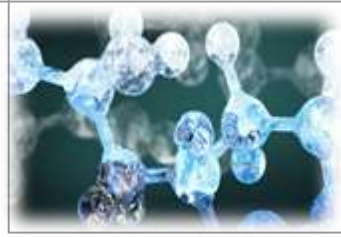
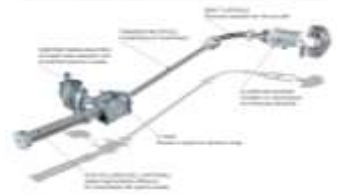
Session 1: Residues in food – Overall situation and regulatory environment

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

Beijing, 18th-19th October 2017





Bruno LE BIZEC, Prof

Laboratoire d'Étude des Résidus et Contaminants dans les Aliments
ONIRIS - France - www.laberca.org

PROHIBITED SUBSTANCES: CONTRASTED SITUATION

PROHIBITED SUBSTANCES: CONTRASTED SITUATION

THE WORLD ANTI-DOPING CODE

INTERNATIONAL STANDARD

PROHIBITED LIST

JANUARY 2017

CODEX ALIMENTARIUS
International Food Standards

World Health Organization

FAO
FIAT PANIS

WTO OMC

Food and Agriculture Organization of the United Nations

THE SCIENTIFIC BASIS OF CODEX

World Health Organization

International Risk Assessment Bodies

Request

Scientific Advice

JECFA	JMPR	JEMNU	JEMRA	Ad Hoc
Joint Expert Committee on Food Additives	Joint Meeting on Pesticide Residues	Joint Expert Meeting on Nutrition	Joint Expert Meeting on Microbiological Risk Assessment	Expert Meetings

JECFA

CODEX Committees

CCRVDF

CODEX ALIMENTARIUS COMMISSION

CAC

International Food Safety Standards

Consumer Protection and Food Trade

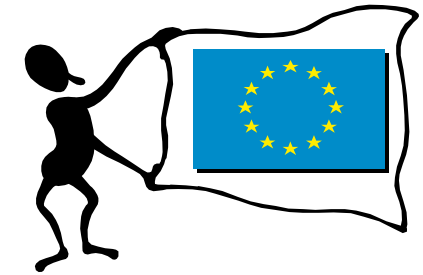
www.fao.org/food/food-safety-quality/scientific-advice/en/

www.who.int/foodsafety/en/

The international rules :

WORLD TRADE ORGANIZATION

- 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



SECTION 1

GENERAL PRINCIPLES OF FOOD LAW

Article 6

Risk analysis

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

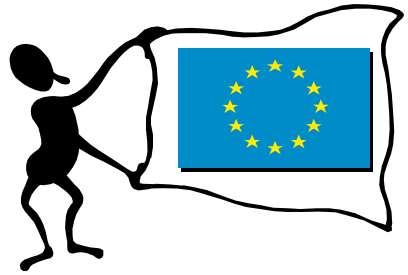
Regulation (EC) No 2009/470/EC

- **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

20.1.2010 EN Official Journal of the European Union L 15/47

Pharmacologically active Substance	Marker residue	Animal Species	MRL	Target Tissues	Other Provisions (*according to Article 14(7) of Regulation (EC) No 470/2009*)	Therapeutic Classification
Methylprednisolone	Methylprednisolone	Bovine	10 µg/kg 10 µg/kg 10 µg/kg 10 µg/kg	Muscle Fat Liver Kidney	Not for use in animals from which milk is produced for human consumption.	Corticoides/ Glucocorticoides



- Forbidden substances (Group A)
  - Substances having anabolic effect
  - Unauthorized substances

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

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

470/2009 +
37/2010: Table 1 → MRL

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

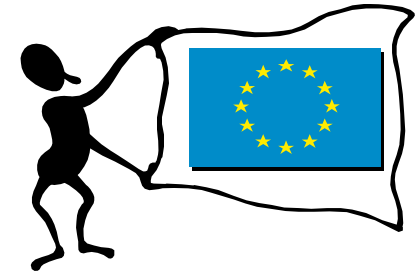
Reg. Contaminants
Reg. Pesticides

LEGISLATION

Dir 96/23/EC

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 — **T, E2, PG, MLGA, TbAc… BOLD**

(4) Resorcylic acid lactones including zeranol — **ZER**

(5) Beta-agonists — **RACTO, ZILPA… CLB**

(6) Compounds included in Annex IV to Council Regulation (EEC) No 2377/90 of 26 June 1990

Commission Regulation (EU) No 37/2010 of 22/12/2009 on pharmacologically active substances and their classification regarding maximum residue limits in foodstuffs of animal origin

Dir 96/22/EC

Steroids, RALs and β-agonists can be used in TCs but imports only acceptable if 'split' system

PROHIBITED LIST

JANUARY 2017

S1 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.

PROHIBITED LIST

JANUARY 2017

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

PROHIBITED LIST

JANUARY 2017

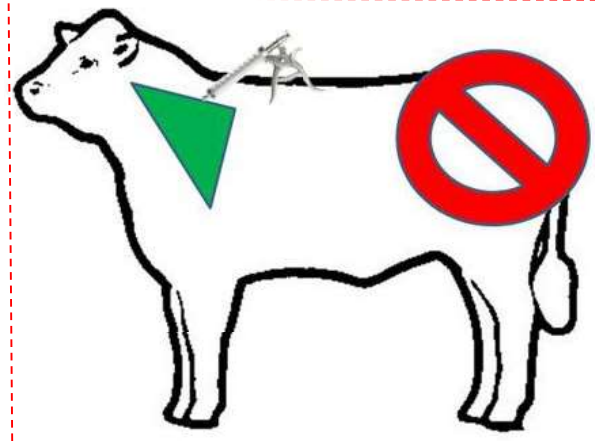
S6 STIMULANTS

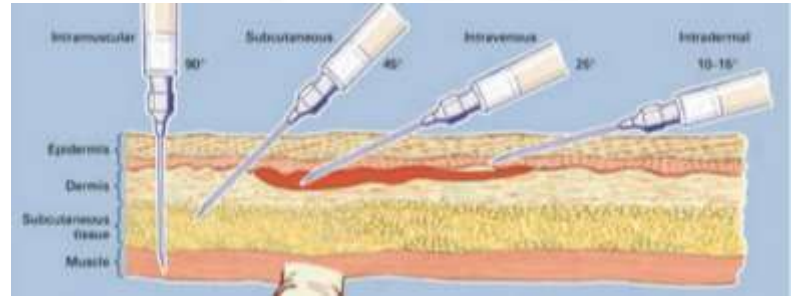
S7 NARCOTICS

S8 CANNABINOIDS

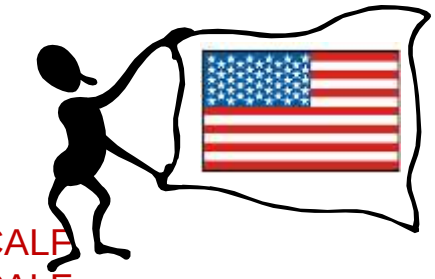
S9 GLUCOCORTICOIDS

All of these implants are not approved for use in dairy cows, nor hogs or poultry



