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THE FIRST TRULY INDEPENDENT WATCHDOG FOR THOSE
WORKING WITH NATURAL AROMATIC MATERIALS

E: info@cropwatch.org T: ++44 (0)7771 872 521

Set out below is the reasoning to re-examine the case for moving Peru Balsam into Annex II/III of the Cosmetics Directive, made by Cropwatch in response to the EU's Public Consultation on the matter. Moving the ingredient should have been based on robust science, not a rag-bag of flawed evidence, as we tried to indicate.

No acknowledgement or feedback from Brussels officials was ever received after this Cropwatch submission. A Peru Balsam manufacturer, who also made his case to the Public Consultation, received a short letter informing him of Peru Balsam's regulatory status - perhaps the lawyers in Brussels thought he didn't already know this (?).

Public Consultation: Proposed Movement of Certain Perfumery Ingredients into Annex II/III of the Cosmetics Directive:

RIGHT OF REPLY ON BEHALF OF A PERU BALSAM MANUFACTURER.

Written & edited by Tony Burfield for Cropwatch Jan 2007.

Executive Summary.

Detailed examination of the published scientific literature on Peru Balsam (PB) and its qualities shows that it is universally recognized & accepted to produce adverse skin reactions / to be a marker for fragrance allergy, in spite of much of the published dermatological material on the subject being of a poor scientific standard. Further collaborative work on the major allergens in PB oil/absolute/tincture - believed, from the work of Hauser (1995) to be coniferyl benzoate, benzyl isoferulate etc. - needs to be done to see if the concentration

of these components can be eliminated or substantially reduced in manufacturing/processing, In this way, PB qualities might eventually be toxicologically reclassified and reintegrated into perfumery as a safer ingredient. As it is, **the banning of PB as a perfumery ingredient** by IFRA in 1982 (RIFM 1982) **may have been an important factor in the resultant halving of global production** in the last two decades. However, in deference to the economic damage done to the PB industry by the recent regulatory muddle over Peru qualities involving Brussels officials, the EU Cosmetics Commissioner should, in our opinion, give the producers a temporary respite from immediate removal of PB oil / absolute into Annex III of the Cosmetics Directive. This temporary respite could enable problems of underlying PB allergenicity to be addressed & hopefully remedied by producers – although they will need external financial input to be able to do this. **Otherwise the PB industry in El Salvador may all but disappear, with loss of employment, maintained PB tree forest, and local community infrastructure.**

Introduction.

The proposal to move PB oil / absolute into Annex III of the Cosmetics Directive, coming on top of the previous banning of PB as a perfumery ingredient and the restriction of PB oil, absolute & anhydrol to 0.4% final concentration on sensitization grounds in perfumery (see below), has badly affected the PB producing industry in El Salvador, as indicated by declining production figures (see table 1). Furthermore the unprofessional regulatory muddle which has engulfed the EU Commission & its advisers in attempting to move PB qualities into an Annex of the Cosmetics Directory (see <http://www.cropwatch.org/peru.htm> & update) has further hurt the PB balsam industry – through no fault of its own. This is because the confusion around its' exact regulatory status has meant that many perfume formulators and industry fragrance safety advisers producers have not fully comprehended the situation, or associated PB qualities with an undeserved tarnished reputation, & played on the safe side, by physically removed the ingredient from existing perfume formulations, or have employed synthetic substitutes instead. The total value of the economic damage caused to the PB industry by this latter escapade is not yet known.

PB is regarded as one of the primary sensitising materials amongst fragrance ingredients. Curiously, reviewing the dermatological evidence, PB has attained this reputation on the back of much incomplete investigation, poor science, appalling experimental technique, conflicting data, etc. etc. and it is perhaps largely the sheer volume of published research material suggesting that PB has these strong sensitising properties, which is the most convincing to the independent observer, rather than the actual quality of much of the published material on the subject. In particular, previous RIFM evaluations of Peru Balsam Oil (PBO) have not been particularly damning, and its use in fragrances was unrestricted until quite recently (1991).

