The European Agency for the Evaluation of Medicinal Products
Veterinary Medicines Evaluation Unit

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COMMITTEE FOR VETERINARY MEDICINAL PRODUCTS

BALSAMUM PERUVIANUM

SUMMARY REPORT

1. *Balsamum peruvianum* or *Peruvianum balsamum* (CAS 8007-00-9) consists of the bark exudate obtained from the large tree *Myroxylon balsamum* (L.) Harms var. *pereirae. Balsamum peruvianum* is a viscous, transparent dark-brown mass with sweet, delicate, lasting odour reminiscent of vanilla.

   The balsam of *Myroxylon pereirae* contains not less than 45% w/w and not more than 70% w/w esters, mainly benzyl benzoate (2/3) and benzyl cinnamate (1/3). Cinnamain - the previous name of the mixture of esters - also contains 3.4% nerolidol and very small quantities of benzyl alcohol. The resin (20 to 30%) also contains alcohol esters of benzoic acid and cinnamaic acid and residues of benzoic acid and its methyl ester, benzyl ferulate cinnamaic acid and its methyl ester, coniferyl benzoate and according to the source outside of dossier some other substances as vanillin, farnesol and probably stilbene in small quantities.

2. *Balsamum peruvianum* is used both in veterinary and human medicine and also for the flavouring of human foodstuffs.

   It is used in veterinary medicine as an antiseptic and for the promotion of the granulation process in combination products (tincture, ointment, and spray) for the healing of wounds in cattle, horses, sheep, goats, swine of every age group. Three products for external use (ointment and tincture), containing 1 to 5% of *Balsamum peruvianum* as part of 5 to 7 active principles are used. The dose needed depends on the size of the skin lesions and the recommended use is twice a day or when needed.

   In human medicine *Balsamum peruvianum* is used for treatment of infected and poorly healing wounds, burns, decubitus ulcers, frostbite, bruises caused by prostheses and haemorrhoids. In pharmaceutical preparations for humans the recommended concentration of *Balsamum peruvianum* is between 5 to 20% of the substance for external use, but when applied on the larger area only 10% is used. Duration of the treatment should not be more than one week.

   One compound of *Balsamum peruvianum*, cinnamic acid is used with benzoic acid and other substances to simulate the flavour of tolu balsam. *Balsamum peruvianum* is also used in cosmetics, perfumes, soaps, hair lotions etc. There is also some use of *Balsamum peruvianum* as repellent.

   Balsamum peruvianum is used as a fragrance in many kinds of food: baked goods, frozen dairy, soft candy, gelatine, pudding, non-alcoholic beverages, alcoholic beverages, hardy candy, chewing gum in concentrations between 6 to 27 mg/kg (172 mg/kg in chewing gum) and the oil of *Balsamum peruvianum* in concentrations between 1 to 13 mg/kg (chewing gum about 10 mg/kg)

3. Pharmacological actions are primarily associated with benzyl benzoate and benzyl cinnamate and also with the alcohol esters of benzoic acid and cinnamaic acid.

4. After topical application on the healthy skin in humans (25% in vaseline), residues of *Balsamum peruvianum* could be seen after one hour using infrared spectroscopy, but no more after 8 hours due to the absorption of the substance. There is no information on the oral administration of the substance, but it is known that after oral administration benzoic acid is quickly absorbed.

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5. The main substances in *Balsamum peruvianum* - benzyl benzoate and benzyl cinnamate - are quickly hydrolysed to benzyl alcohol, which is oxidised to benzoic acid. In liver the benzoic acid is conjugated with glycine to hippuric acid, which is quickly excreted by the kidneys. After oral administration 75 to 80% of the substance is eliminated in 6 hours in humans. No information of the metabolism in animals is available.

6. The LD_{50}-values of the oil of *Balsamum peruvianum* are 2.4 mg/kg bw after oral administration in rats and more than 5 g/kg for rabbits after dermal application. Information on repeated dose toxicity, reproductive toxicity and teratogenicity, mutagenicity and carcinogenicity was not available, but their provision was not considered necessary in view of the very limited veterinary use and the wide-spread use of the substance in human foodstuffs.

7. Potential for a photosensitising effect of *Balsamum peruvianum* has been described.

   In animals after the dermal application of undiluted perubalsam oil there were strong signs of irritation on the skin of the rabbit after 24 hours.

8. The data on the antibacterial activity of the undiluted volatile oil indicated that there is some activity against 9 of 10 Gram-positive and Gram-negative strains of bacteria tested and some fungicide and fungistatic effect against 15 pathogen spores. In view of the limited veterinary uses no further information was requested.

9. In humans, after dermal application or oral ingestion of *Balsamum peruvianum* (doses not specified) severe kidney disorders have been observed (uraemic coma, fatty kidneys, nephritis, etc.). It was also reported the death of one infant because the mother has used the balsamum as nipple cream. No details about the exposure are given.

   Balsamum peruvianum is one of most potent contact allergens used in epicutan-test. The hypersensitivity reactions are more severe after dermal application of *Balsamum peruvianum* than those after oral use. In one study, when *Balsamum peruvianum* (8% in vaseline) was applied topically, 8 of 25 persons showed sensitivity reactions. According to the literature 3.4 to 6.6% of patients (numbers not mentioned) were sensitive. It is not really known which substance is responsible for these allergic reactions, but it could be the ester of coniferyl alcohols. In human after the dermal application of *Balsamum peruvianum* (8% in vaseline) there were no signs of irritation after 24 or 48 hours (Patch-Test).

   Clinical symptoms (including anaphylactoid reactions) have been mentioned also after the use of food containing *Balsamum peruvianum.* No detailed information on these exposures is available.

10. *Balsamum peruvianum* has previously been included in the category N2 of aroma-substances by the Council of Europe, which means that the use of *Balsamum peruvianum* as food-additive is acceptable in small quantities. The current category of *Balsamum peruvianum* according to the Council of Europe is not known, but this body still considers *Balsamum peruvianum* acceptable in small quantities.

    The FDA has published the “List of Substances Generally Recognised as Safe” (as revised of 1 April 1993) including Balsam of Peru.

    Benzyl benzoate has already been included in Annex II of Council Regulation (EEC) No 2377/90. In EU the Food Additive Code E-445 is the glycerol ester of wood resin (a complex mixture of tri- and diglycerol esters of resin acids from wood resin).

11. In view of the limited veterinary uses of *Balsamum peruvianum* and its widespread presence in human foodstuffs, no information on residue depletion or residues was requested.

Conclusions and recommendation

Having considered the criteria laid down by the Committee for the inclusion of substances in Annex II to Council Regulation (EEC) No 2377/90 and in particular that:

- *Balsamum peruvianum* is widely present in human foodstuffs and is thus a normal component of the human diet,
- *Balsamum peruvianum* is of low acute toxicity,
- benzyl benzoate, the main component of *Balsamum peruvianum* is rapidly absorbed and excreted and is already included in Annex II;
- *Balsamum peruvianum* is used only for infrequent and non-regular topical treatment of individual animals,
- the animals are unlikely to be sent for slaughter during or immediately after treatment;

the Committee concludes that there is no need to establish an MRL for *Balsamum peruvianum* and recommends its inclusion in Annex II to Council Regulation (EEC) No 2377/90 in accordance with the following table:

Pharmacologically active substance(s)	Animal species	Other provisions
Balsamum peruvianum	All food producing species	For topical use only