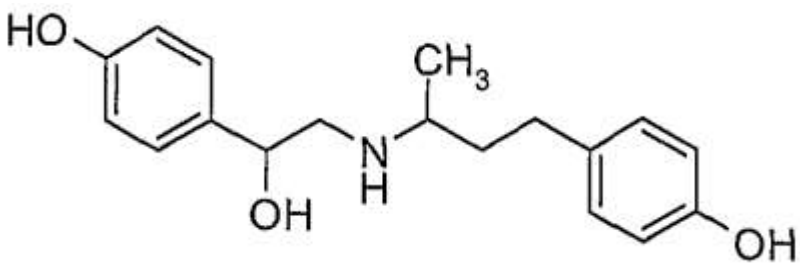


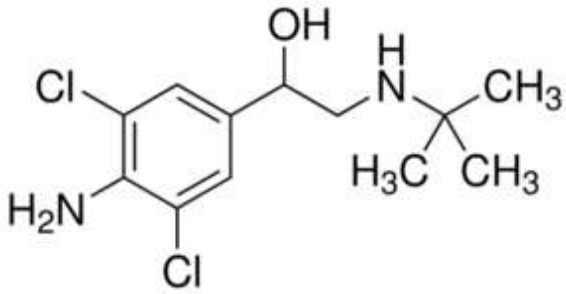
ANABOLIC STEROIDS

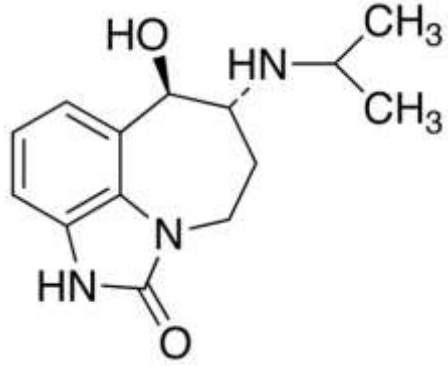


	Marque	Composition		
UPJOHN	Calf-oid	10 mg d'œstradiol + 100 mg de progestérone	1990	CALF
-	Component C	10 mg d'œstradiol + 100 mg de progestérone		CALF
-	Component H	20 mg d'œstradiol + 200 mg de testostérone		HEIFER
-	Component S	20 mg d'œstradiol + 200 mg de progestérone		STEER
-	Component TH	200 mg d'acétate de trenbolone		HEIFER
ELANCO	Compudose	25,7 mg d'œstradiol	1982	STEER & HEIFER
-	Encore	43,9 mg d'œstradiol		STEER
ROUSSEL-UCLAF	Finaplix-H	200 mg de testostérone	1987	HEIFER
ROUSSEL-UCLAF	Finaplix-S	140 mg de testostérone	1987	STEER
-	Forplix	36 mg de zéranol + 140 mg d'acétate de trenbolone		STEER
UPJOHN	Heifer-oid	20 mg d'œstradiol + 200 mg de testostérone		HEIFER
HEIFER	Implix	20 mg d'œstradiol + 200 mg de testostérone		HEIFER
UPJOHN	Implus-C	10 mg d'œstradiol + 100 mg de progestérone		CALF
UPJOHN	Implus-H	20 mg d'œstradiol + 200 mg de testostérone	1984	HEIFER
UPJOHN	Implus-S	20 mg d'œstradiol + 200 mg de progestérone	1982	STEER
UPJOHN	MGA	acétate de mélengestrol	1977	HEIFER
MALLINCKRODT	Ralgro	36 mg de zéranol	1969	CALF, HEIFER, STEER
ROUSSEL-UCLAF	Revalor	20 mg d'œstradiol + 140 mg d'acétate de trenbolone		STEER
ROUSSEL-UCLAF	Revalor-G	8 mg d'œstradiol + 40 mg d'acétate de trenbolone	1991	STEER & HEIFER
UPJOHN	Steer-oid	20 mg d'œstradiol + 200 mg de progestérone		STEER
SYNTEX	Synovex C	10 mg d'œstradiol + 100 mg de progestérone	1984	CALF
SYNTEX	Synovex H	20 mg d'œstradiol + 200 mg de testostérone	1958	HEIFER
SYNTEX	Synovex S	20 mg d'œstradiol + 200 mg de progestérone	1956	STEER
SYNTEX	Torelor	40 mg d'œstradiol + 200 mg d'acétate de trenbolone		STEER
SYNTEX	Torevex-S	20 mg d'œstradiol + 200 de progestérone		STEER