Temesvari *et al* (1978) are typical of researchers who have previously comment on “the widespread use of Peru Balsam and chemically related materials which cross-react with it” comprising, apparently “cosmetics, soaps, deodorants, perfumes, foods (pastry, Coca-Cola, ice cream, vanilla, orange !!) and preservatives (parabens and benzoic acid).” Schienman (2002) noted that the prevalence of (overall) fragrance allergy apparently rose in Denmark, Singapore, Slovenia & the USA (but not in the UK) and quotes Fisher (1990) that (a PB patch test) will detect 50% of patients with a fragrance allergy. Larsen *et al.* (1998) have suggested that the addition of a natural mixture of fragrances (2% each of jasmine absolute, ylang-ylang oil, narcissus absolute, sandalwood oil and spearmint oil) will detect 95% of patients with fragrance allergy [– N.B. Cropwatch has previously pointed out that narcissus absolute and spearmint oil are quite uncommon fragrance ingredients, and that genuine sandalwood oil is now a rare commodity through commercial over-exploitation of the species. A picture is therefore building up that cross-reactivity is responsible for a least a part, if not a considerable part, of these reactions].

The fact is that the annual production volume of PB has at least halved since the time of Temesvari’s paper above, & the introduction of the notorious “26 allergens” legislation has (presumably) reduced exposure/notified cosmetics consumers to the presence of PB-like chemicals (benzyl benzoate, benzyl cinnamate etc.) - yet the frequency of apparent allergic reactions to PB is not abating. Cropwatch is playing with the notion that if the logic of this situation is that banning/restricting an ingredient does not prevent an allergic reaction occurring in small susceptible minority of the population, then why ban it at all?

Production – New Information.

PB is an exudate produced from the large tree *Myroxylon pereirae* (Royle) Klotzsch (Fam. Fabaceae) [syn. *M. balsamum* L. (Harms) var. *pereirae* (Royale) Harms.] that grows up to 25m. in South, Central America & Mexico. Balsam production now mainly occurs in El Salvador in an area (approx. 400 square kilometers) of worked trees called ‘the Balsam Coast’), with some former production in Guatemala and from Belize in Honduras. Since PB was shipped to Peru in earlier times for export, it came to be known under this name.

Production of PB is carried out after the rains in November/December until May, by fire-scorching and wounding the bark of the tree, leaving approx. 1 week, before slashing and removing rectangular strips of outer layers of bark (typically some 30cm. x 15 cm.), which are crushed, boiled into hot water and pressed (giving ‘Balsam of Cascara’, Balsam of the Bark). As well as the bark, the tree is also worked – according to Poucher (1936), after the outer layers of bark are removed, exposing the wood. This is covered with cloths or rags to collect the exudates over 15-20 days, the cloths or rags being subsequently boiled to recover the balsam and pressed in a rope press, (giving ‘Balsam de Pañal’, the major part of the yield). In a few days a third exudation (‘Balsam de Contrapique o Tacuazonte’) is collected with cloths that are boiled and pressed to recover the resin. In the pressing process the balsam sinks to the bottom (S.G. 1.150 to

1.170) and the water is decanted off and the resin strained. A combination of these three tapping in definite proportions is a 'Raw Balsam' that then is boiled to evaporate the residual water (this called the "Purification Process"). This "Purification" gives PB as we know it commercially. The tree may be tapped in this way at fortnightly intervals up to 8-9 months per year. Average yields have been reported to be between 0.25 to 0.50Kg per tree per annum around 60 years of age giving maximum yields (Manual of Good Practice in the Production of Balsam of El Salvador, OIRSA 2006).

Year.	Average Production of Peru Balsam per Year.
1976-1980	140 Tons
1985-1989	146 Tons
1996-2000	91 Tons
2001-2005	73 Tons

Table 1: Annual Production Figures for Peru Balsam (years where available) Source: Centrex, El Salvador Gob.

Api (2006), speaking of PB quality usage volumes amongst IFRA members (member response factor not reported) and states: "The worldwide volume of use of the oil is less than 10 metric tons and the worldwide volume of use of the absolute is less than 1 metric ton (IFRA Volume of Use Survey, 2000)." *N.B. It has to be remembered, however, that IFRA membership does not include every commercial concern within the world's perfumery industries, however much Api gives the impression that it does. These figures may, therefore, understate actual fragrance global usage – TB.*

Applications – where is Peru Balsam used?

