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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

MELISSA OIL - Cropwatch's Archive.

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§1. Extract from *Cropwatch Newsletter 4, July 2006.*

Melissa oil. IFRA have decided this minor essential oil (please note: which is actually derived from *Melissa officinalis* subsp. *officinalis* L. to distinguish it from *M. officinalis* oils of other subspecies which have different compositions) rests in the category of 'not to be used as or in perfumery/safe conditions of use have not established'. It was previously listed amongst 14 recommended essential oils (correct subspecies indicated) to generate income for developing countries in FAO's Agricultural Services Bulletin 94 *Minor Oil Crops*.

Baker (2006) comments that Melissa oil (subspecies not defined) is 'not used in perfumery', presumably based on IFRA's conclusions from a usage enquiry of trade organisation members. However its top-note profile was previously used in the creation of the perfume "Coeur-Joie" (Nina Ricci) who's launch date some put at late 1930's (e.g. Arctander 1961), others later at 1946. The comment quoting IFRA, saying that Melissa oil is not used in perfumery is different from saying that the ingredient is not used at all in the whole of perfumery (i.e. in natural perfumery or in artisan crafted cosmetics where it is used to fragrance creams & lotions etc.). If Corporate Perfumery has shown little current interest in the oil of *M. officinalis* subsp. *officinalis* – the use of which dates back to the Ancient Egyptians, and which has monographs in respected reference tomes like Arctander & Guenther - it may simply be because its' keeping qualities are poor, that it is difficult to find unadulterated & its fresh citrus note can be mimicked more cost effectively by alternative materials (i.e. it's over-expensive!). Estimates of annual production figures for *Melissa officinalis* subsp. *officinalis* L. vary widely, ranging from 2.5Kg/year (FAO), 40Kg/annum (Aqua-Oleum, undated). Cropwatch has 200Kg/annum for 2004 for *Melissa officinalis* subsp. *officinalis* L.*; but for the different oil *Melissa officinalis* subsp. *altissima* Dawson the annual output for 2004 was estimated at 30Kg (Cropwatch, unpublished information). RIFM would presumably be reluctant to spend valuable research funds on such a minor aroma material, and a request for a SCCP Opinion would not therefore be likely to materialise.

* N.B. This figure reflects an initiative by a number of UK farmers to grow medicinal crops on setaside land. Unfortunately, much of the essential oil produced remained unsold and interest in growing *Melissa officinalis* (and production volumes) waned.

However, Melissa oil is a **flagship aromatherapy essential oil**, has useful properties in aromatherapy & herbal medicine, & any doubts about its' safety in a perfumery application would appear inconsistent with its widespread & fairly untroubled history of use in aromatherapy practice for the past several decades. There is something wrong when Corporate estimates of usage start to determine our attitudes to ingredients (although, of course, provided you are not a member of IFRA there is nothing to stop you using it in fragrances or cosmetics within the EU).

§2. IFRA Reveals its Toxicological “Evidence” against Melissa Oil.

(First published on *Aromaconnection* 24th May 2009).

Pre-amble.

It has always been something of a curiosity that IFRA has previously seen fit to prohibit melissa oil (lemon balm oil) which derives from *Melissa officinalis* L. ssp *officinalis*, as an ingredient of fragrances. The reasoning behind this, according to the published IFRA Standard for melissa oil, issued on 16-07-2008, was said to be:

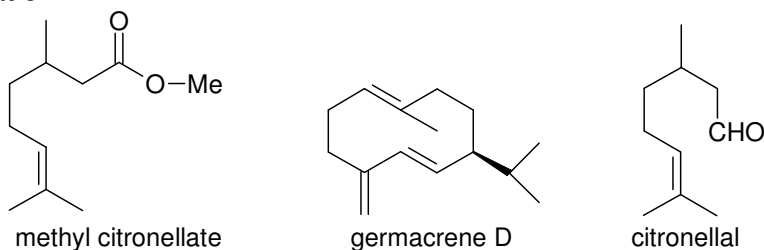
- 1) presence of structural alerts as defined in the Human Health Criteria Document (Ford *et al.*, 2000), and/or
- 2) adverse data on the material itself, and/or
- 3) adverse data for a structurally related material based on toxicological concerns about its contained components from structural point of view.

