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Health & Consumer Protection
Directorate-General

Legislación sobre residuos de sustancias farmacológicamente activas en la UE Establecimiento de LMRs

Ana Blass Rico

COMISIÓN EUROPEA

DIRECCIÓN GENERAL SANIDAD Y PROTECCIÓN DE LOS CONSUMIDORES

II Ronda negociación entre CA y la UE

Bruselas 25 al 29 de febrero de 2008

Summary

- EU residue control framework
- Risk analysis
- EU MRLs
  - EMEA
  - EFSA
  - Procedures
  - Marketing authorisation
- MRPLs

Articulo 152 TRATADO DE LA UNIÓN EUROPEA

Al definirse y ejecutarse todas las políticas y acciones de la Comunidad se garantizará un alto nivel de protección de la salud humana

EU residue framework food control perspective

Regulation 2002/178/EC "Food Law"

Food safety requirements (Art 14)

Responsibilities (Art 17)

Regulation 2004/882/EC on official controls

Art 2: Official Control means any form of control that the competent authority perform for the verification of compliance with the feed and food law, animal health and welfare rules

Directive 96/23/EC "Residue Control Directive"

Decision 2002/657/EC analytical requirements + performance limits

2377/90: human safety evaluation of residues of pharmacologically active substances

96/22/EC and 2003/74/EC
Authorisation and use restrictions

2002/82/EC: *Veterinary Medicinal Products Directive*

Definitions

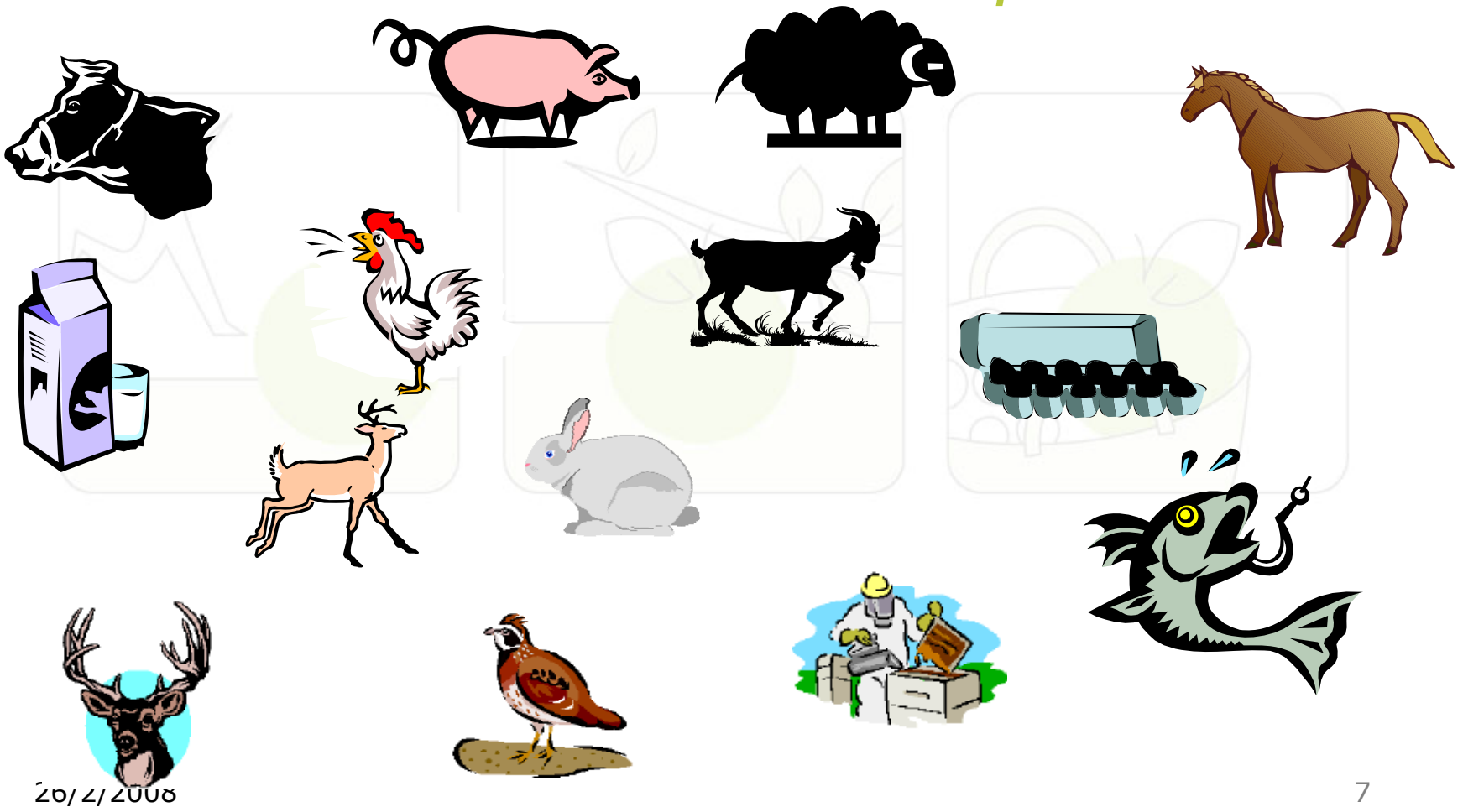
- **Residuos de medicamentos veterinarios**: todas las sustancias farmacológicamente activas que permanezcan en los productos alimenticios obtenidos a partir de animales a los que se les hubiere administrado dichos medicamentos;
- **Límite máximo de residuos** (LMR):

The maximum concentration of residue resulting from the use of a veterinary medicinal product (expressed in mg/kg or µg/kg on a fresh weight basis) which may be accepted by the Union to be legally permitted or recognised as acceptable in or on a food".

