Session 1: Residues in food – Overall situation and regulatory environment

A GENERAL PERSPECTIVE ON THE USE OF WADA PROHIBITED SUBSTANCES FOR ANIMAL HUSBANDRY

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ONIRIS - France - www.laberca.org
PROHIBITED SUBSTANCES: CONTRASTED SITUATION
PROHIBITED SUBSTANCES: CONTRASTED SITUATION

THE WORLD ANTI-DOPING CODE
INTERNATIONAL STANDARD

PROHIBITED LIST
JANUARY 2017
The international rules:

- WTO determined international trade rules (GATT 1948-1994)
- Intergovernmental institution with committees
  - Agreement (SPS, TBT…)
  - Procedures of dispute settlement
- SPS: Application of sanitary and phytosanitary measures
  - To facilitate international trade by reducing sanitary barriers
  - To help countries to protect themselves against sanitary hazards due to trade
- If measures are based on international standards (OIE, Codex Alimentarius, IPPC)… they are automatically presumed to be consistent with the provisions of the SPS agreement
- If measures are more restrictive, members shall justify that they are based on scientific principles.
- RA is compulsory
3. Where international standards exist or their completion is imminent, they shall be taken into consideration in the development or adaptation of food law, except where such standards or relevant parts would be an ineffective or inappropriate means for the fulfilment of the legitimate objectives of food law or where there is a scientific justification, or where they would result in a different level of protection from the one determined as appropriate in the Community
**Regulation (EC) No 2009/470/EC**

- **Commission classification** of pharmacologically active substances **shall establish either:**
  - a MRL
  - a provisional MRL (*defined period of time – completion of scientific studies in progress*)
  - the absence of the need to establish a MRL (*not necessary for the protection of human health*)
  - a prohibition on the administration of a substance

**Regulation (EC) No 2010/37/EC**

<table>
<thead>
<tr>
<th>Pharmacologically active Substance</th>
<th>Marker residue</th>
<th>Animal Species</th>
<th>MRL</th>
<th>Target Tissues</th>
<th>Other Provisions (according to Article 14(7) of Regulation (EC) No 470/2009)</th>
<th>Therapeutic Classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methylprednisolone</td>
<td>Methylprednisolone</td>
<td>Bovine</td>
<td>10 µg/kg</td>
<td>Muscle</td>
<td>Not for use in animals from which milk is produced for human consumption.</td>
<td>Corticoides/ Glucocorticoides</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>10 µg/kg</td>
<td>Fat</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>10 µg/kg</td>
<td>Liver</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>10 µg/kg</td>
<td>Kidney</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
• Forbidden substances (Group A)
  • Substances having anabolic effect
  • Unauthorized substances

• Veterinary medicines (Groups B1, B2) mainly with MRLs
  • Antibiotics,
  • Anthelminthic,
  • NSAI drugs
  • Corticosteroids

• Contaminants (Group B3)
  • Pesticides, dioxins, mycotoxins
  • Heavy metals...

Dir. 96/22 or
37/2010: Table 2 → no MRL

470/2009 +
37/2010: Table 1 → MRL

Reg. Contaminants
Reg. Pesticides
LEGISLATION

Council directive 96/23/EC on measures to monitor certain substances and residues thereof in live animals and animal products of 29 April 1996

ANNEX I

GROUP A — Substances having anabolic effect and unauthorized substances

(1) Stilbenes, stilbene derivatives, and their salts and esters

(2) Antithyroid agents

(3) Steroids

(4) Resorcylic acid lactones including zeranol

(5) Beta-agonists


Steroids, RALs and β-agonists can be used in TCs but imports only acceptable if ‘split’ system
ANABOLIC AGENTS
Anabolic agents are prohibited.

1. ANABOLIC ANDROGENIC STEROIDS (AAS)
   a. Exogenous* AAS, including:
   b. Endogenous** AAS when administered exogenously:

2. OTHER ANABOLIC AGENTS
   Including, but not limited to:
   - Clenbuterol;
   - Selective androgen receptor modulators (SARMs, e.g. andarine and ostarine);
   - Tibolone;
   - Zeranol;
   - Zilpaterol.
S2 PEPTIDE HORMONES, GROWTH FACTORS, RELATED SUBSTANCES, AND MIMETICS

S3 BETA-2 AGONISTS
All selective and non-selective beta-2 agonists, including all optical isomers, are prohibited.