Whilst melissa oil enjoys a considerable reputation in aromatherapy for its alleged beneficial properties, the usage volume of melissa oil in corporate perfumery nowadays has to be vanishingly small, perhaps running to no more than a few kilos per annum, since many perfumers consider the high cost of the ingredient is not justified by any contained unique notes, overall odour value, stability, or performance in product. In the days of early perfumery, the situation may have been different, for example *Melissa officinalis* was said to be an ingredient of the 17th Century cordial Eau des Carmes. Melissa extracts on the other hand contain classes of compounds not found in the essential oil, which may have acetylcholinesterase inhibiting, anti-oxidant, anti-viral (e.g. exhibit action against herpes simplex viruses: Wolbling & Leonhardt 1994). and other useful properties Melissa leaf (under 'lemon balm') is official in the European Pharmacopoeia.

The Composition / Authenticity of Melissa Oil.

There is a considerable amount of scientific literature on the composition & authenticity of melissa oil, and this brief review should only be taken as merely illustrative rather than fully comprehensive. Melissa oil rarely been commercially available in unadulterated form in the past, and was often a construct of citronella

oil, litsea cubeba oil, lemon oil and various isolates & synthetics (Burfield 2008). Tisserand & Balacs (1995) had only identified possible toxicological concerns for melissa oil via its citral content, which they maintained was in the range 35-55%, concerns which presumably also apply to other high citral containing oils such as lemongrass oil & litsea cubeba oil. Previously Schultze (1992) had investigated melissa flower oil, and found the corolla oil (yield 0.002%) to be different from the calyx oil, the latter resembling more the oil of the leaves. The main constituents of melissa leaf oil (Schultze 1989) were found to be citronellal (36.2%), germacrene D (13.5%), β -caryophyllene (10.9%), geranial (7.6%), and methyl citronellate (4.9%). Clery (1992) drew up some pointers to distinguish authentic melissa oil (including estimation of the geranial: citronellol ratio), in order to distinguish it from lemon-scented catnip oil from *Nepeta cataria* var. *citriodora*; this same topic was subsequently re-investigated by Klimek *et al.* (2000). In addition Clery indicates that the β -caryophyllene: geranial ratio is also important for the verification of authenticity, and the author cites a checklist of components normally found in genuine melissa oil. The position is further complicated by the ratio of top leaves to bottom leaves gathered, as the neral / geranial content is higher in the top leaves, whereas the sesquiterpenes are relatively higher in the bottom leaves – a topic further investigated by Mrlianova *et al.* (2001), who investigated essential oil composition at various harvest cut heights. Further, oil produced from the dried herb is claimed to be higher in neral & geranial, and lower in β -caryophyllene & caryophyllene oxide, than the fresh herb (Salaby *et al.* 1995). Melissa plants grown near the equator usually only grown in vegetative (non-flowering) form and so slight compositional differences may also arise from this consideration.



The evaluation of criteria for melissa oil authenticity was also discussed by Hener (1995) who used enantioselective gas chromatography, isotope ratio mass spectroscopy on-line coupled with capillary gas chromatography. Soresen (2000) reviewed the analysis, composition and pharmacological uses of *Melissa officinalis* extracts. Later, Lawrence (2008) reviewed a number of publications on melissa essential oils showing differences in composition due to the effect of different geographical sourcing, differing stages of maturity etc. Other melissa oils produced commercially include *Melissa romana* Mill.

Melissa Oil under IFRA's 44th Amendment.

Under the draft proposals for IFRA's 44th Amendment, melissa oil (which they describe as 'genuine *Melissa officinalis* L.')

has been downgraded from an outright ban in fragrances, to a concentration restriction in the fragrance compound (as opposed to the finished cosmetic product). QRA data for melissa

oil, which is categorised as a weak sensitiser, is presented by IFRA for the various established product categories, based on a No Expected Sensitization Induction Level (NESIL) of 1400 µg/cm². The problem for those of us who like to consider the robustness of the “evidence” supporting these proposed restrictions, is that it is alluded to in the form of 3 unpublished reports, not available in the public domain. These are as follows:

- RIFM (Research Institute for Fragrance Materials, Inc.), 2001. Human repeated insult patch test. Unpublished study from Robertet, 21 February. Report number 36641. (RIFM, Woodcliff Lake, NJ, USA).
- RIFM (Research Institute for Fragrance Materials, Inc.), 2008. Local Lymph Node Assay. Unpublished study from Robertet. (RIFM, Woodcliff Lake, NJ, USA).
- RIFM (Research Institute for Fragrance Materials, Inc.), 2008. Human repeated insult patch test. Unpublished study from Robertet. (RIFM, Woodcliff Lake, NJ, USA).