Control de residuos. Base legal

- **Directive 96/22/EC** = prohibition on the use in stockfarming of certain substances having hormonal or thyrostatic action and of beta-agonists. Amended by Directive 2003/74/EC
- **Directive 96/23/EC** = measures to monitor certain substances and residues in live animal and animal products (residue monitoring plans)

Scope of residue control
Live animals and *animal products*



Planes de vigilancia para la detección de residuos:

- los Estados miembros someten a la Comisión los planes relativos a la detección de grupos de residuos
- la Comisión informa a los Estados miembros, en el marco del Comité Permanente
- cada año la Comisión envía al Parlamento Europeo y al Consejo una comunicación que recoge los resultados de las acciones llevadas a cabo en el ámbito regional, nacional y comunitario

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Residue monitoring plan

General information

- Legislation for substances indicated in Annex I
- Infrastructure for official services
- List of approved laboratories
- National tolerances for authorized substances
- Substances to be detected and method of analysis
- Official sampling procedures
- Measures when residues detected

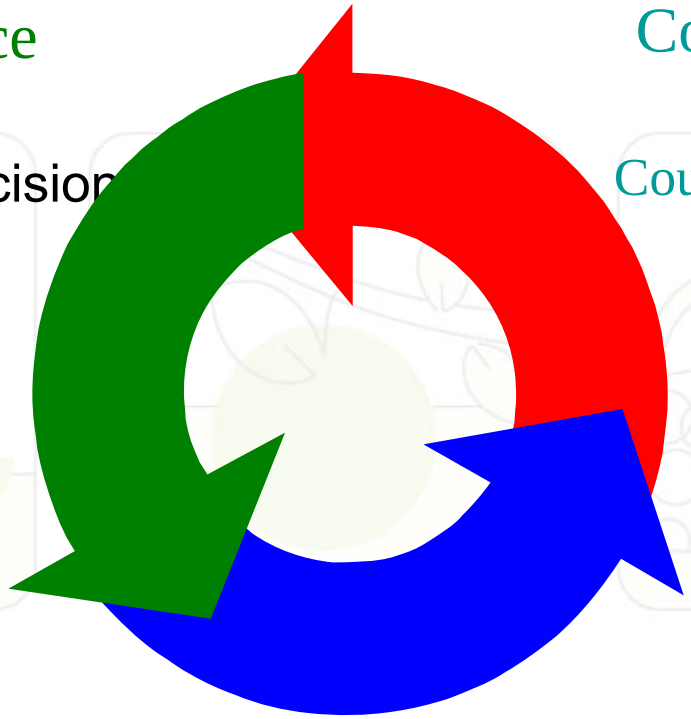
Residue monitoring plan

- Production figures previous year
- Groups and Substances
- Laboratories
- Analytical methods: screening and confirmation
- Animal species/ Matrixes/ Number of samples

Laboratory network

National Reference Laboratories

NRLs Commission Decision 2006/130/EC



Community Reference Laboratories

Council Directive 96/23/EC, Chapter 2, Annex V.

Routine Laboratories

Groups of substances

Directive 96/23/EC

Banned substances
- Stilbenes
- Thyrostats
- Steroids and zeranol
- Chloramphenicol
- Nitrofurans

Veterinary medicines
- Antibacterials (B1)
- Antihelmintics
- Anticoccidials
- Carbamates
- Sedatives
- NSAIDs
- Other pharmacologically active substances

Contaminants
- Organochlorine
- Organophosphorous
- Chemical elements
- Mycotoxines
- Dyes
- Others

Two categories of substances

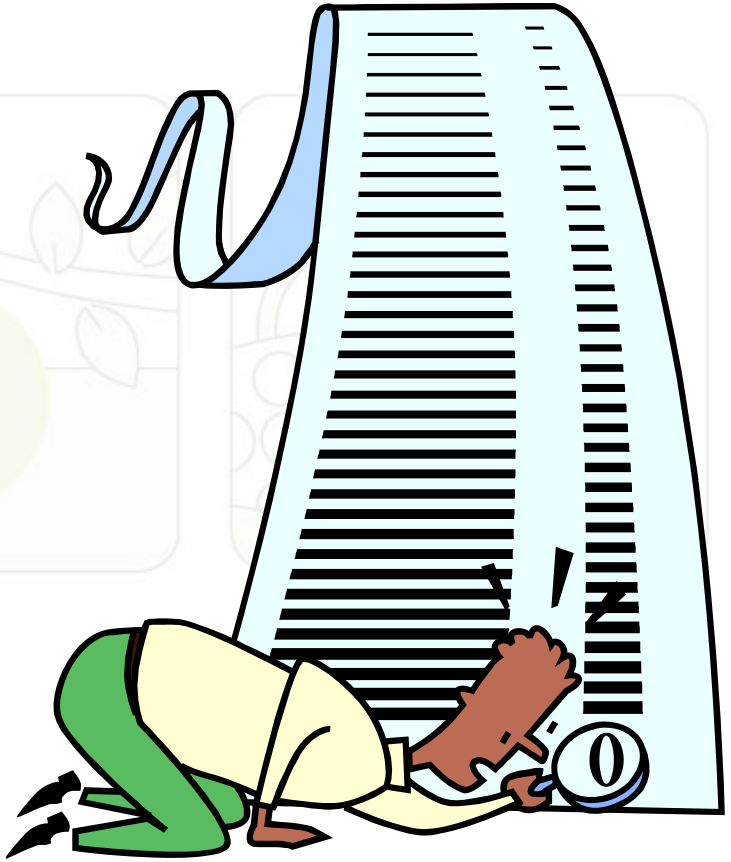
- substances that have not intentionally used but = result of production, packaging, transport or holding or environment = **contaminants**
- substance intentionally used in animals, plants and foods or contact material = **residues, additives, contact materials**

Prohibition of use not a choice

Use may be prohibited

Targeting criteria

- More than 1000 substances

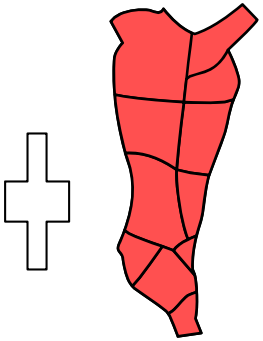


Scope of residue control

Targeted samples

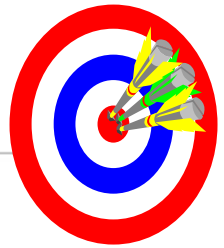
- Samples must be targeted with the aim of detecting illegal treatment or controlling compliance with MRLs

Testing at farms and slaughterhouses



Suspect samples

- Consequence of non-compliant results
- presence of prohibited substances
- Evidences of illegal treatment or non-compliance withdrawal period



National plans should be targeted with the aim of detecting illegal treatment or controlling compliance with:

- **Regulation 2377/90** = Establishes Maximum Residue Limits (MRLs) for substances and animal species (veterinary medicines)
- **Regulation 466/2001**= Establishes Maximum levels for certain contaminants in foodstuff:
  - Heavy metals (Pb, Hg, Cd) , other contaminants
- **Pesticides residues** with MRLs (76/895/EEC, 86/362/EEC, 86/363/EEC & 90/642/EEC.