S4 HORMONE AND METABOLIC MODULATORS

S5 DIURETICS AND MASKING AGENTS
STIMULANTS

NARCOTICS

CANNABINOIDs

GLUCOCORTICOIDs
All of these implants are not approved for use in dairy cows, nor hogs or poultry.
# ANABOLIC STEROIDS

<table>
<thead>
<tr>
<th>Marque</th>
<th>Composition</th>
<th>Année</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>UPJOHN</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Calf-oid</td>
<td>10 mg d’œstradiol + 100 mg de progestérone</td>
<td>1990</td>
</tr>
<tr>
<td>- Component C</td>
<td>10 mg d’œstradiol + 100 mg de progestérone</td>
<td>CALF</td>
</tr>
<tr>
<td>- Component H</td>
<td>20 mg d’œstradiol + 200 mg de testostérone</td>
<td>HEIFER</td>
</tr>
<tr>
<td>- Component S</td>
<td>20 mg d’œstradiol + 200 mg de progestérone</td>
<td>STEER</td>
</tr>
<tr>
<td>- Component TH</td>
<td>200 mg d’acétate de trenbolone</td>
<td>HEIFER</td>
</tr>
<tr>
<td><strong>ELANCO</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Compudose</td>
<td>25,7 mg d’œstradiol</td>
<td>1982</td>
</tr>
<tr>
<td>- Encore</td>
<td>43,9 mg d’œstradiol</td>
<td>STEER</td>
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<tr>
<td><strong>ROUSSEL-UCLAF</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Finaflex-H</td>
<td>200 mg de testostérone</td>
<td>1987</td>
</tr>
<tr>
<td>Finaflex-S</td>
<td>140 mg de testostérone</td>
<td>STEER</td>
</tr>
<tr>
<td>- Forplex</td>
<td>36 mg de zéranol + 140 mg d’acétate de trenbolone</td>
<td>STEER</td>
</tr>
<tr>
<td><strong>UPJOHN</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heifer-oid</td>
<td>20 mg d’œstradiol + 200 mg de testostérone</td>
<td>HEIFER</td>
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<tr>
<td><strong>HEIFER</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Implix</td>
<td>20 mg d’œstradiol + 200 mg de testostérone</td>
<td>HEIFER</td>
</tr>
<tr>
<td><strong>UPJOHN</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Implus-C</td>
<td>10 mg d’œstradiol + 100 mg de progestérone</td>
<td>CALF</td>
</tr>
<tr>
<td><strong>UPJOHN</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Implus-H</td>
<td>20 mg d’œstradiol + 200 mg de testostérone</td>
<td>HEIFER</td>
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<tr>
<td><strong>UPJOHN</strong></td>
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<td></td>
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<tr>
<td>Implus-S</td>
<td>20 mg d’œstradiol + 200 mg de progestérone</td>
<td>STEER</td>
</tr>
<tr>
<td><strong>UPJOHN</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MGA</td>
<td>acétate de mélangestrol</td>
<td>1977</td>
</tr>
<tr>
<td><strong>MALLINCKRODT</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ralgro</td>
<td>36 mg de zéranol</td>
<td>1969</td>
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<tr>
<td><strong>ROUSSEL-UCLAF</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Revalor</td>
<td>20 mg d’œstradiol + 140 mg d’acétate de trenbolone</td>
<td>STEER</td>
</tr>
<tr>
<td><strong>ROUSSEL-UCLAF</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Revalor-G</td>
<td>8 mg d’œstradiol + 40 mg d’acétate de trenbolone</td>
<td>1991</td>
</tr>
<tr>
<td><strong>UPJOHN</strong></td>
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<td></td>
</tr>
<tr>
<td>Steer-oid</td>
<td>20 mg d’œstradiol + 200 mg de progestérone</td>
<td>STEER</td>
</tr>
<tr>
<td><strong>SYNTEx</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Synovex C</td>
<td>10 mg d’œstradiol + 100 mg de progestérone</td>
<td>1984</td>
</tr>
<tr>
<td><strong>SYNTEx</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Synovex H</td>
<td>20 mg d’œstradiol + 200 mg de testostérone</td>
<td>1958</td>
</tr>
<tr>
<td><strong>SYNTEx</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Synovex S</td>
<td>20 mg d’œstradiol + 200 mg de progestérone</td>
<td>1956</td>
</tr>
<tr>
<td><strong>SYNTEx</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Torelor</td>
<td>40 mg d’œstradiol + 200 mg d’acétate de trenbolone</td>
<td>STEER</td>
</tr>
<tr>
<td><strong>SYNTEx</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Torevex-S</td>
<td>20 mg d’œstradiol + 200 mg de progestérone</td>
<td>STEER</td>
</tr>
</tbody>
</table>
β-AGONISTS