Medicinal

PB has been traditionally used by the Inca and is still used by Columbia ethnic peoples to treat wounds and arrest bleeding; healing is reported to occur with little or no scarring. It has been used as an anti-parasitic especially for scabies (Anon 1986) & generally for ulcers, pruritis, eczema & ringworm (Wren 1988). It has been, and still is, used extensively for topical preparations for treatment of wounds (Leung & Foster 1996). PB has also been used in Western medicine in profuse bleeding and in plastic surgery (Lewis W. H. & Lewis M. P. F 2003). PB's properties to promote granulation and as a disinfectant are utilized in combinations of PB, trypsin & castor oil are marketed under various trade names (Granulex™, Granul™, Balsa-Derm™, Xenaderm™ etc.) and recent published studies (Noble *et al* 1989, Narayanan *et al* 2005, McDougall *et al* 2005, Gray & Jones 2004 etc.) demonstrate considerable its success in difficult wound care situations, in skin graft healing (Carson *et al* 2003), in pressure ulcers (Maas-Irslinger *et al* 2003) etc. It is also used frequently in haemorrhoidal preparations. For a review of PB's considerable beneficial role in wound healing see Hammond (1999).

PB was official in the USP (1820); also formerly official in NF XII. It is official in the BP (2007); DAB 7 & OAP 9, Ph Helv VI & Eu Pharm 5.2. A Commission E Monograph on 'Peruvian Balsam' can be seen at http://www.herbalgram.org/bodywise/commissione/Monographs/Monograph_0292.html.

Perfumery: The balsam/balsam oil/tincture has been traditionally used for "warmth" and sweetness in perfume compositions, particularly as part of oriental themes. It was noted for its fixative properties & had significant uses in incense perfumes, being blended with musks, coumarin and animal notes. It is particularly useful in incense and formerly also in soap perfumes.

Food Flavourings: PB oil/tincture enjoys extensive use in flavorings (chocolate, confectionary, alcoholic beverages etc.), where its employment is unrestricted in many countries [FDA: §182.20 GRAS]. It was formerly official in the FCC.

Composition. Genuine PB balsam as sold commercially from producers consists of a heterogeneous mixture of approximately 4 parts of material obtained by boiling rags and 1 part of material obtained from the bark. The composition of these 2 separate component origins of PB **have never been separately analysed** to our knowledge (this is currently being organised by Cropwatch). The composition of PB balsam is variable (Veien *et al* 1996); 75% of the total number of components of PB is unknown. Specific allergens in PB are not well defined ((Veien *et al.* 1996). Hausen however has identified a number of minor components as severe sensitizers - coniferyl benzoate, benzyl isoferulate etc. (Hausen 1995).

Adulteration of Peru Balsam and extracts/distillates in Perfumery.

This is **a problem virtually unaddressed by toxicologists** & health & safety officials, who presumably (& mistakenly) take all products as authentic. However, since there is a test in the 1923 BPC which distinguishes between artificial and natural Peru balsams, the problem has actually been recognized for some time! Many commentators remark that Peru balsam oil complete is actually solid, or contains semi- solid material which contains non-volatile components (e.g. Billot & Wells 1975). Further, the author's remark that Peru balsam oil as sold commercially is of variable composition, and could contain co-distillates such as added benzyl benzoate. With modern methods of Peru balsam oil, production such as molecular distillation, the addition of co-solvents, such as balsamic esters, is commonplace.

Any effects of the commercial practice of adulteration of Peru oil etc. on adverse skin reactions, has yet to be properly evaluated.

Regulatory position. According to Api (Api 2006) - of RIFM - PB "has not been used in perfumery since 1982 when IFRA first banned this material in perfumery". This is, of course, again somewhat wishful thinking since the not all the world's perfumery concerns belong to IFRA, and of those that do, not all of them rigorously observe IFRA's Standards/Code of Practice. Further, Api states (Api

2006) that a 0.4% concentration limit in fragrances for Peru extracts/distillates has been in place since 1991, although text books of the same year (e.g. Poucher 1991) still report on its safe & unrestricted use.

Now we understand that murine local lymph node assay gives EC3 values of 4.0% for either PBO or PB absolute and absolute, against <0.5% for PB (RIFM unpublished data, according to Api 2006). Presumably this will require IFRA members to observe yet another Code of Practice policy change in ingredients usage - but this very Public Consultation is concerned **with approval of a 0.4% PBO level**. It really is intolerable for industry to be tossed around according to the whims of the latest toxicological techniques – the results of which anyway, are to be critiqued in a forthcoming Cropwatch Opinion, as several inconsistencies have been observed.

A Closer Look At RIFM's earlier work on Peru Balsam Oil (PBO).