Risk Analysis

determines the acceptable level of risk

Scientific evaluation + Other legitimate factors ⇒ measures determining food safety in a country = level of protection deemed appropriate

Opinion:

- NOEL/ADI
- tolerance proposal (MRL/ML)
- knowledge gaps
- consideration factors

- feasibility of control
- societal
- economic
- traditional
- ethical
- environmental factors

Recital 19, Art. 6+7 of 2002/178/EC Food Law

MRLs Human safety evaluation:

Toxicological studies = > SF Daily food basket ⇒ Maximum residue limits/food commodities

NOAEL No observed adverse effects level

ADI Acceptable daily intake (µg or mg/kg BW)
arbitrary average human bodyweight 60 kg

carcinogenic/ genotoxic = > no safe limit

prohibition of use (MRPL)

Contaminants ALARA → Maximum Level

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European Medicines Agency

- The European Medicines Agency (EMEA) is a decentralised body of the European Union with headquarters in London.
- Its main responsibility is the protection and promotion of public and animal health, through the evaluation and supervision of medicines for human and veterinary use.
- The EMEA is responsible for the scientific evaluation of applications for European marketing authorisation for medicinal products (centralised procedure). Companies submit one single marketing authorisation application to the EMEA.
- For veterinary medicinal products the Agency has the responsibility to establish safe limits for medicinal residues in food of animal origin.
- 440 staff members in 2007 + scientific resources of over 40 national competent authorities in 30 EU and EEA-EFTA countries in a network of over 4,000 European experts
- Annual budget 163 m €/ Community budget ± 45 m €

http://www.emea.europa.eu/

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European Medicines Agency

Committee for Medicinal Products for Veterinary use (CVMP)

- responsible for preparing the Agency's opinions on all questions concerning veterinary medicinal products,
- responsible for conducting the initial assessment of veterinary medicinal products for which a Community-wide marketing authorisation is sought.
- also responsible for several post-authorisation and maintenance activities, including the assessment of any modifications or extensions ('variations') to the existing marketing authorisation.

The CVMP is composed of:

- a chairman, elected;
- one member (and an alternate) nominated by each of the 27 EU Member States;
- one member (and an alternate) nominated by each of the EEA-EFTA states Iceland and Norway;
- up to five co-opted members, chosen among experts nominated by Member States or the EMEA and recruited, when necessary, to gain additional expertise in a particular scientific area.

Procedures for marketing authorisation

- **1. MRL**

A veterinary medicinal product intended for administration to food-producing animals and containing an existing pharmacologically active substance can only be authorised if any pharmacologically active substance contained within it is placed in Annexes I, II or III of Council Regulation (EEC) No 2377/90 2. Marketing authorisation procedure

- 2. Marketing authorisation procedure

http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/vol-6/a/vol6a_chap4_2006_05.pdf

Marketing authorisation

- 1. MRL
- 2. **Marketing authorisation procedure**

1. Centralised Community procedure:

for the authorisation of veterinary medicinal products, for which there is a single application, single evaluation and a single authorisation allowing direct access to the single market of the Community.

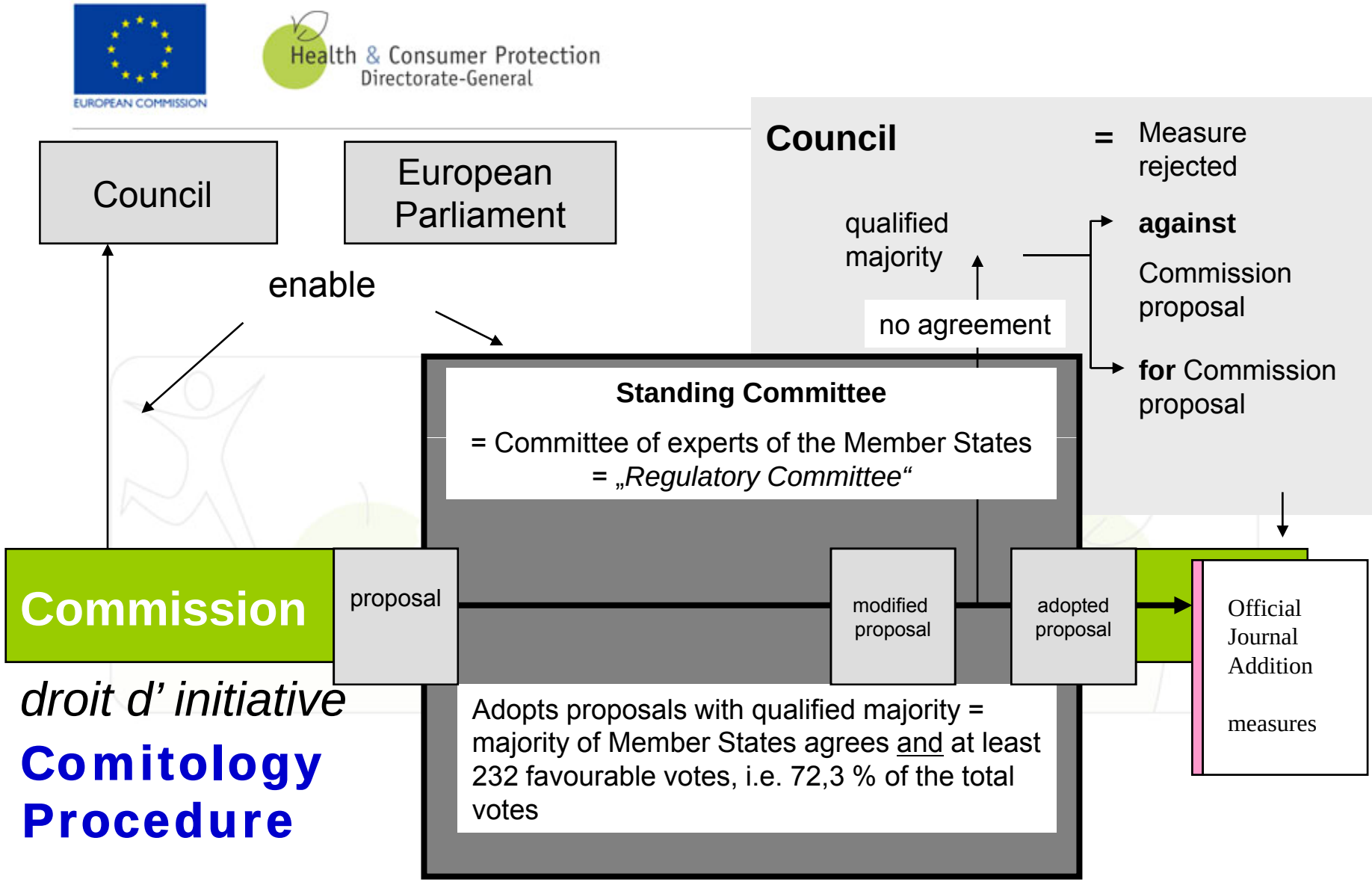
2. Mutual recognition and decentralised procedure