• Action
  – Repartitioning agent
  – For increased carcass leanness
  – For improved rate of weight gain and feed efficiency (up to 25% each)
β-AGONISTS

CONTROL

TREATED

ZILPATEROL

1993
cattle

SOUTH AFRICA
MEXICO

RACTOPAMINE*

1999
finishing swine

PAYLEAN®

RACTOPAMINE*

2003
cattle & turkey

OPTAFLEXX®

ZILPATEROL*

2006
cattle

TOMAX®

ZILMAX®

*Approved by FDA
ZILPATEROl
**Commercial formulation**

Zilmax®: 4.8% w/w zilpaterol hydrochloride, 8% polyoxyl castor oil, 4.3% polyvinylpyrrolidone, and 82.9% ground corn cob.

**Distributed by:** Intervet Inc., (d/b/a Merck Animal Health), made in France

**Indication:** For increased rate of weight gain, improved feed efficiency, increased carcass leanness in cattle fed in confinement for slaughter

**Usage:** Feed continuously to cattle during the last 20-40 days on feed, containing 6.8 g/ton zilpaterol, to provide 60 to 90 mg zilpaterol hydrochloride per head per day. Withdrawal period: 3 days prior to slaughter.

**Precautions:** Not for use in animals intended for breeding, *equidae*, dairy cattle, veal calves.
Zilmax® registration is approved in 17 countries: Brazil, Canada, Columbia, Costa Rica, the Dominican Republic, Ecuador, Guatemala, Honduras, Kazakhstan, Mexico, Nicaragua, Panama, Peru, South Africa, South Korea and United States.

Import licenses: Lebanon and Pakistan.

Registration is in process in 8 additional countries: Argentina, Australia, Belarus, Chile, Indonesia, New Zealand, Pakistan, Taiwan and Uruguay.

Japan have established an import MRL for ZILPATEROL in 2014.
Table 10.22. Measurement of $[^{14}C]$zilpaterol and $[^{14}C]$deisopropyl-zilpaterol residues in cattle tissues, mean ±SD expressed as zilpaterol HCl equivalents in µg/kg (Tulliez, 1999)

<table>
<thead>
<tr>
<th>Withdrawal time</th>
<th>Residues of $[^{14}C]$zilpaterol and $[^{14}C]$deisopropyl-zilpaterol (µg/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Liver</td>
</tr>
<tr>
<td></td>
<td>zilpaterol</td>
</tr>
<tr>
<td>12   ①</td>
<td>104.7 ±33.3</td>
</tr>
<tr>
<td>12   ②</td>
<td>84.4 ±19.8</td>
</tr>
<tr>
<td>24   ①</td>
<td>48.4 ±5.3</td>
</tr>
<tr>
<td>48   ①</td>
<td>22.9 ±13.3</td>
</tr>
<tr>
<td>96   ①</td>
<td>7.5 ±3.4</td>
</tr>
</tbody>
</table>

NOTES: (1) Group was fed medicated feed for 12 days. (2) Group was fed medicated feed for 15 days. (3) ND = Not detectable. (4) Only one value available for the 96-h samples, so no mean and SD were calculated.
As a result, JECFA proposed draft MRLs for zilpaterol hydrochloride of 3.3 μg/kg in cattle kidney, 3.5 μg/kg in cattle liver and 0.5 μg/kg in cattle muscle.

The Committee agreed that parent zilpaterol was an appropriate marker residue in M, L, K. Liver and kidney contained the highest concentration of zilpaterol at all sampling times, followed by muscle. There are no measurable residues in adipose fat.