Cropwatch has written to Robertet, Grasse, and to RIFM N.J., requesting that they make these reports publicly available, in the interests of transparency. We feel that this is particularly important in this case, in view of the devastating criticisms concerning the use of the QRA technique outlined in SCCP Opinion SCCP/1153/08, which directly related to the submitted RIFM / IFRA-generated data concerning citral as an alleged sensitiser (see feature on SCCP Opinion SCCP/1153/08 in *Cropwatch Newsletter* August 2008).

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- Sorensen J.M. (2000) “*Melissa officinalis*.” *Int. J. Aromatherapy* **10**(1-2), 7-15
- Tisserand R. & Balacs T. (1995) *Essential Oil Safety*. Churchill-Livingstone 1995.
- Wolbling R.H. & Leonhardt K. (1994) “Local therapy of herpes simplex with dried extract from *Melissa officinalis*” *Phytomedicine* **1**. 25-31.

§3. Update on Melissa Oil

[First published on *Aromaconnection* 31st May 2009]

You may recall the recent Cropwatch posting to Aromaconnection on a proposed IFRA restriction for Melissa oil, and the non-availability of the relevant evidence in the public domain. Following separate Cropwatch requests to the holders of the privately-held information (Robertet & RIFM), Catherine Gadras, in charge of the regulatory and safety department of Robertet, Grasse, has mailed promising to forward a summary to Cropwatch by 15th June 2009, in respect of the LLNA and HRIPTs tests that have been conducted on behalf of Robertet, 'in order to allow the use of this EO for perfumery use'. This is a welcome development. RIFM have not, as yet, either replied or acknowledged the request.

§4. Robertet Reveals its Evidence on Melissa Oil to Cropwatch.

by Tony Burfield July 2009.

You may remember that Cropwatch was quite puzzled by any need for IFRA's new restrictive Standard for Melissa oil in IFRA's 44th Amendment, and had requested details of three unpublished toxicology reports from both RIFM & Robertet, Grasse, which were not available in the public domain, but which were cited by IFRA as containing evidence sufficient to restrict its use in perfumery. The back-story on this matter is available in the Cropwatch Files at <http://www.cropwatch.org/Melissa%20officinalis%20-%20Cropwatch%20article%20archive.pdf>, but to briefly recap, although Melissa oil & extracts occupy an important place in aromatherapy and herbal medicine, Melissa oil is virtually unused in corporate perfumery. Nevertheless IFRA had previously seen fit to ban it as an ingredient on the basis of undisclosed evidence. There seemed to be no such body of evidence within the RIFM database to support such a ban, and it is a complete mystery to many of us how REXPAN could have come to such a conclusion. The ban has now been transformed into a concentration restriction under IFRA's hyper-bureaucratic QRA system. In the interests of *Freedom of Information*, Cropwatch has compiled a comprehensive bibliography of the available literature on Melissa oil in the *Cropwatch Files* section of its website, to enable any interested parties amongst the general public at large to make their own minds up about the need for any restriction.

Although RIFM has ignored Cropwatch's request for the withheld evidence on Melissa oil as noted above, Catherine Gadras of Robertet, Grasse very kindly responded with a summary of the test data, which is displayed at <http://www.cropwatch.org/Melissa%20EO%20testing%20summary.pdf>, and offered to answer any further points. Accordingly we asked Robertet (on 14th June) to accurately define the botanical nomenclature of the Melissa species employed (was it, for example, the oil from *Melissa officinalis* L. subsp. *officinalis*?), the geographical origin of the Melissa herbage used to steam distill the essential oil, and the compositions of the oils employed in the research (since commercial Melissa oils vary widely – see Cropwatch's Melissa oil bibliography). We also asked, in as many words, if the Robertet team would like venture any

comments on the fact that there was a complete lack of adverse human reactions in the Robertet HRIPT studies, contrary to the numerical indications of possible sensitiser activity shown by the EC3 value? Without going into too many further details, this data would seem to offer further support as to the flawed ability of the LLNA test to accurately predict sensitiser potency for aromatic ingredients, and its questionable place of this animal-based test within the over-bureaucratic QRA system. But presumably, unless a notable such as Professor Axel Schnuch stands up and gives a paper on perfume ingredients with indicatory EC3 values which *do not* produce a significant number of adverse reactions per 10,000 dermatitis patients, no action will be taken by IFRA or by the `EU's 'expert' committees to scrap this flawed QRA system (we make this comment since Schnuch's evidence seems to have contributed to the pressure on the EU Cosmetics Commission to belatedly review the situation regarding notorious 26 Allergens debacle - see *Cropwatch Files*).