Centralised Community procedure 1. EMEA

- Pre-submission; 6 months in advance, recommended.
- MRLs
  - Rapporteur/co-rapporteur+ experts
  - Fees: 58 000 €
  - CVMP opinion
  - EMEA transmission of Opinion to the Commission (within 30 days after adoption by CVMP)
  - Commission: draft Commission Regulation to amend Annex I, II , II, IV and submission to the Standing Committee on Veterinary Medicinal Products

Centralised Community procedure
2. Adoption Commission Decisions

- Within 15 calendar days of receipt of an opinion of the EMEA, the Commission prepares a draft decision taking the opinion and any relevant provisions of Community law into account. Where the draft decision is not in accordance with the opinion of the EMEA, the Commission shall annex a detailed explanation of the reasons for the differences.
- In the area of veterinary medicinal products, the Commission is assisted by the Standing Committee on Veterinary Medicinal Products (the "Standing Committee"). The Standing Committee is chaired by the Commission representative, who does not vote. (Decision by a qualified majority of 232 out of 321 votes).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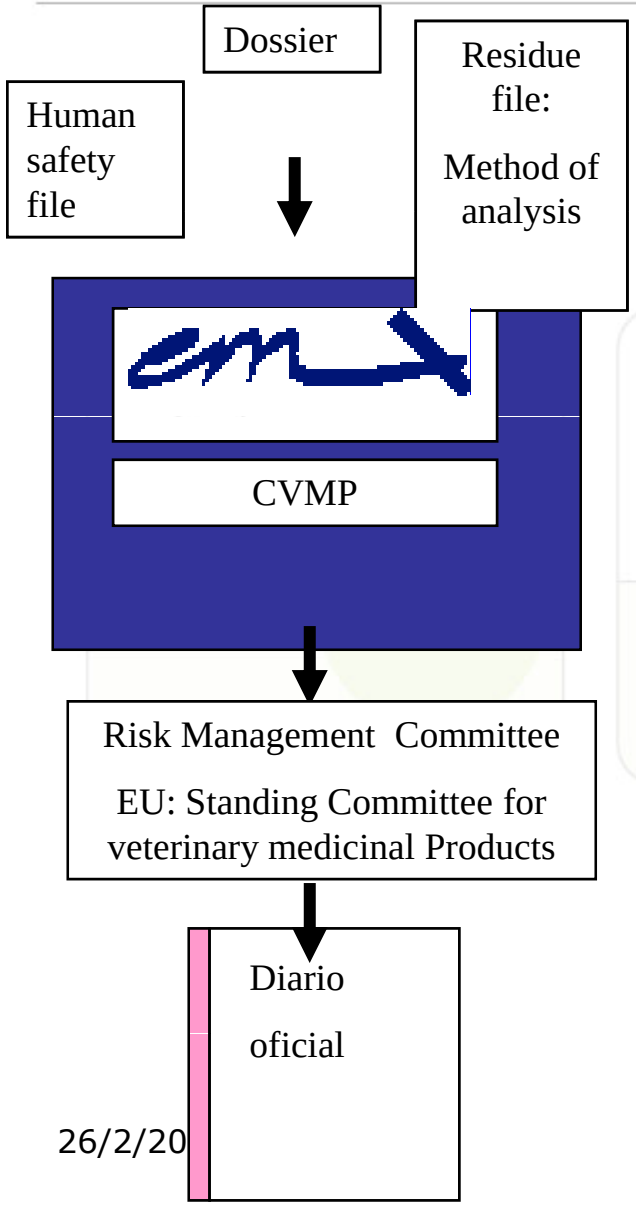
Council
European Parliament
enable
Council
= Measure rejected
qualified majority
against Commission proposal
no agreement
for Commission proposal
Standing Committee
= Committee of experts of the Member States
= „Regulatory Committee“
Commission
proposal
modified proposal
adopted proposal
Official Journal Addition
measures
Adopts proposals with qualified majority = majority of Member States agrees and at least 232 favourable votes, i.e. 72,3 % of the total votes
droit d’ initiative
Comitology Procedure

EU MRLs



Requirements

Annex V of 2377/90 + Volume 8 Guidelines

http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/vol-8/pdf/vol8_10-2005_.pdf

Result:

EU: Classification in Annex I to IV of 2377/90

http://pharmacos.eudra.org/F2/mrl/index.htm

Official Journal: http://europa.eu.int/eur-lex/en/oj/

Summary Reports on: http://www.emea.eu.int/

Marketing authorisation

MRLs+quality/safety/efficiency

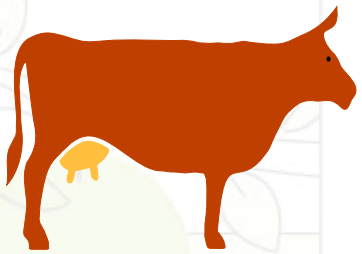
Limitaciones de uso

- indicación

- prescripción

-especies

-Withdrawal periods:



is the time after the last administration of the veterinary medicinal product during which the animal must not be slaughtered or during which milk or eggs must not be taken for human consumption, ensuring that residues will not exceed the MRLs

determined as part of the process of evaluation of the application for marketing authorisation