Zilpaterol is now currently at Step 3 in the Codex processes and will be discussed at the upcoming JECFA meeting (Geneva, nov 2017) and CCRVDF meeting (2018)

<table>
<thead>
<tr>
<th>Species</th>
<th>Kidney (μg/kg)</th>
<th>Liver (μg/kg)</th>
<th>Muscle (μg/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cattle</td>
<td>3.3</td>
<td>3.5</td>
<td>0.5</td>
</tr>
</tbody>
</table>

*There were insufficient zilpaterol residue data to adequately consider exposure to residues in lungs and other edible offal of cattle apart from liver and kidney.*
LIKELIHOOD OF POSITIVE ANTI-DOPING TESTS?

Hypothesis: consumption of an edible tissue at the MRL value.

Comment: the non respect of the withdrawal period, the non respect of the zootechnical dosage must be considered as illegal practices and therefore as marginal attitudes

Scenario muscle: 0.5 ng.g\(^{-1}\) → 300 g is equivalent to 150 ng. Conservative scenario: consumer’s urine collected 12 h after the meal, 100% bio-accessibility, 100% bio-availability, 1 L urine, no metabolization… concentration should not exceed 0.1-0.2 ng.mL\(^{-1}\) in consumer urine.

Scenario offal: 3.5 ng.g\(^{-1}\) → 300 g is equivalent to 1000 ng. Conservative scenario: consumer’s urine collected 12 h after the meal, 100% bio-accessibility, 100% bio-availability, 1 L urine, no metabolization… concentration can reach 1 ng.mL\(^{-1}\) in consumer urine.
RACTOPAMINE
The commercial ractopamine preparation is a racemic (RR-, RS-, SR-, and SS-) used as a growth promoter in livestock.

RR-ractopamine is the most potent enantiomer

**Commercial formulation:** Paylean® and Optaflexx®

**Distributed by:** Elanco (≠ Engain 20 & Actogain 100 by Zoetis Canada Inc.)

**Indication:** For increased rate of weight gain, improved feed efficiency, increased carcass leanness in cattle fed in confinement for slaughter

**Usage:** Feed continuously to animal during the last 28-42 days (Optaflexx®, in steers or market heifers), 20-40 days (Paylean®, in swine) and 7-14 days (Paylean®, in turkey) on feed. **No withdrawal period prior to slaughter.**

**Dosage:** swine→5-20 mg/kg feed. Cattle→10-30 mg/kg feed (70-400 mg per head.d⁻¹). Turkey→5-9 mg/kg feed

**Precautions:** not for use in breeding animal (swine, heifers or bulls).
Ractopamine is approved in 24 countries: Brazil, Canada, Columbia, Costa Rica, the Dominican Republic, Ecuador, Guatemala, Honduras, Mexico, Nicaragua, Panama, Peru, South Africa, South Korea and United States + Argentina, Belarus, Chile, New Zealand, Taiwan and Uruguay.
Ractopamine metabolizes mainly by conjugation. Metabolic profiles in tissues (zero-withdrawal) of pig and bovine indicate a different quantitative distribution of ractopamine and ractopamine conjugates in the two species. The ratio-free vs. conjugated being lower in cattle (0.14 in L and K) when compared to pig (0.51 and 0.31 in L and K).
At its 35th Session in Rome (2012), the Codex Alimentarius Commission adopted an Acceptable Daily Intake (ADI) and Maximum Residue Level (MRL) for pig and cattle tissues (muscle, fat, liver and kidney)… on a close 69 to 67 vote. Opposition was concentrated in the EU, but also included China, India, Turkey, Iran, Egypt and Russia
CLENBUTEROL
On June 15, 1978, FDA granted permission to Boehringer-Ingelheim Ltd to test its new stimulant drug (Ventipulmin®) for treating respiratory disease in horses.

In 1988, public health and meat inspection officials suspected the use of clenbuterol in livestock in the USA&Canada. In Texas, it was used in livestock animal shows while in Quebec, the drug was found in veal calves. In Europe +++ NC samples from 1990 to 1995.

**Ventipulmin®** → treatment of acute and chronic respiratory illness caused by bronchospasm and/or mucus accumulation. It can be used both orally and intravenously.

**Planipart®** → induces relaxation of the uterine musculature and thus dilation of the birth canal. By single intravenous or intramuscular injection → 2 mL (60 µg)/100 kg bw.