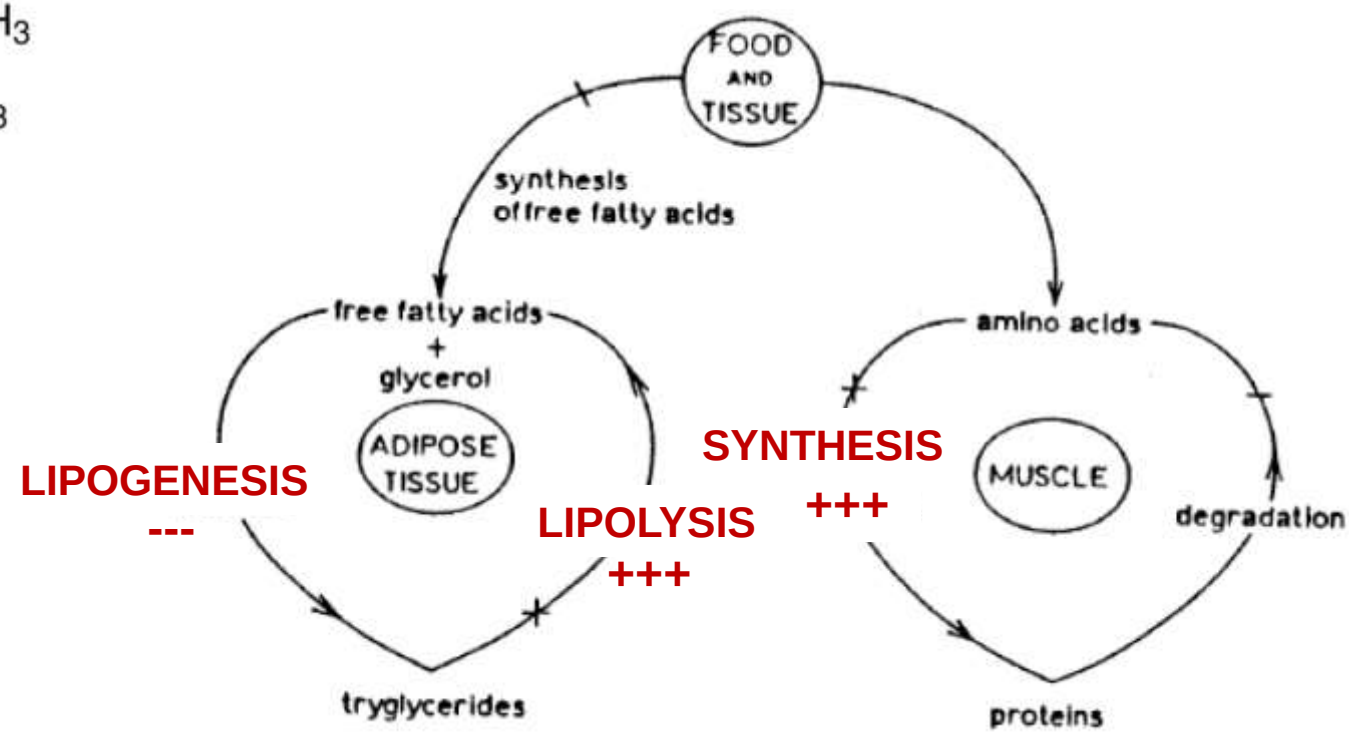
β-AGONISTS



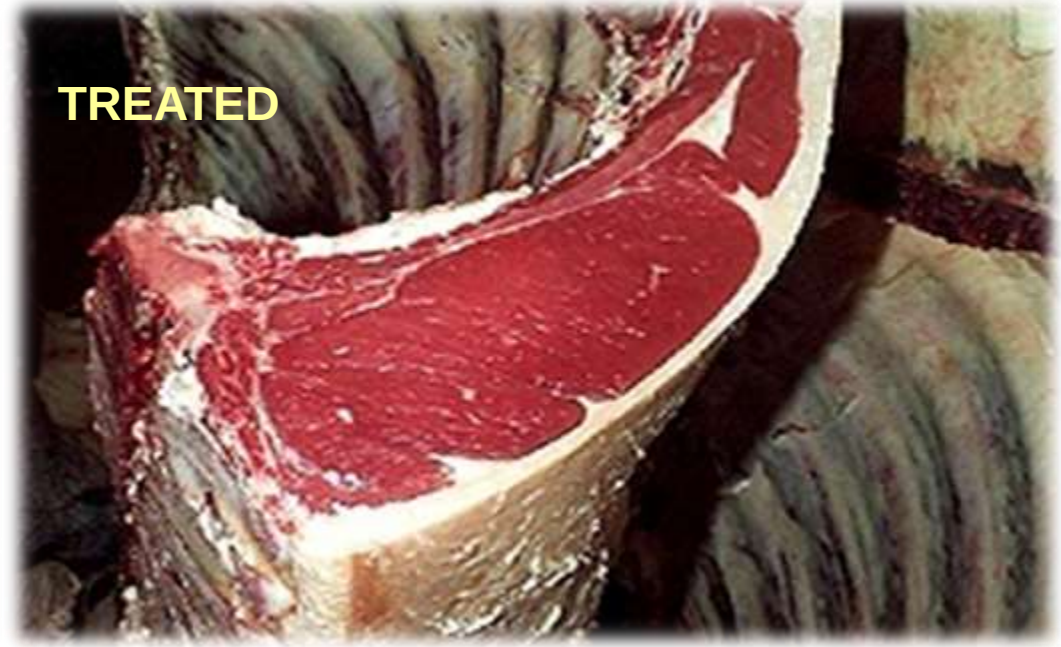




- **Action**
  - –Repartitioning agent
  - –For increased carcass leanness
  - –For improved rate of weight gain and feed efficiency (up to 25% each)



β-AGONISTS



ZILPATEROL — 1993 — cattle — *SOUTH AFRICA, MEXICO*

RACTOPAMINE* — 1999 — finishing swine — **PAYLEAN®**

RACTOPAMINE* — 2003 — cattle & turkey — **OPTAFLEXX®** **TOMAX®**

ZILPATEROL* — 2006 — cattle — **ZILMAX®**

**Approved by FDA*

WORLD ANTI-DOPING AGENCY
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CHINADA
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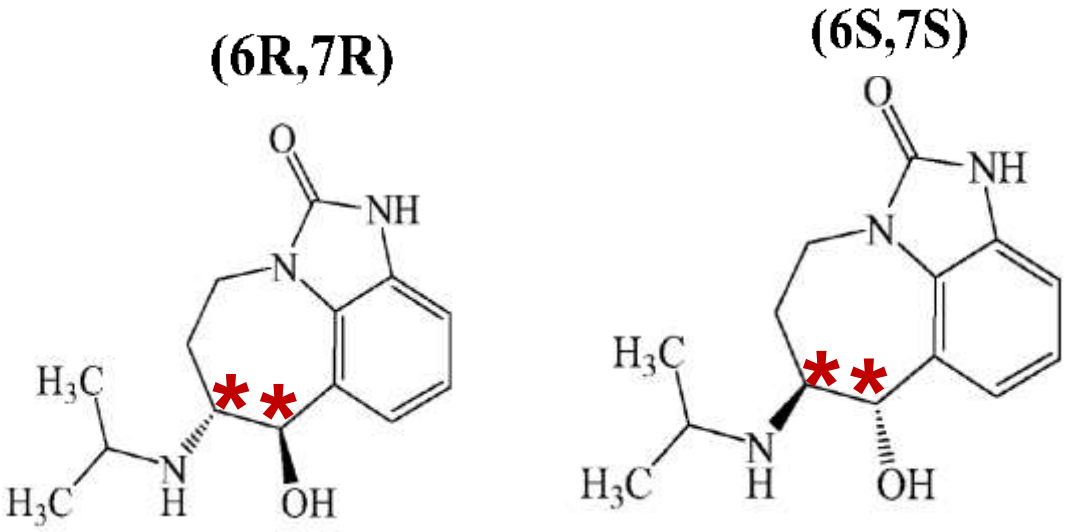
ZILPATEROL



RU 42173 corresponds to racemic trans zilpaterol hydrochloride, a mixture of the (6R,7R) and (6S,7S) enantiomers

Zilmax® (zilpaterol hydrochloride 4.8%)

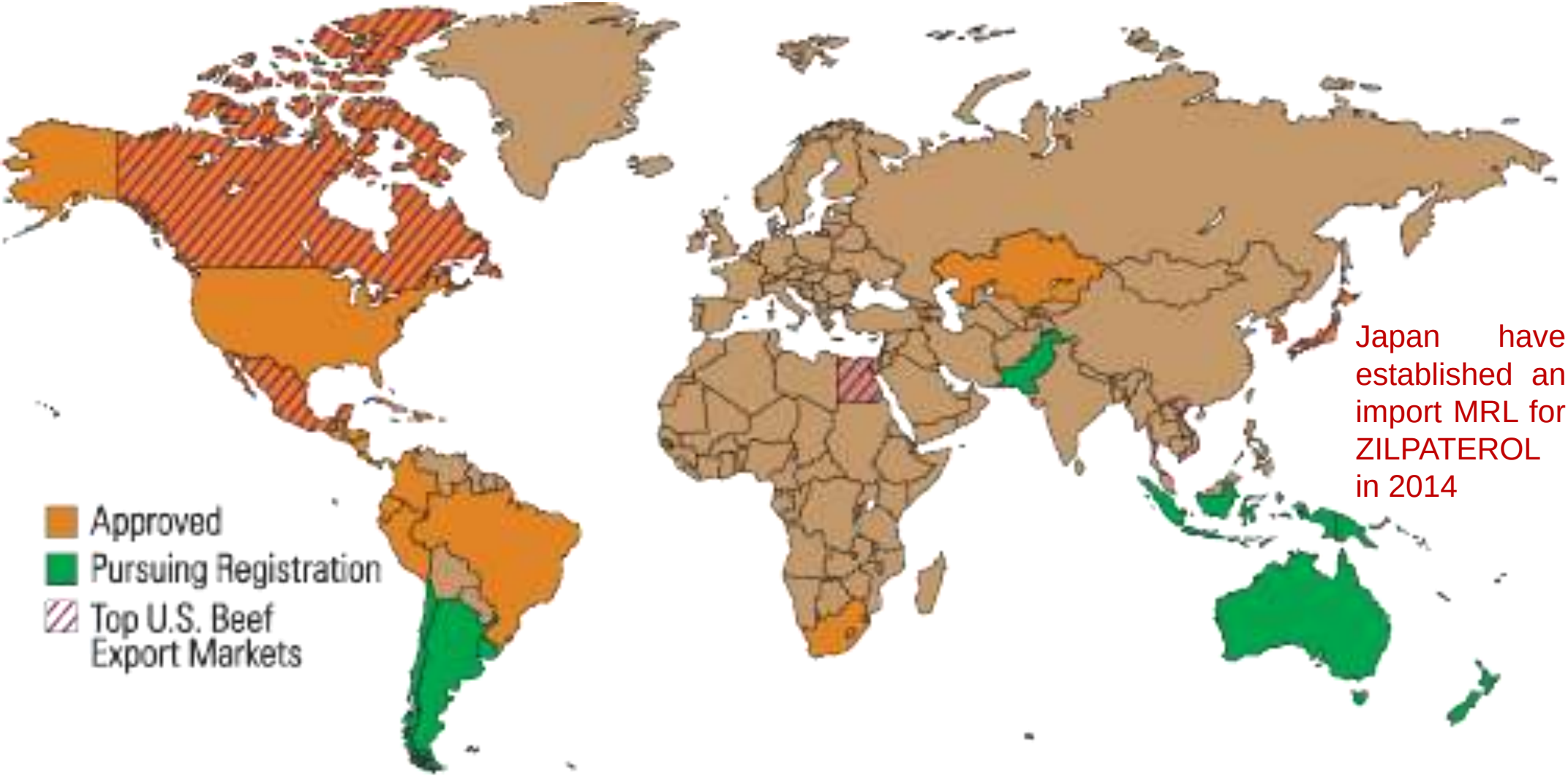
Commercial formulation
Zilmax®: 4.8% w/w zilpaterol hydrochloride, 8% polyoxyl castor oil, 4.3% polyvinylpyrrolidone and 82.9% ground corn cob.