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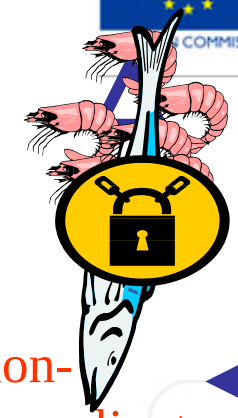
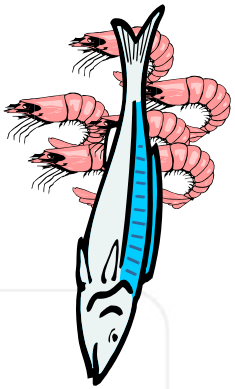
MRPLs for controls





test → no residues detected => compliant

test → residues

residues ≥ MRPL → non-compliant rejected

residues < MRPL → Consignment compliant

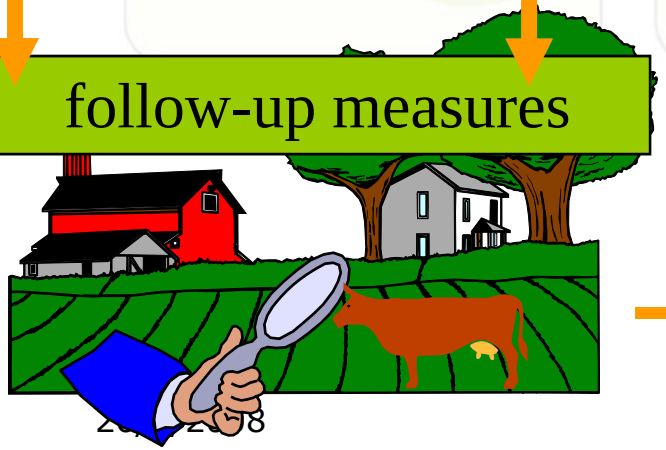
Consignment compliant => in circulation

Consignment compliant => in circulation

Consignment compliant => in circulation

reference point for action

follow-up measures



Questionnaire measures taken ☑

Report

Plan 200X+1

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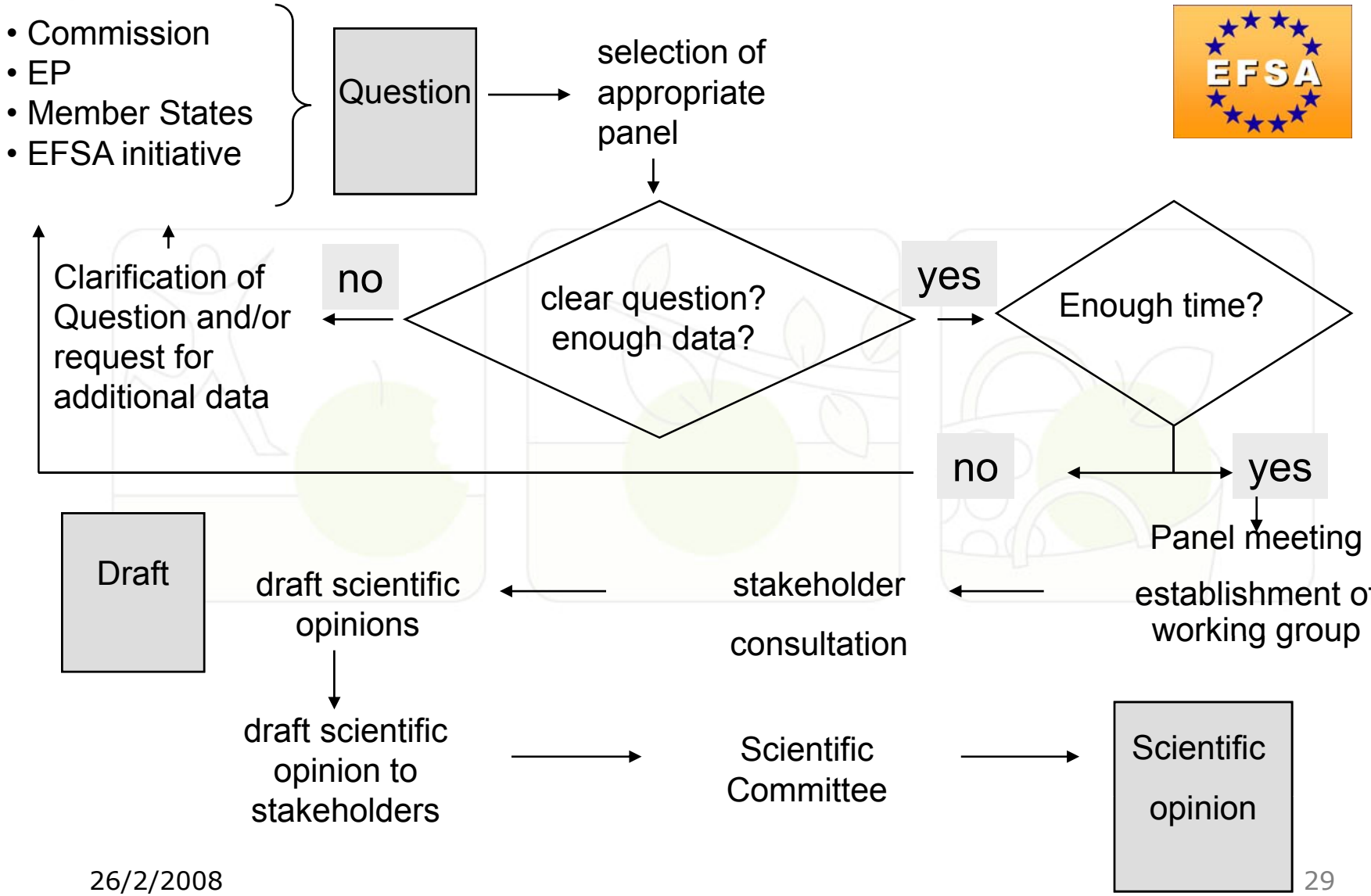
EFSA scientific advice



third countries

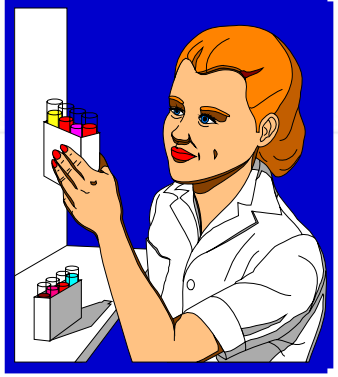
- must submit residue control plans and results to Commission
- must offer equivalent guarantees to those provided for in Community Legislation
- Are not subject to Community law
  - Do not have to use 96/23 model e.g. Codex however…..
  - as per 96/22 must have either total ban on use of hormones & beta-agonists for growth promotion or split system

Elements of a regularly system to ensure food safety in terms of residues

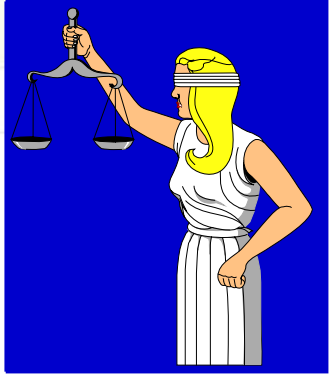
food safety is ensured by

Legis-lation

Control



Enforce-ment



More Info?