**Black market preparations** → mainly oral route, drinking water of animal
HUMAN INCIDENTS ASSOCIATED TO TAINTED CLENBUTEROL MEATS
WADA POSITIVE TESTS ATTRIBUTED TO TAINTED CLENBUTEROL MEATS

Portugal, 1998-2002, n=50, lamb and bovine meat

Spain, 1990 & 1994, n=135 and n=140, beef liver

China, Guangdong, 2009, n=70, pig organs

“lean meat powder” or “shouroujing”

China, Shanghai, 2006, n=330, pig

Spain

France, 1990, n=22, veal liver

Mexico

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**EU and USA**
CLB has been banned in meat in the U.S. since 1991 and in the EU since 1996 because of health concerns including increased heart rate, muscular tremors, headache, nausea, fever and chills.

**In China**
The government banned the production, the use and the sale of CLB in 2011. The ban was announced shortly after a major contamination event involving CLB in pork and that sickened hundreds of people.

**In Mexico**
CLB has been banned in meat products for a number of years, the drug was found in the urine of numerous soccer players from different countries who were participating in the under-17 world soccer championship in 2011. Government inspectors in Mexico shut down livestock markets where a vast majority (>90%) of the thousands meat samples were tested positive for CLB.
<table>
<thead>
<tr>
<th>Study No.</th>
<th>Calf</th>
<th>WT (days)</th>
<th>No.</th>
<th>No. of cattle</th>
<th>Muscles</th>
<th>Liver</th>
<th>Kidney</th>
<th>Fat</th>
<th>Injection Site</th>
<th>Reference Table 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td>3</td>
<td>0.86 ± 0.39</td>
<td>ND</td>
<td>9.20 ± 3.33</td>
<td>9.09 ± 3.74</td>
<td>0.96 ± 0.58</td>
<td>0.98 ± 0.33</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>7</td>
<td>2</td>
<td>3</td>
<td>ND</td>
<td>1.39 ± 0.19</td>
<td>0.41 ± 0.02</td>
<td>0.27 ± 0.07</td>
<td>ND</td>
<td>0.13 ± 0.16</td>
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<tr>
<td></td>
<td>3</td>
<td>10</td>
<td>3</td>
<td>3</td>
<td>0.85 ± 0.10</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>0.08 ± 0.10</td>
<td>ND</td>
</tr>
<tr>
<td>2</td>
<td>3</td>
<td>0.25</td>
<td>1</td>
<td>3</td>
<td>2.17 ± 0.27</td>
<td>36.6 ± 9.5</td>
<td>38.7 ± 8.4</td>
<td>0.82 ± 0.42</td>
<td>2.49 ± 0.70</td>
<td>Cameron et al. 1987</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>6</td>
<td>2</td>
<td>3</td>
<td>0.09 ± 0.10</td>
<td>7.37 ± 2.2</td>
<td>3.16 ± 0.5</td>
<td>2.15 ± 0.6</td>
<td>0.32 ± 0.20</td>
<td>ND</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>10</td>
<td>3</td>
<td>3</td>
<td>4.32 ± 0.5</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>0.28 ± 0.20</td>
<td>ND</td>
</tr>
<tr>
<td>3</td>
<td>4</td>
<td>0.25</td>
<td>1</td>
<td>4</td>
<td>0.79 ± 0.2</td>
<td>20.7 ± 4.8</td>
<td>16.1 ± 2.3</td>
<td>0.55 ± 0.1</td>
<td>1.66 ± 0.3</td>
<td>Hawkins et al. 1993b</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>5</td>
<td>2</td>
<td>4</td>
<td>0.16 ± 0.03</td>
<td>3.9 ± 0.7</td>
<td>2.2 ± 0.5</td>
<td>0.12 ± 0.2</td>
<td>0.39 ± 0.1</td>
<td>ND</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>28</td>
<td>3</td>
<td>4</td>
<td>ND</td>
<td>0.89 ± 0.1</td>
<td>0.46 ± 0.2</td>
<td>ND</td>
<td>0.18 ± 0.03</td>
<td>ND</td>
</tr>
</tbody>
</table>

Total residues (mean +/- sd ng.g⁻¹) of radioactivity after administering ¹⁴C-clenbuterol to calves.
In reaching its decision on MRLs for CLB, the CCRVDF took the following factors into account:

- The ADI of 0-0.004 µg.kg\(^{-1}\) bw.d\(^{-1}\), which is equivalent to a max ADI of 0.24 µg for a 60-kg person.
- Muscle and liver are the target tissues.
- The parent drug is the marker residue and is the only residue of public health concern. It accounts for 100% of the total residues in muscle, fat and milk (cows), 60% of the total residues in bovine liver and kidney.
- The Committee recommended that clenbuterol should not be used as a growth-enhancing agent.