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.

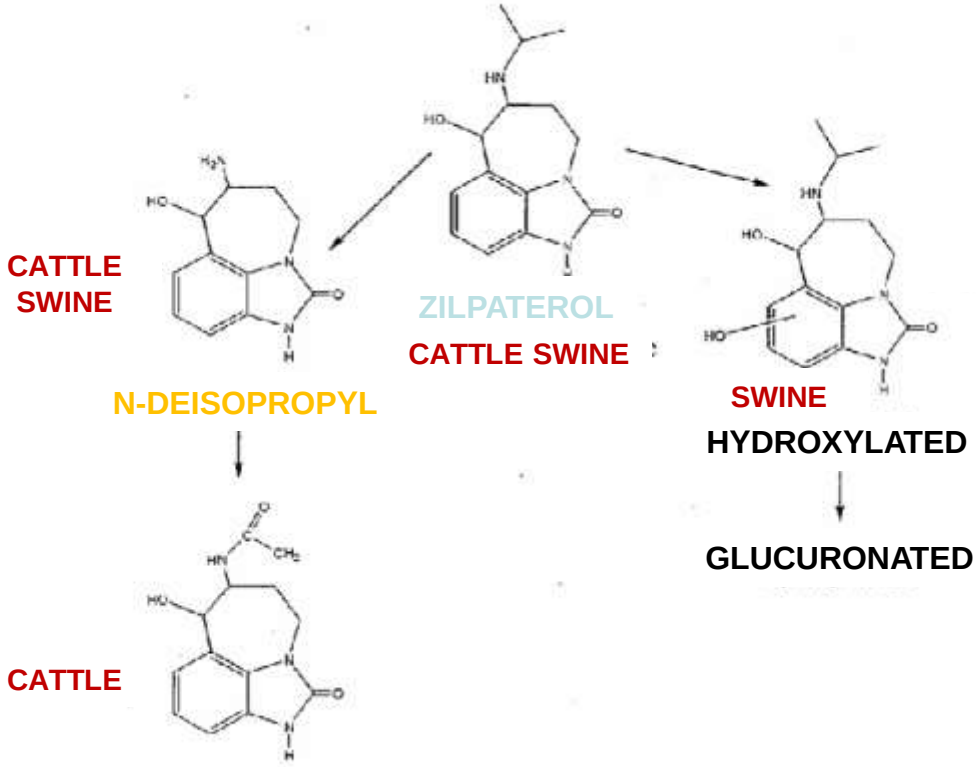


Figure 10.3. Depletion of zilpaterol residues in cattle liver.

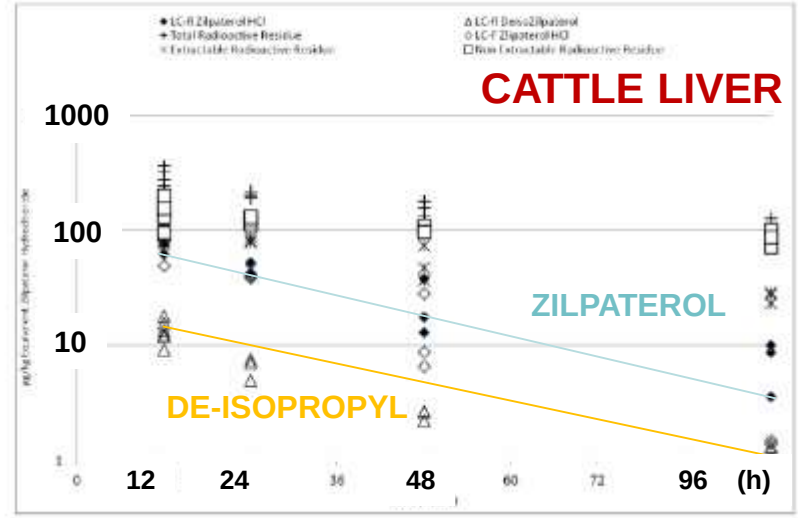
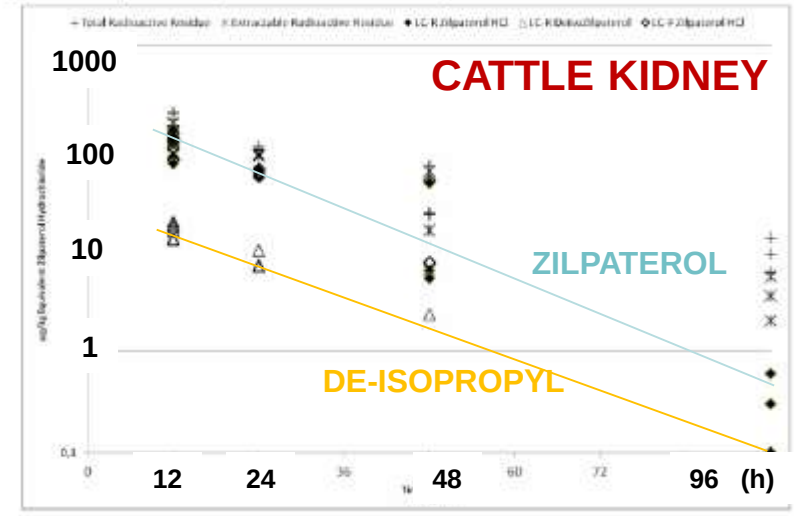


Table 10.22. Measurement of [^{14}C]zilpaterol and [^{14}C]deisopropyl-zilpaterol residues in cattle tissues, mean ±SD expressed as zilpaterol HCl equivalents in µg/kg (Tulliez, 1999)

Withdrawal time	Residues of [^{14}C]zilpaterol and [^{14}C]deisopropyl-zilpaterol (µg/kg)					
	Liver		Kidney		Muscle	
	zilpaterol	deisopropyl-zilpaterol	zilpaterol	deisopropyl-zilpaterol	zilpaterol	deisopropyl-zilpaterol
12 (1)	104.7 ±33.3	11.2 ±1.7	127.1 ±22.3	14.9 ±1.9	13.3 ±1.8	1.6 ±0.1
12 (2)	84.4 ±19.8	15.7±2.3	92.6 ±28.5	16.3 ±3.4	12.7 ±3.8	3.7 ±0.4
24 (1)	48.4 ±5.3	6.5 ±1.4	57.9 ±5.0	7.8 ±1.7	4.8 ±2.0	ND (3)
48 (1)	22.9 ±13.3	2.5 ±0.3	18.9 ±22.8	1.4 ±0.8	ND	ND
96 (1)	7.5 ±3.4	1.1 (0.2) (4)	0.3 (0.3) (4)	0.14	ND	ND

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.