On the EU in General:
http://europa.eu.int and
Freephone Number: 00 800 6 7 8 9 10 11

Directorate General Health and Consumer Protection
sanco-mailbox@ec.europa.eu

Residue Control Legislation:

http://europa.eu.int/comm/food/fs/sfp/fcr/residues_en.html

Scientific Evaluation:

http://www.efsa.eu.int/ and http://www.emea.eu.int/ (veterinary residues)

General guidance for third country authorities on procedures to be followed when importing live animals and animal products into the European Union
http://europa.eu.int/comm/food/fvo/pdf/guide_thirdcountries_en.pdf

Guidelines on the implementation of the main General Food Law requirements.
http://europa.eu.int/comm/food/food/foodlaw/guidance/index_en.htm

Animal health
http://europa.eu.int/comm/food/animal/animalproducts/index_en.htm

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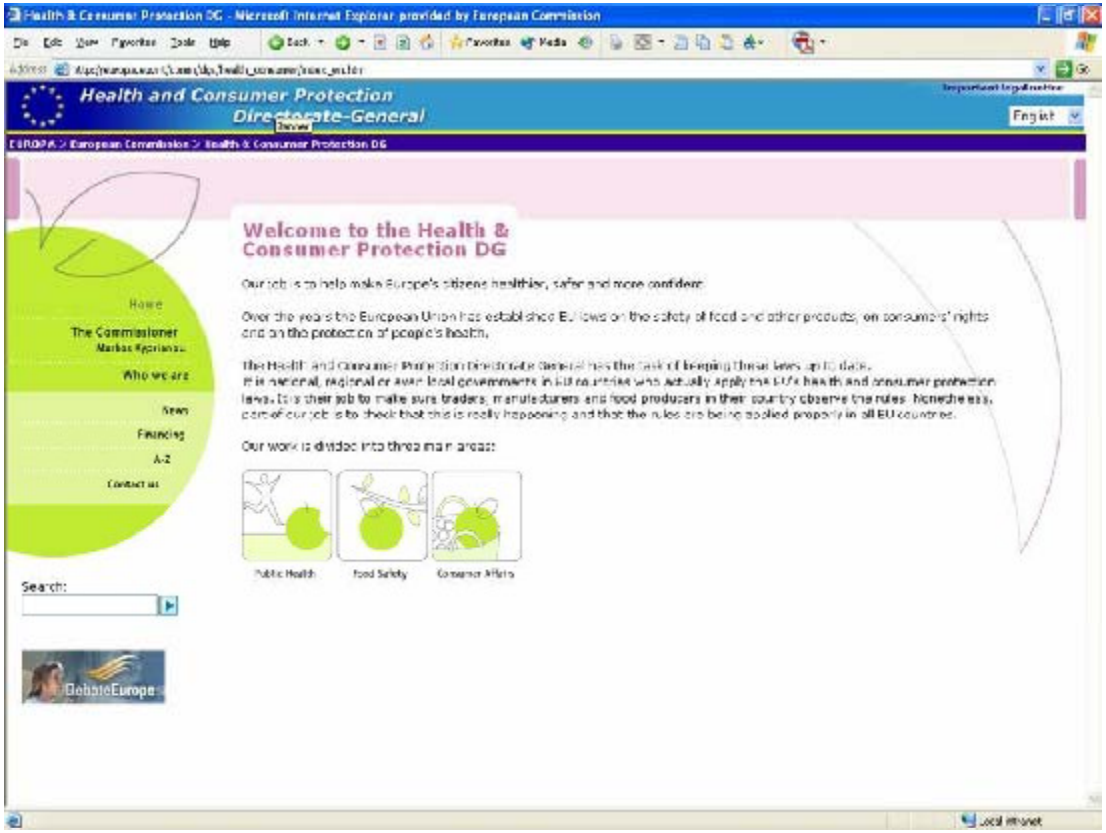

http://europa.eu.int/comm/dgs/health_consumer/index_en.htm

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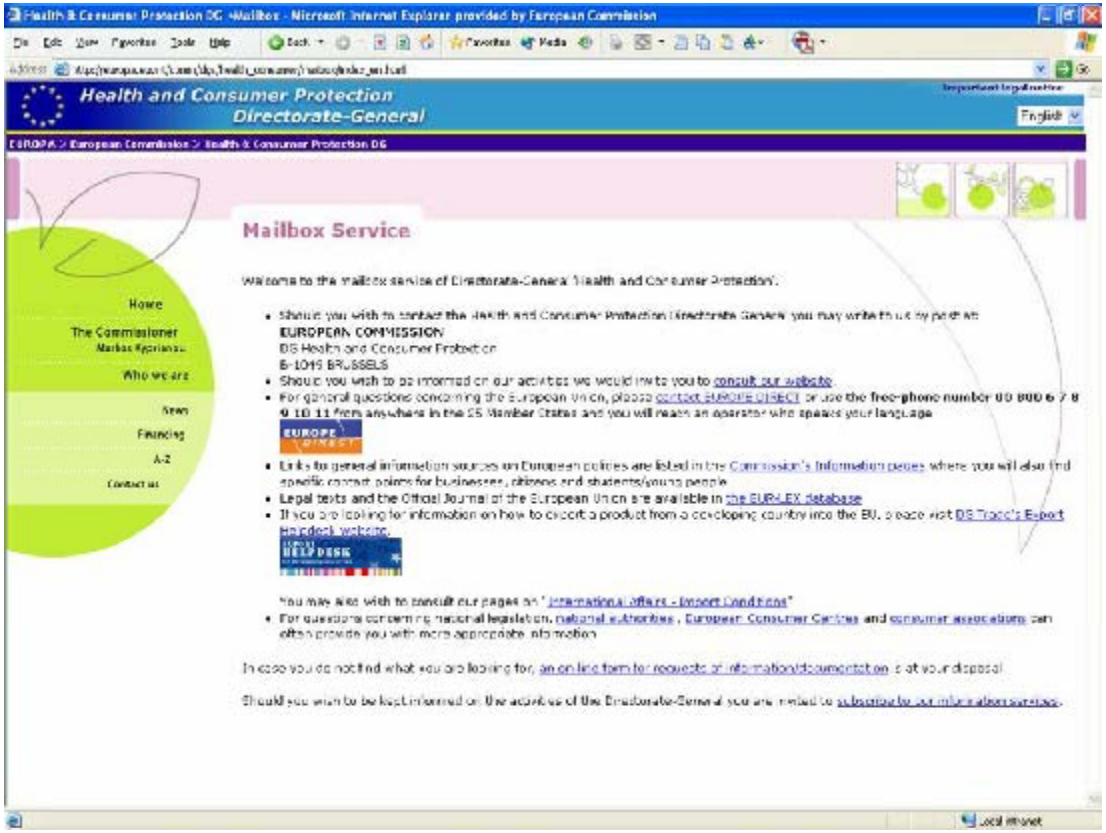