<table>
<thead>
<tr>
<th>Animal</th>
<th>Tissue</th>
<th>MRL (µg/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cattle</td>
<td>Fat</td>
<td>0.2</td>
</tr>
<tr>
<td>Cattle</td>
<td>Kidney</td>
<td>0.6</td>
</tr>
<tr>
<td>Cattle</td>
<td>Liver</td>
<td>0.6</td>
</tr>
<tr>
<td>Cattle</td>
<td>Milk</td>
<td>0.05</td>
</tr>
<tr>
<td>Cattle</td>
<td>Muscle</td>
<td>0.2</td>
</tr>
<tr>
<td>Horse</td>
<td>Fat</td>
<td>0.2</td>
</tr>
<tr>
<td>Horse</td>
<td>Kidney</td>
<td>0.6</td>
</tr>
<tr>
<td>Horse</td>
<td>Liver</td>
<td>0.6</td>
</tr>
<tr>
<td>Horse</td>
<td>Muscle</td>
<td>0.2</td>
</tr>
</tbody>
</table>
CONCLUSION
GH (rbST, SOMATOTROPINE)

Discovery by Russian scientists Asimov et al., 1937
Recombinant DNA technology
European Commission Decision (1999/879/CE)
Monsanto sells its rbST business


Attempts to purify bGH from pituitary cows
Authorization in 1988 in South Africa
Commercialization of Posilac in 1994
Pressure from consumers and producers groups

SARMS
Selective Androgen Receptor Modulators

NOVEL FOODS

Lactating performances
Feed conversion
Lean meat
Growth rate up

Ecdysone

CODEX

JECFA evaluation
Interdication of use by Health Canada
European Commission Decision (1999/879/CE)
Pressuring from consumers and producers groups
JECFA evaluation

Attemps to purify bGH from pituitary cows
Authorization in 1988 in South Africa
Commercialization of Posilac in 1994
Pressure from consumers and producers groups

CODEX

Sarms and method of use thereof
US 20140221479 A1
RÉSUMÉ
This invention is directed to a feed composition and method of affecting the carcass composition by increasing the lean mass, reducing the fat mass, and/or reducing the percent fat mass comprising SARM compounds.

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Feed conversion

Lactating performances
Growth rate up

NOVEL FOODS

Ecdysone

Growth rate up
Lactating performances
Feed conversion
Lean meat
CONCLUSIONS

WHEREAS IMPLANTS DO NOT CONSTITUE A REAL ISSUE (*EASY ELIMINATION*), INJECTION SITES REMAIN A SENSIBLE ACCUTE SOURCE OF EXPOSURE FOR CONSUMERS

URGENT NEED FOR NEW STRATEGIES ABLE TO DETERMINE RESIDUE’S ORIGIN, i.e. FOOD CONSUMPTION vs DOPING (*\(^{13}\text{C}/^{12}\text{C}\), ENANTIOMERS, EXCIPIENT/IMPURITIES, SPECIFIC ANIMAL METABOLITES INCLUDING BOUND RESIDUES, HUMAN BIOLOGICAL MATRICES REVEALING CHRONIC vs ACCUTE EXPOSURE…)

CLEAR RISK FOR ATHLETES TO BE TESTED POSITIVE WHEN CONSUMING TAINTED MEAT OR EVEN RESIDUES AT THE MRL CONCENTRATION.

CONTRASTED SITUATIONS = \( f(\text{COUNTRIES}) \)
谢谢
Thank you!
A GENERAL PERSPECTIVE ON THE USE OF WADA PROHIBITED SUBSTANCES FOR ANIMAL HUSBANDRY

Bruno LE BIZEC, Prof