Figure 10.4. Depletion of zilpaterol residues in cattle kidney



Zilpaterol hydrochloride (β_2-adrenoceptor agonist)

Acceptable daily intake — The Committee reaffirmed the ADI of 0–0.04 µg/kg body weight established at the seventy-eighth meeting (WHO TRS No. 988, 2014).

ADI 0-0.04 µg.kg^{-1} bw

ZILPATEROL: MARKER

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.

Recommended maximum residue limits (MRLs)[a]

Species	Kidney (µg/kg)	Liver (µg/kg)	Muscle (µg/kg)
Cattle	3.3	3.5	0.5

[a] 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.

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

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)

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

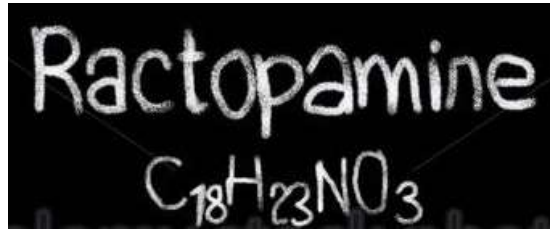
Scenario muscle: 0.5 $ng.g^{-1}$ → 300 g is equivalent to 150 ng. Conservative scenario: consumer's urine collected 12 h after the meal, 100% bio-accessibility, 100% bio-availability, 1 L urine, no metabolization… concentration should not exceed 0.1-0.2 $ng.mL^{-1}$ in consumer urine.

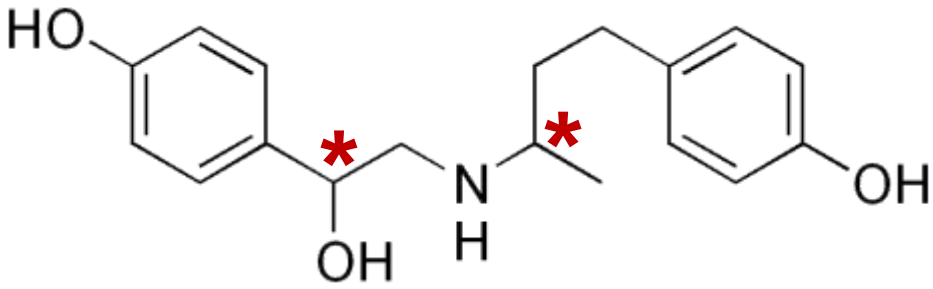
Scenario offal: 3.5 $ng.g^{-1}$ → 300 g is equivalent to 1000 ng. Conservative scenario: consumer's urine collected 12 h after the meal, 100% bio-accessibility, 100% bio-availability, 1 L urine, no metabolization… concentration can reach 1 $ng.mL^{-1}$ in consumer urine.

WORLD ANTI-DOPING AGENCY
play true

CHINADA
CHINA ANTI-DOPING AGENCY

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

Elanco Paylean® 20

Elanco Optaflexx®

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

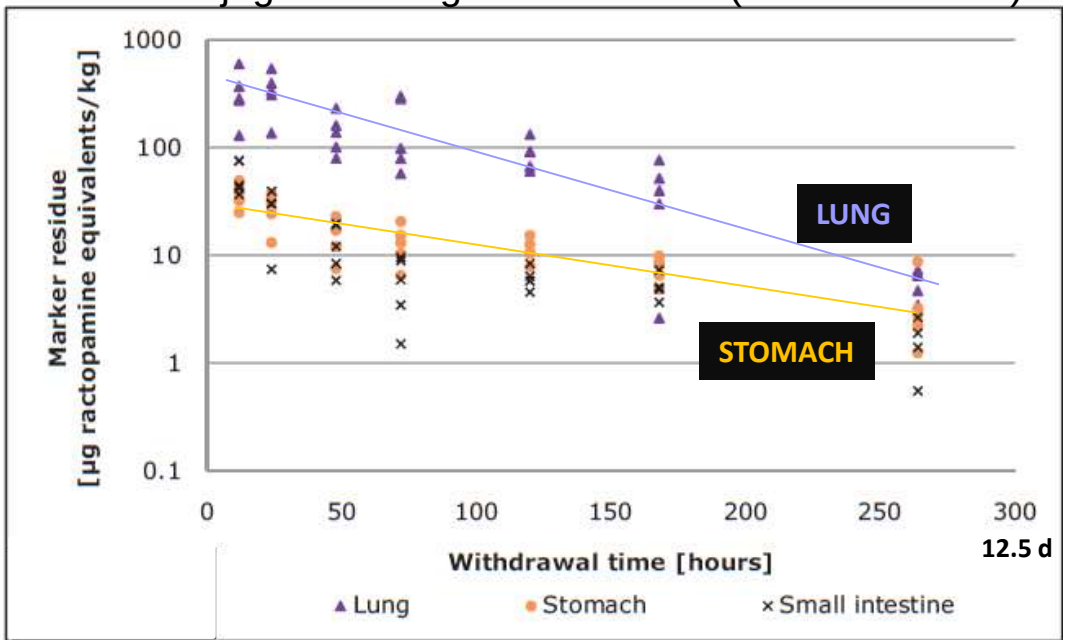
Usage: Feed continuously to animal during the last 28-42 days (Optaflexx®, in steers or market heifers), 20-40 days (Paylean®, in swine) and 7-14 days (Paylean®, in turkey) on feed. No withdrawal period prior to slaughter.

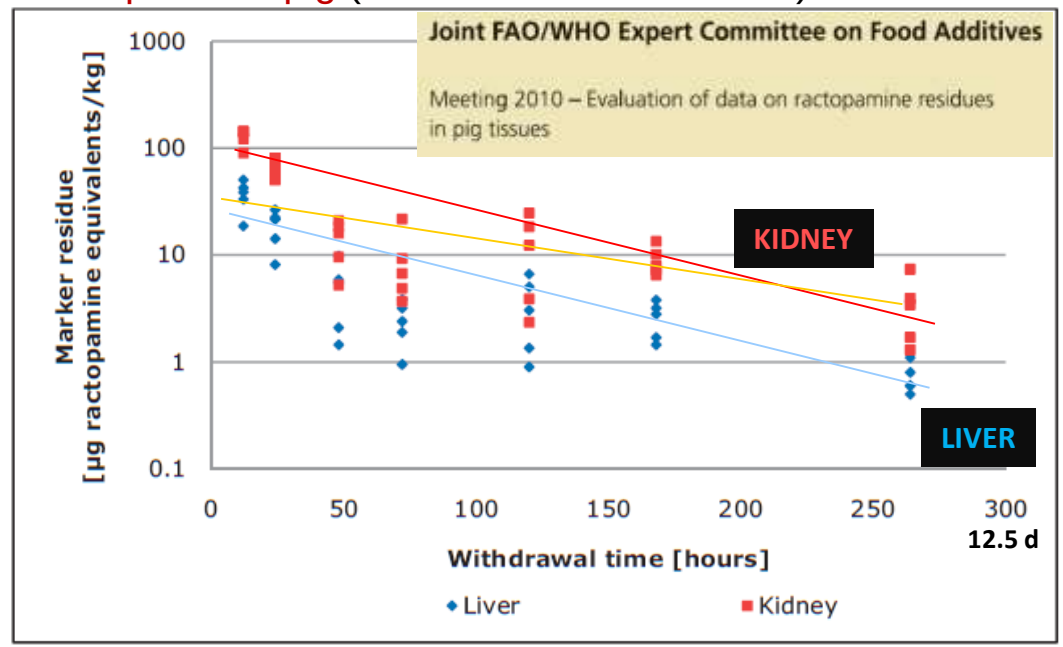
Dosage: swine→5-20 mg/kg feed. Cattle→10-30 mg/kg feed (70-400 mg per head.d^{-1}). Turkey→5-9 mg/kg feed