RIFM tested several samples of PBO - see *FCT* (1974) **12**, p953 -954. The **irritation** studies were assembled using from two to five numbered samples of PBO (manufacturing methods not stated), not tracked from a botanically verified source, nor batch-tracked by unique identifying code, nor confirmed tested as 100% botanically derived (although the monograph reports that analysis was carried out). **The lack of proper botanical authentication of the test materials would nowadays consign these studies to the dustbin.** One researcher found that 100% PBO applied to intact or abraded rabbit skin for 24 hr. under occlusion was slightly irritating; however another researcher using a different sample under the same conditions & same animal species found that PBO wasn't irritating. Two different samples of 100% Peru balsam applied to the backs of hairless mice were found non-irritating. Irritation tests on human volunteers using five different 8% Peru balsam oil in a closed patch test produced no irritation in 24 hrs.

The **sensitization** studies were carried out using maximisation tests employing five similarly non-authenticated PBO samples (8% in petroleum) in closed patch tests - **which produced no reactions in 25 human volunteers.**

Unsatisfactory Aspects to Peru Balsam Oil's (PBO's) Regulatory Position.

IFRA restricted Peru balsam oil to 0.4% in the final product in 1991 quoting the above RIFM 1974 work – work which in fact gives the oil a fairly clean bill of health. As noted above, up to now there have been no study details available in the public domain which clearly shows the necessity to restrict PBO concentration in perfumes, based on adverse human skin reactions - but we understand that RIFM data from murine local lymph node may change this situation shortly - but disappointingly this information was not available in time for this Public Consultation. Certainly there are a multitude of scientific publications indicating why PB (usually of undefined origin) should be in Annex II, and these can be divided into three separate categories:

1. Those studies of insufficient scientific merit not to be considered. These include many case studies in *Contact Dermatitis* employing insufficient scientific detail, analysis, bad experimental design etc.
2. Those more rigorous studies which support the findings of adverse skin reactions for PB or PBO. The number of studies specifically dealing with PB qualities (oil, absolute, tincture etc). are unsatisfactorily small.
3. Those studies which (perhaps embarrassingly) do not quite show the expected adverse skin reactions of PB qualities (e.g. Rudzki E. & Grzywa Z. 1977), or indicate that PB patch testing is not of value in a patients' experience of allergy (Johansen *et al* 1997). More work needs to be done to show the reasons why this happens.

The unequal playing field: regulations for flavourings vs. perfumes

It is known that flavourings can be responsible for allergenicity issues: "hypersensitivity reactions to PB from oral uptake in systemic contact allergy cases are often overlooked " (Pfutzner *et al.* 2003a; Pfutzner *et al.* 2003b). However evidence of the benefits of specifically avoiding flavourings in special diets, which may include the total avoidance Peru balsam, is not clear e.g. has been found beneficial by Veien (1985), but not beneficial in all delayed-type allergy cases by Niinimaki (1995). Salam *et al.* (2001) publish evidence on a reported improvement in 50% of contact allergy patients on a balsam-avoidance diet, but alleged improvements rely on telephone self-reporting – an unsatisfactory assessment system with built-in fallibility.

Any practical inhibitory measures to prevent PB being universally used as a flavourings ingredient are not immediately apparent, thus PB balsam and its qualities are, or will be, more tightly regulated in cosmetics. This unfair legislative imbalance between regulations that apply to flavourings against those that affect fragrances needs to be resolved, preferably after a new evidence review.

New Hopes for Peru Balsam as a Safer Ingredient.

Cropwatch have previously expressed disappointment at the Brussels regulatory culture, which happily bans or restricts natural ingredients in cosmetics without working with industry to find a way forward to produce a safer version of the product.

1. Cropwatch has already indicated an avenue of investigation for the possible elimination of more allergenic materials from PB (such as coniferyl benzoate), via modifications of the preparation process (it is that a process for the elimination of the presence of naturally occurring coniferyl benzoate 'is known in the art' i.e. during the preparation of hypoallergic ylang-ylang oil). We intend to petition world bodies for funding to set up a project to investigate whether a safer form of PB can be produced using this principle.

2. Another (perhaps slightly less satisfactory) approach is reflected by patents which refer to the ability of various preparations which can reduce adverse skin reactions caused by cosmetic ingredients e.g. Smith *et al.* (1998) for Estee Lauder, referring to the beneficial properties hydro-alcoholic extracts of *Cola nitida*. Goyarts *et al.* (2000) indicate that cyclic adenosine monophosphate phosphodiesterase inhibitors have moderate effect in reducing irritation of 8% PB balsam in petrolatum. Ford & Maibach (2005) say there is a problem with this approach as PB irritation is not a typical irritation but is a non-immunological contact urticaria. It remains to be seen whether by employing these types of materials in fragrance formulations, a way forward to reduce the frequency of adverse skin effects in susceptible individuals can be established.

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