary Drugs and Contaminants</b>                             |  |             |
| B1   | Antibacterial substances, incl. sulphonamides, quinolones, tetracyclines.      | ✓           |
| B2a  | Anthelmintics (parasitic worms/helminths)                                      | ✓           |
| B2b  | Anticoccidals  |             |
| B2c  | Carbamates and pyrethroids   |             |
| B2d  | Sedatives  |             |
| B2e  | Non-steroidal anti-inflammatory drugs (NSAIDs)                                 | ✓           |
| B2f  | Other pharmacologically active substances (e.g. teflubenzuron, diflubenzuron)  |             |
| B3a  | Organochloride compounds (incl. PCBs)  | ✓           |
| B3b  | Organophosphorus compounds   | ✓           |
| B3c  | Chemical elements (lead, cadmium, mercury, arsenic)                            | ✓           |
| B3d  | Mycotoxins   | ✓           |
| B3e  | Dyes (e.g. malachite green)  |             |
| B3f  | Others (brominated flame retardants, PAHs)                                     |             |

Ref: National Food Residue Database Report 2010/11. M. Danagher & J. Rae,J.

see [http://nfrd.teagasc.ie/pdf/NFRD\\_Annual\\_Report\\_2011.pdf](http://nfrd.teagasc.ie/pdf/NFRD_Annual_Report_2011.pdf)

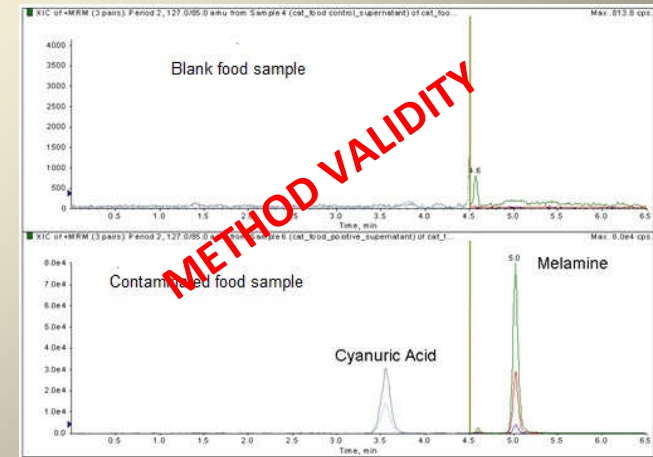
# Analysis Challenges



The Level of Contamination



Food matrix complexity



Verification and validation

# Biomarker Methodology

Requires demonstration of a quantitative relationship between intake of a substance and the amount of the substance or a metabolite in the body tissue or fluid of an animal - e.g., in blood, adipose tissue, urine, or milk

**BioCop Project (2005 – 2009)<sup>1</sup>**  
detecting chemical contaminants in food

- Involved measuring of the effect of the contaminant(s) rather than the more traditional single target compound concentrations
- Developed using rapid and efficient transcriptomics, proteomics and biosensor-based technologies
- Examples include detection of:-
  - Pesticides
  - Mycotoxins such as produced by fungi
  - Therapeutic drugs (growth promoters, quinolone antimicrobials)
  - Endocrine disrupters (phytoestrogens)

<sup>1</sup> For more see [http://www.teagasc.ie/publications/2009/1075/biocop\\_detecting\\_chemical\\_contaminants\\_in\\_food\\_5442.pdf](http://www.teagasc.ie/publications/2009/1075/biocop_detecting_chemical_contaminants_in_food_5442.pdf)  
or <ftp://ftp.cordis.europa.eu/pub/food/docs/elliott.pdf>

# Acknowledgement

Some concepts and illustrations used herein are based on a presentation entitled  
FOOD SAFETY MANAGEMENT SYSTEM FOR CONTAMINANTS  
AND DRUG RESIDUES IN THE DAIRY PRODUCTS  
by Prof. Dr. Bruno LE BIZEC, École Nationale Vétérinaire,  
Agroalimentaire et de l'Alimentation Nantes-Atlantique  
given at the **2013 IDF World Dairy Summit** in Yokohama,  
Japan.

However, the views and opinions expressed herein are my own and should not be taken as being those of Dr. LE BIZEC and his co-workers.

**THANK YOU**