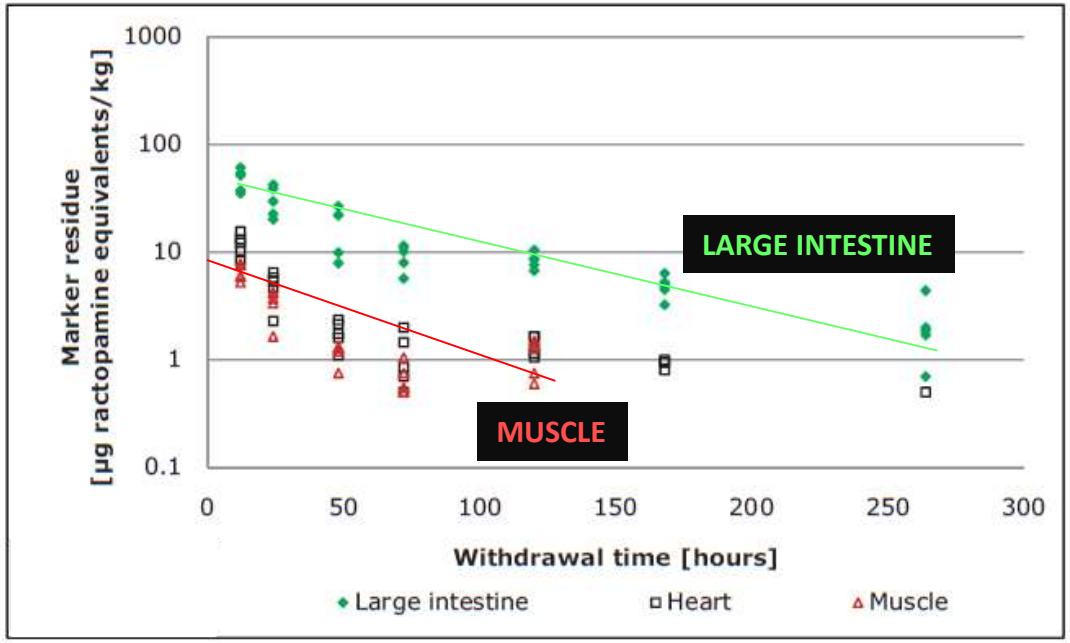
Precautions: not for use in breeding animal (swine, heifers or bulls).

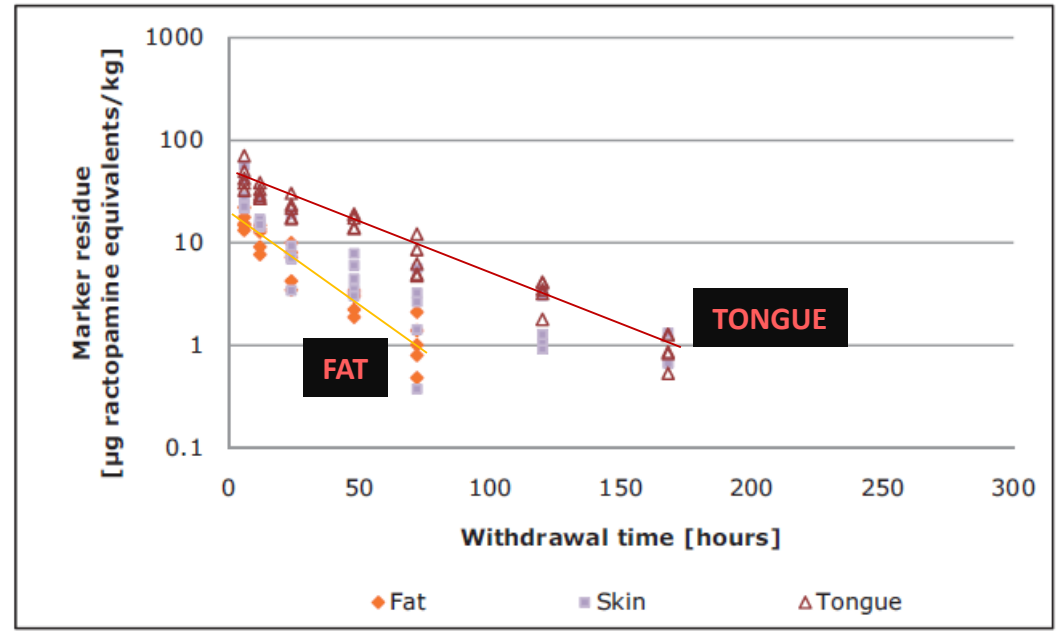
Ractopamine is approved in 24 countries: Brazil, Canada, Columbia, Costa Rica, the Dominican Republic, Ecuador, Guatemala, Honduras, Mexico, Nicaragua, Panama, Peru, South Africa, South Korea and United States + Argentina, Belarus, Chile, New Zealand, Taiwan and Uruguay.

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).









European Food Safety Authority

The EFSA Journal (2009) 1041, 1-52

SCIENTIFIC OPINION

Safety evaluation of ractopamine[1]

Scientific Opinion of the Panel on Additives and Products or Substances used in Animal Feed

(Question No EFSA-Q-2008-433)

Adopted on 2 April 2009

PANEL MEMBERS*

Georges Bories, Paul Brantom, Joaquim Brufau de Barberà, Andrew Chesson, Pier Sandro Cocconcelli, Bogdan Debski, Noël Dierick, Jürgen Gropp, Ingrid Halle, Christer Hogstrand, Joop de Knecht, Lubomir Leng, Anne-Katrine Lundebye Haldorsen, Sven Lindgren, Alberto Mantovani, Miklós Mézes, Carlo Nebbia, Walter Rambeck, Guido Rychen, Atte von Wright and Pieter Wester

SUMMARY

Ractopamine hydrochloride is pharmacologically classified as a phenethanolamine β-adrenoceptor agonist. The use of the substance as a feed additive is authorised in different countries (USA, Canada, Japan and Mexico) for growth promotion of fattening pigs and cattle. Ractopamine has not been assessed in the EU so far.

Following a request from the European Commission, the European Food Safety Authority (EFSA) was asked to provide an opinion on the JECFA evaluation for ractopamine hydrochloride, having consulted and closely co-operated with other organisations such as EMEA and the Community Reference Laboratory responsible for β-agonists (BVL in Berlin).

