European Medicines Agency
Veterinary Medicines and Inspections

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COMMITTEE FOR MEDICINAL PRODUCTS FOR VETERINARY USE (CVMP)

Substances considered as not falling within the scope of Council Regulation (EEC) No 2377/90

Council Regulation (EEC) No 2377/90 defines "*residues of veterinary medicinal products*" as "*pharmacologically active substances, whether active principles, excipients or degradation products, and their metabolites which remain in foodstuffs obtained from animals to which the veterinary medicinal product in question has been administered"*.

Following the publication of Council Regulation 2377/90 a number of companies submitted applications for substances used in veterinary medicinal products, irrespective of the level of pharmacological action shown by such substances. The CVMP having reviewed the lists of substances to be considered as candidates for Annex II of Council Regulation 2377/90, considered that some substances were normal components of human food, biologically inert when orally taken, or not classified as chemicals. Consequently, taking account of the scope of Council Regulation 2377/90, the Committee issued in 1995 a list of substances not falling within the scope of Council Regulation 2377/90. This list included also substances for which no formal MRL application had been made and substances which were originally the subject of an intention to submit or even an actual application but subsequently classed as not within the scope of Council Regulation 2377/90.

Where MRL applications had been submitted for substances used as excipients these substances were, following their assessment, mostly included in Annex II of Council Regulation 2377/90.

The CVMP further discussed the concept of "pharmacologically active substances" in particular considering the approach to be taken for excipients. The CVMP adopted a Position Paper on the definition of substances capable of pharmacological action in the context of Council Directive 2001/82/EC with a particular reference to excipients and manufacturing materials (EMEA/CVMP/072/97-Rev.1[1]), concluding that "*substances capable of pharmacological action are substances pharmacodynamically active at the dose at which they are administered to the target animal by means of the veterinary medicinal product in which they are included"*.

Furthermore, as no legal status has been attributed to the so-called "out of scope" list established by CVMP when Council Regulation 2377/90 was amended in March 1997, the CVMP agreed in November 1997 to recommend the inclusion all the active principles in that particular list in Annex II, where appropriate.

[1] Initially adopted in April 1997 and further revised in July 2004

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Having concluded the assessment of applications for the establishment of MRLs for “old substances” the EMEA published in the year 2000 a list of those substances which remained as not being within the scope of Council Regulation 2377/90. This list of substances is, particularly with regard to excipients, in no way exhaustive and includes only substances for which requests in this respect were made to CVMP by a company or a national authority.

Since then, several amendments have been introduced following consideration of further requests and the document has been updated accordingly.

Any enquiries may be directed to the attention of Dr Kornelia Grein, Head of Sector (Safety of Veterinary Medicines) at the EMEA, 7 Westferry Circus, Canary Wharf, London E14 4HB, e-mail kornelia.grein@emea.europa.eu, telephone +44 20 7 418 8432.

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Excipients

Aqua purificata
2-(2-n-Butoxyethoxy)ethanol
Carbomer
Casein hydrolysate
Chlorobutanol (at concentrations up to 1%)
Coconut oil
Collagen hydrolysate
Corn oil
Cotton seed oil
Diethanolamine (at doses up to 0.3 mg/kg bw/day)
Ethoxyquin (at concentrations up to 0.1 mg/g)
Fibrous materials of plant origin
Gelatin
Glycerol dimethylketal (at concentrations up to 150 mg/ml)
4-(2-hydroxyethyl)-1-piperazineethanesulfonic acid (HEPES) - for use as a buffering agent in vaccines and vaccine diluents
Isopropyl myristate (at doses up to 5 mg/kg bw)
Maleic acid (for use in buffering systems at doses up to 0.39 mg/kg bw)
Meglumine (at doses up to 1.5 mg/kg bw)
Metacresol (at concentrations up to 0.2%)
2-Octyl-dodecanol (when administered topically at doses up to 20 mg/kg bw)
Olive oil
Peanut oil
Polysaccharides naturally occurring such as celluloses and hydroxycelluloses, dextrans and glucans
Polymyxin B - for use as an endotoxin neutralising agent in vaccines at doses of not more than 60 µg/dose (approximately 500 IU per dose) or not more than 6 µg/kg bw (approximately 50 IU/kg bw), whichever is the lower
Sesame oil
Silicones
Soybean (milled and hulled)
Soybean oil, including epoxidized soybean oil
Squalane (as a component of the adjuvant system)
Starches normally found in food and food grade starches
Sulfolipo-cylclodextrin
Triethanolamine (at doses up to 0.25 mg/kg bw)
Trometamol (for use in buffering systems at doses up to 0.65 mg/kg bw)
Vermiculite (including expanded vermiculite)
Zymosan A – for use as an adjuvant at doses of up to 0.12 mg/kg bw

Normal foodstuffs

Avena (oats)
Carbohydrates naturally occurring
Cereals
Chocolate flavour
Coffea arabica
Honey
Royal jelly
Petroselium crispum (parsley)
Peptides and proteins as constituents of the human diet
Pulses

Chemically unidentified substances of natural origin
Organ autolysates
Immunoglobulines
Probiotic components including bacteria and yeasts
Dried dialysate derived from blood
Lyophylised ruminal fluid

Natural substances essential for animal and human life
Oxygen