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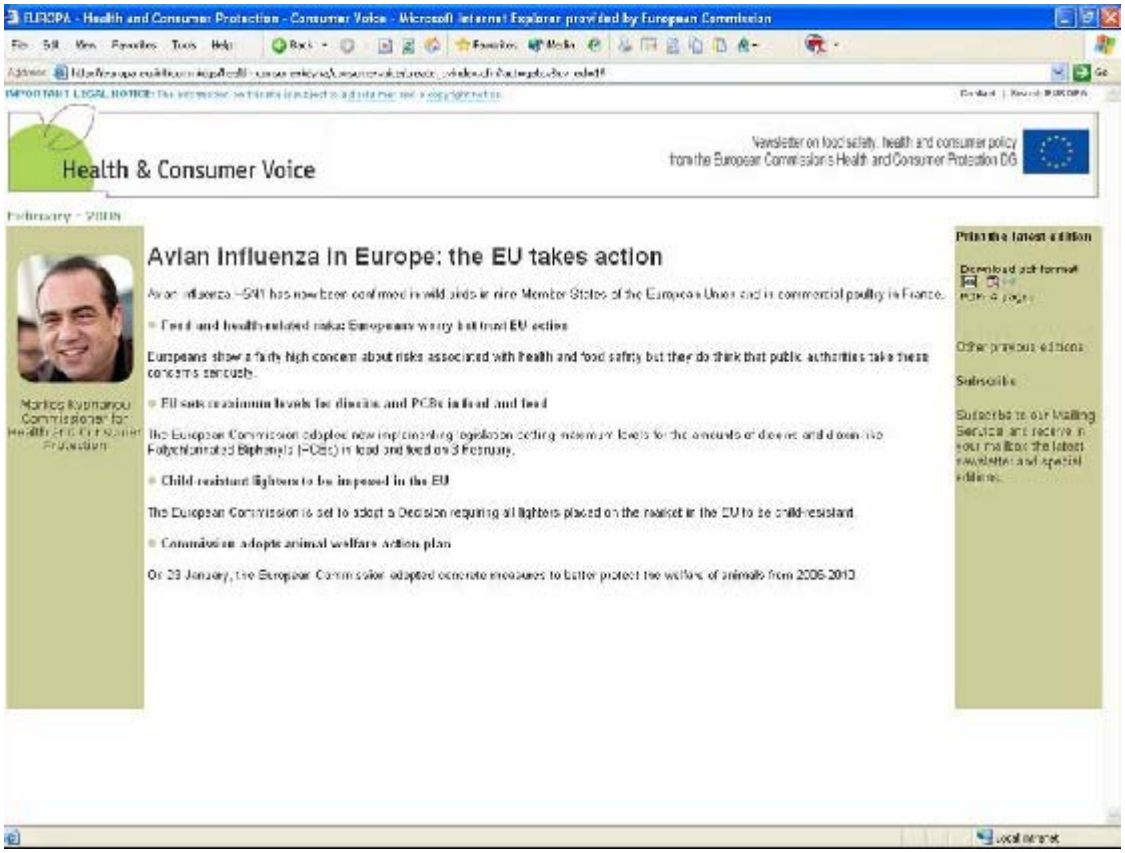

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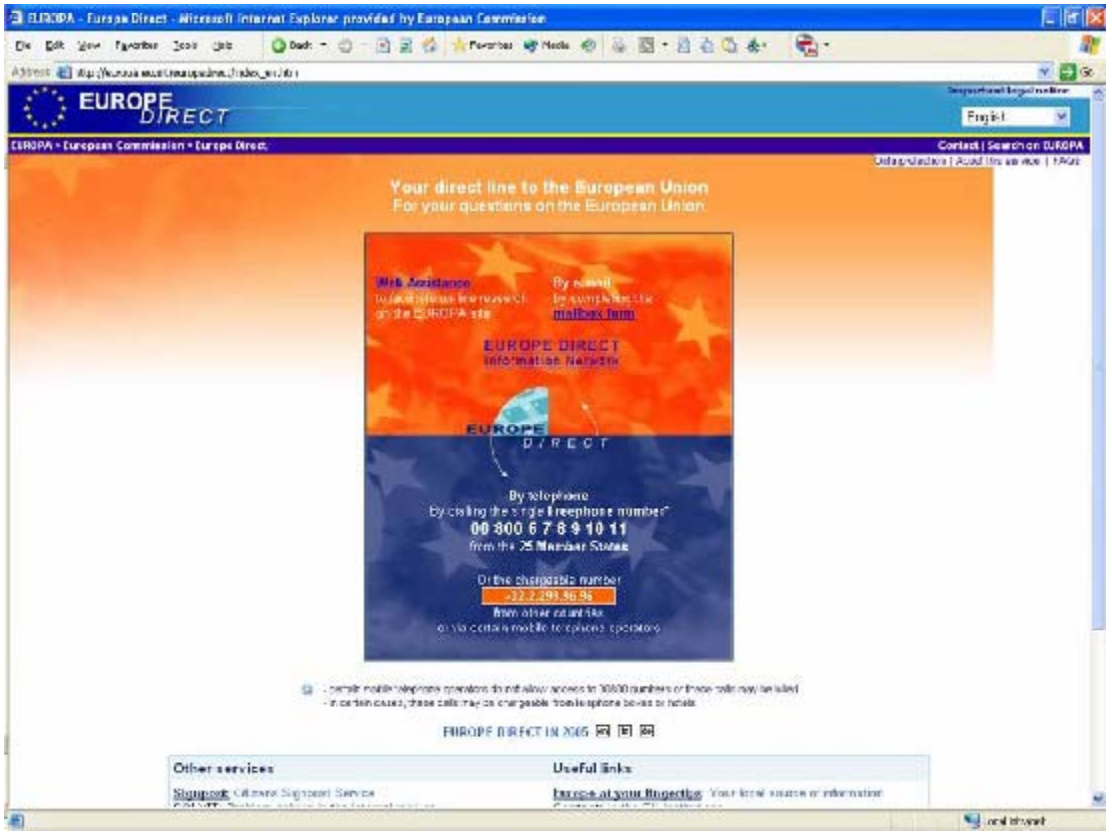