The metabolic fate of ractopamine hydrochloride is similar in the target species (pig and cattle), laboratory animals and humans.

The FEEDAP Panel concluded from an acute study in dogs that tachycardia and peripheral vasodilatation observed are in line with the expected pharmacological action. From another acute study in dogs, with limited statistical power, a pharmacological NOAEL of 2 μg kg^{-1} bw could be derived.

Comparing dog and monkey data it appeared that the dog could be considered as more sensitive to ractopamine (β-adrenergic substances). However, the FEEDAP Panel considered that there was not enough data to support this conclusion.

NOAEL's derived from pharmacological repeated dose studies should not be regarded as a meaningful basis for an ADI because of the observed down regulation of lung β-adrenergic

[1] For citation purposes: Scientific Opinion of the Panel on Additives and Products or Substances used in Animal Feed (FEEDAP) on a request from the European Commission on the safety evaluation of ractopamine. *The EFSA Journal* (2009) 1041, 1-52

* One member of the Panel did not participate in the discussion on the subject referred to above.

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

RACTOPAMINE (production aid)

JECFA Evaluation: 40 (1992); 62 (2004); 66 (2006)

Acceptable Daily Intake: 0-1 μg/kg body weight (66th JECFA, 2006).

Residue Definition: Ractopamine.

Species	Tissue	MRL (μg/kg)	CAC
Cattle	Muscle	10	35th (2012)
Cattle	Liver	40	35th (2012)
Cattle	Kidney	90	35th (2012)
Cattle	Fat	10	35th (2012)
Pig	Muscle	10	35th (2012)
Pig	Liver	40	35th (2012)
Pig	Kidney	90	35th (2012)
Pig	Fat	10	35th (2012)

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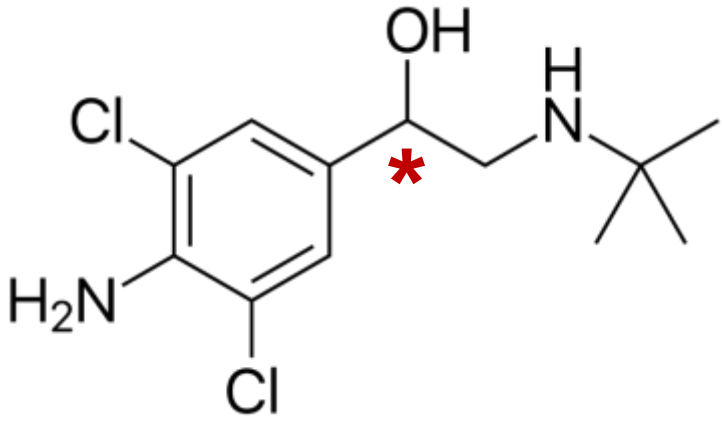
CHINA ANTI-DOPING AGENCY

CLENBUTEROL



TOCOLYTIC

BRONCHODILATOR

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

Spain

France, 1990, n=22, veal liver

China

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

Mexico

"lean meat powder" or "shouroujing"

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

China, Shanghai, 2006, n=330, pig

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

EU and USA

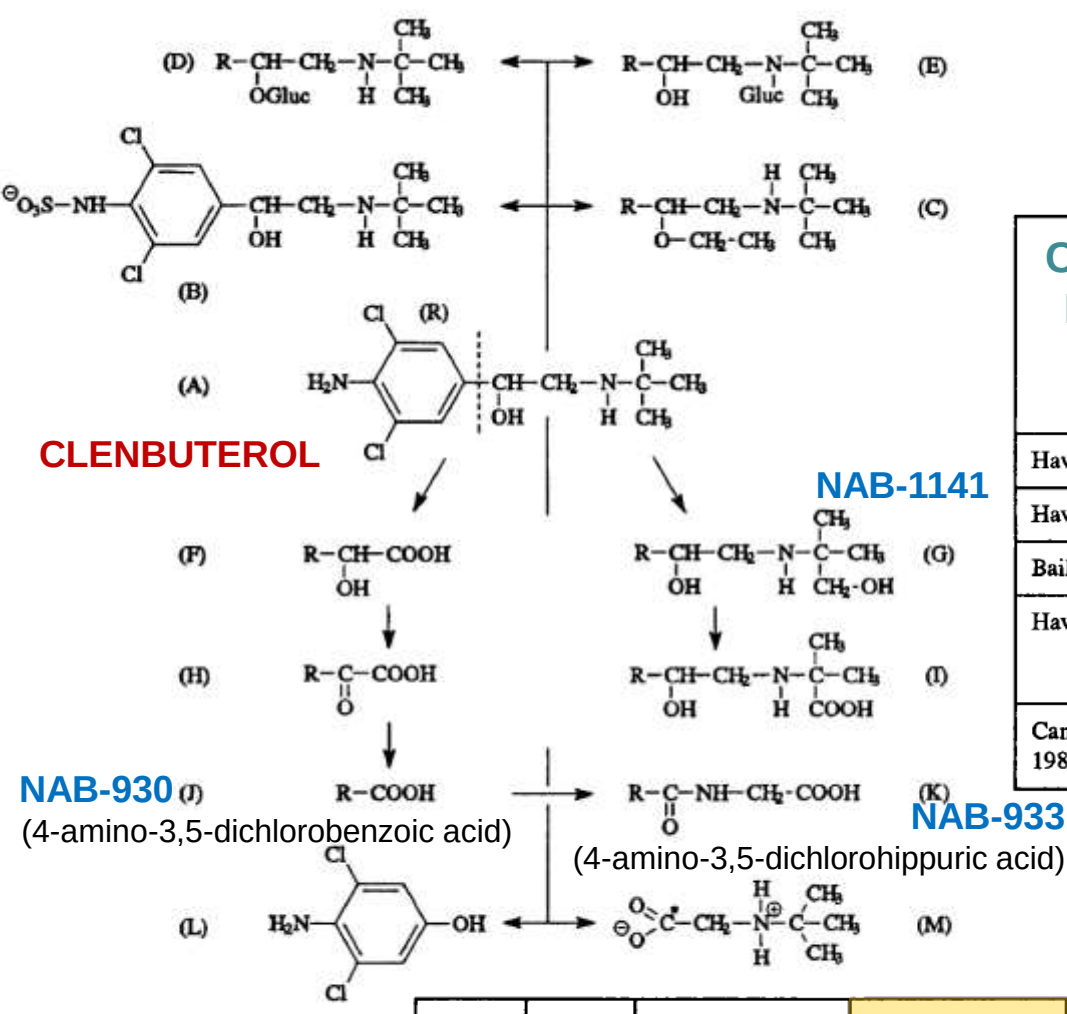
CLB has been banned in meat in the U.S. since 1991 and in the EU since 1996 because of health concerns including increased heart rate, muscular tremors, headache, nausea, fever and chills.

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.



CLENBUTEROL NAB-930 NAB-933 NAB-1141

CATTLE LIVER	WT (h)	TR extractable (%)	as a % extractable TR					
			NAB 365 (UD)	NAB 930	NAB 931	NAB 933	NA 1141	Polar/base -line
Hawkins et al, 1985b	24	50	64	ND	ND	ND	ND	26
Hawkins et al, 1985a	2	89	65	ND	ND	ND	ND	35
Baillie et al., 1980	3	89	52*	ND	ND	4	11	34
Hawkins et al, 1993b	6	81	90	0.3	1.4	1.5	2.1	4
	120	87	49	4.7	ND	4.8	ND	42
Cameron & Phillips, 1987	6	84	95	ND	ND	ND	ND	5

Total residues (mean +/- sd ng.g^{-1}) of radioactivity after administering ^{14}C-clenbuterol to calves

Study No.	No. cattle	WT (days)	Muscle	Liver	Kidney	Fat	Injection Site	Reference Table 2.
Calf 1	3	1	0.86 ± 0.39	9.20 ± 3.33	9.09 ± 3.74	0.96 ± 0.58	0.98 ± 0.33	Hawkins et al. 1985b
	3	7	ND	1.39 ± 0.19	0.41 ± 0.02	ND	0.13 ± 0.16	
	3	10	ND	0.85 ± 0.10	0.27 ± 0.07	ND	0.08 ± 0.10	
2	3	0.25	2.17 ± 0.27	36.6 ± 9.5	38.7 ± 8.4	0.82 ± 0.42	2.49 ± 0.70	Cameron et al. 1987
	3	6	0.09 ± 0.10	7.37 ± 2.2	3.16 ± 0.5	ND	0.32 ± 0.20	
	3	10	ND	4.32 ± 0.5	2.15 ± 0.6	ND	0.28 ± 0.20	
3	4	0.25	0.79 ± 0.2	20.7 ± 4.8	16.1 ± 2.3	0.55 ± 0.1	1.66 ± 0.3	Hawkins et al. 1993b
	4	5	0.16 ± 0.03	3.9 ± 0.7	2.2 ± 0.5	0.12 ± 0.2	0.39 ± 0.1	
	4	28	ND	0.89 ± 0.1	0.46 ± 0.2	ND	0.18 ± 0.03	

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.

Cattle	Fat	0.2 µg/kg
Cattle	Kidney	0.6 µg/kg
Cattle	Liver	0.6 µg/kg
Cattle	Milk	0.05 µg/l
Cattle	Muscle	0.2 µg/kg
Horse	Fat	0.2 µg/kg
Horse	Kidney	0.6 µg/kg
Horse	Liver	0.6 µg/kg
Horse	Muscle	0.2 µg/kg

CONCLUSION

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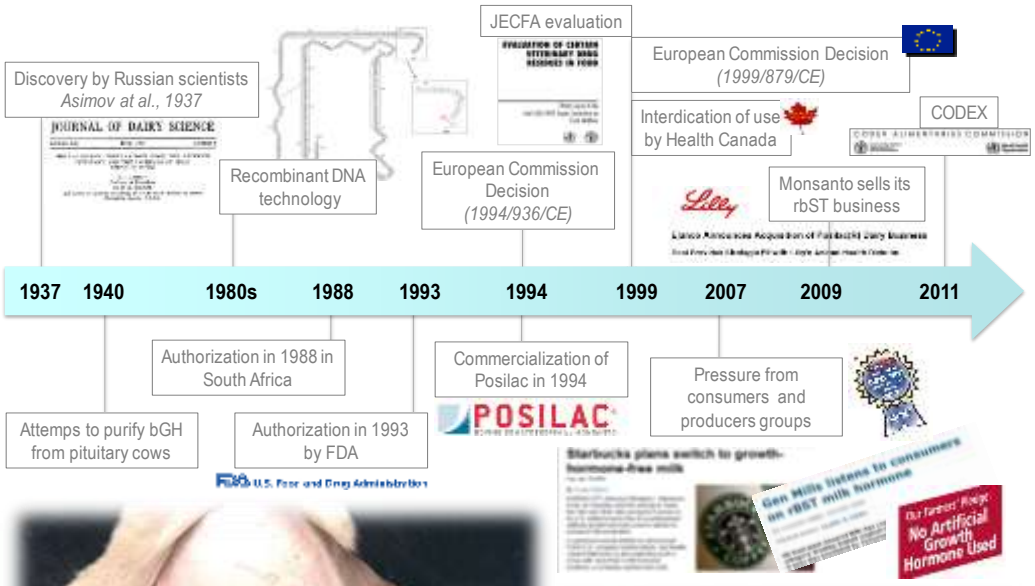
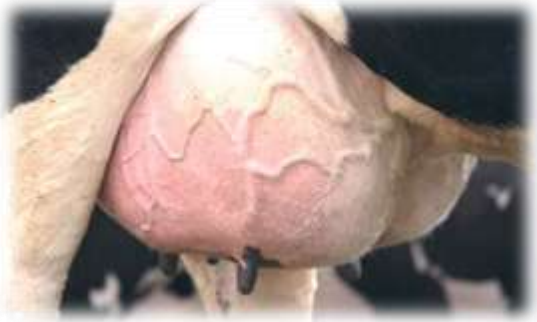
GH (rbST, SOMATOTROPINE)





Lactating performances

Feed conversion
Lean meat

Growth rate up

SARMs

Selective Androgen Receptor Modulators

Sarms and method of use thereof

US 20140221479 A1

RÉSUMÉ

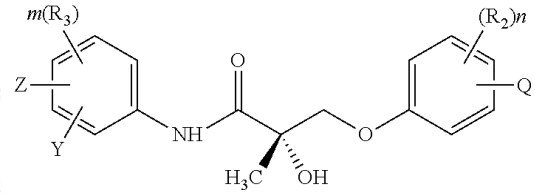
This invention is directed to a feed composition and method of affecting the carcass composition by increasing the lean mass, reducing the fat mass, and/or reducing the percent fat mass comprising SARM compounds.

Numéro de publication	US20140221479 A1
Type de publication	Demande
Numéro de demande	US 14/166,993
Date de publication	7 août 2014
Date de dépôt	30 janv. 2014
Date de priorité	7 juin 2004
Autre référence de publication	CA2793999A1, 7 autre(s) »
Inventeurs	James T. Dalton, Duane D. Miller, Jeffrey D. Kearbey
Cessionnaire d'origine	University Of Tennessee Research Foundation
Exporter la citation	BiBTeX, EndNote, RefMan

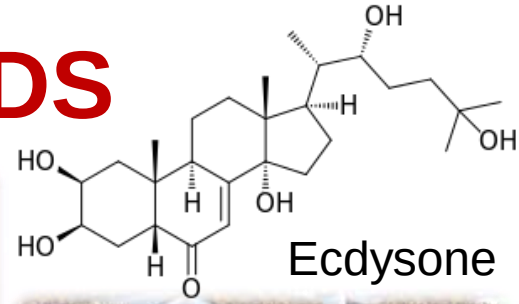
Citations de brevets (1), Citations hors brevets (1), Classifications (8), Événements juridiques (1)

Liens externes: USPTO, Cession USPTO, Espacenet

https://www.google.com/patents/US20140221479



NOVEL FOODS



Ecdysone

CONCLUSIONS

A.

CLEAR RISK FOR ATHLETES TO BE TESTED POSITIVE WHEN CONSUMING TAINTED MEAT OR EVEN RESIDUES AT THE MRL CONCENTRATION.
CONTRASTED SITUATIONS = f(COUNTRIES)

B.

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

C.

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

谢谢

Thank you!

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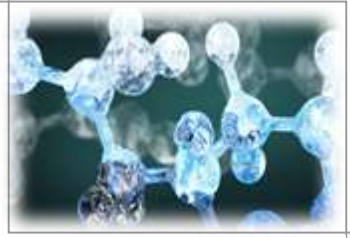
Session 1: Residues in food – Overall situation and regulatory environment

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

Beijing, 18th-19th October 2017



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