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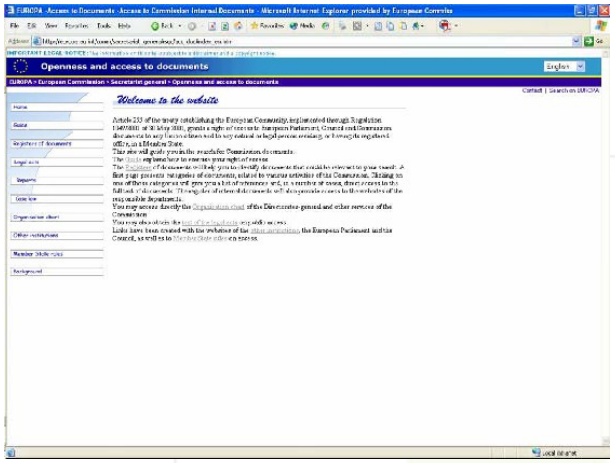
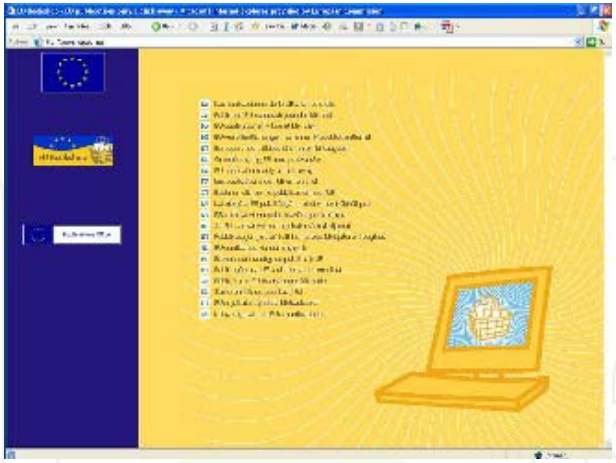
Other useful websites



Access to documents



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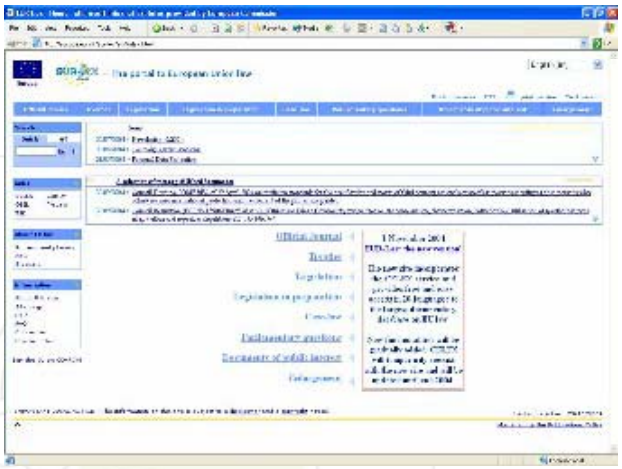
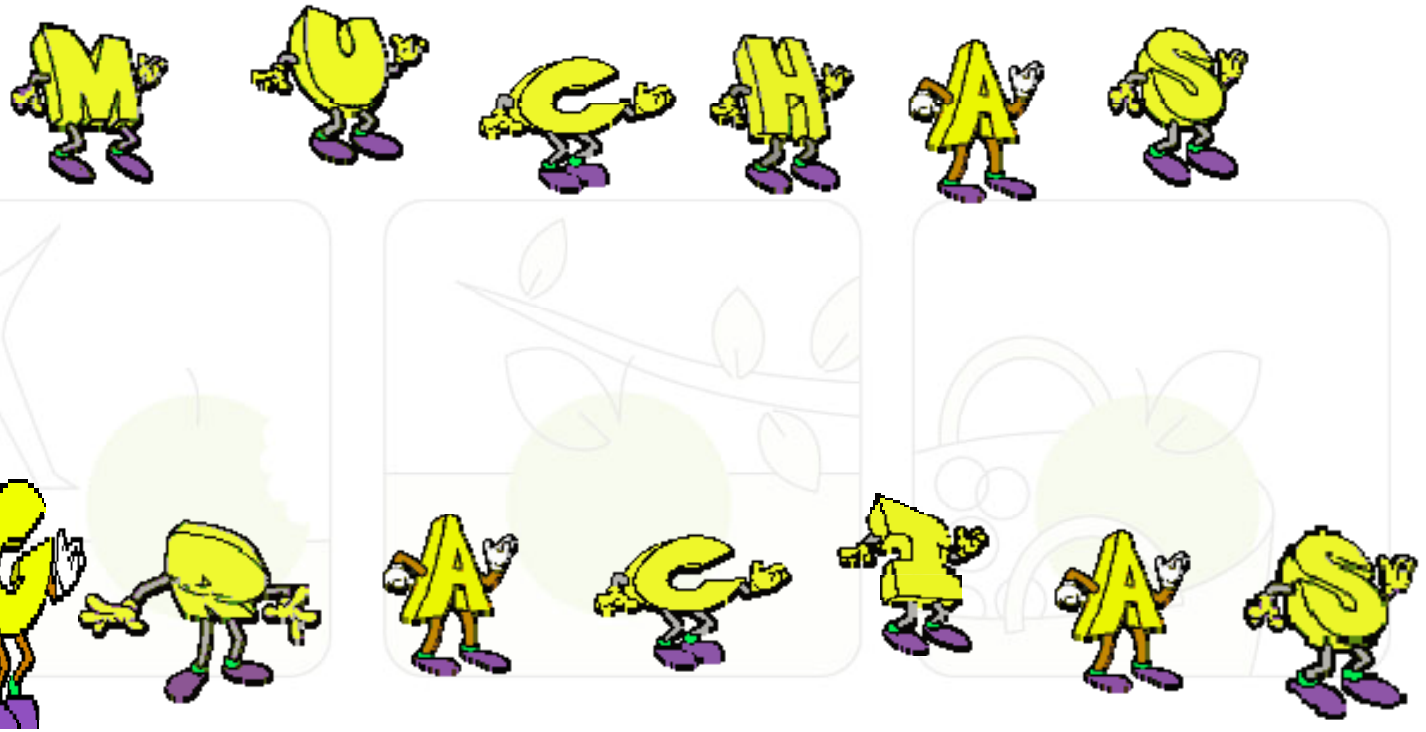


EURLEX for legislation

http://europa.eu.int/comm/secretariat_general/sgc/acc_doc/index_en.htm

http://europa.eu.int/publications

http://europa.eu.int/eur-lex/en/index.html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