If we receive a further reply from Robertet regarding further details of the toxicological studies on Melissa oil, we will post it in the public interest. We should point out that in asking these questions, we did not mean to place Robertet in an awkward position (Robertet being a Direct Company Member of IFRA). However as Martin Watt noted when presented with the Robertet studies summary recently: "(the data presented)... is all typical in-house testing and certainly NOT suitable for ANY scientific evaluation purposes." And further: "My key point is that RIFM data is only trade recommendations. The EU committee is attempting to turn those 'recommendations' into EU law. So far without success, but they keep trying. Only publicly discrediting that committee and the administrators in the European court will anything change."

Cropwatch's feeling is that the IFRA/RIFM/REXPAN conglomerate is struggling: better toxicological facilities & superior expertise in specialized subject areas are available outside the organisation, and this situation together with the fact that people are better informed on toxicological matters is stretching the credibility of many of IFRA's policies and its decision-making generally. The perfume industry certainly needs a safety organisation to protect its interests – but maybe not this one, which is guilty of over-regulating the industry, and confuses the career interests of its composite toxicologists over and above its function to be a balanced safety policy-making unit for the trade.

§4. Melissa Oil & IFRA Policy (cont'd): The Further Details.

(First published on Aromaconnection 6th Sept 2009; then in *Cropwatch Newsletter* 16).

Pre-amble.

Those of us who have worked in the aroma trade for most of their working lives, have, at times, been highly skeptical of the knowledge & abilities of those unelected officials who would impose baffling & seemingly nonsensical regulations and codes of practice upon the trade. Sometimes we felt that we were being regulated by those who had little in-depth knowledge or experience of the subject - a feeling which has never really gone away.

Perhaps safety-orientated organisations like IFRA would have gained more credibility from some of us old-timers if they had more openly owned up to their previous errors. Yes, we accept that with improvements in experimental design and better techniques, many of IFRA's earlier (nineteen seventies') findings on ingredient toxicology are now suspect, or have been superseded. Most importantly, the failure to use rigorously purified aroma chemicals for toxicology testing by researchers reporting to RIFM, and the use of complex botanical materials from non-expertly identified botanical sources, has thrown large sections of IFRA's previous toxicological findings into doubt since impurities and adulterants have often been responsible for adverse effects rather than the pure ingredients. From a personal standpoint, when you have been drenched in perfume & essential oils on a daily basis for 30-odd years, as many of us at the coalface have, you may feel some intuition (rightly or wrongly) for what aroma materials might be posing any handling risks. This is why many of us laughed openly over IFRA's Quenching Hypothesis (now discredited). It is why we are still cynical over the disproportionate IFRA classifications of many materials which are supposed to be sensitising, according to the corporate-toxicological methodology involved in the QRA approach. But many of these ingredients indicated as sensitisers have failed to produce any significant numbers of adverse reactions amongst the end-users of fragranced cosmetic & household products in which they occur.

Melissa Oil: Lessons Learned.

The curious case of the previous banning of Melissa oil as a fragrance ingredient by IFRA, gave Cropwatch an opportunity to explore IFRA's ingredient policies in detail (see previous Cropwatch reports). In so many instances, a veil of secrecy obscures the detailed experimental facts on which IFRA/REXPAN ingredient status decisions are made. Following requests by Cropwatch, Robertet Grasse, to their immense credit, were willing to share their toxicological findings on Melissa oil testing, referred to in the RIFM data-base, but otherwise not available to the general public. Subsequently we can now clearly see (in our opinion) that there was no good reason to ban Melissa oil from perfumery use in the first place, and a case for its continued restriction is heavily based on Robertet's evidence, which was not comprehensive across a range of dosages, but based on a strategy to reduce costs. This involved contriving experiments at doses which were likely to produce a positive safety outcome, rather than the prospect of funding a more extensive range of tests proving its skin safety at higher dosages. That's OK - we can easily deal with this, because it represents the truth. It's just that IFRA didn't previously reveal these particular facts about the economic restraints which have materially affected the testing strategies, for this particular ingredient.

Where do we go from here? It is apparent that we need an independent body to openly ascertain the facts about 'pure' toxicological science – as against the corporate-funded version of toxicology which we are forced to follow. It is also apparent from the mail that Cropwatch receives that there are other expert opinions out there – why must these individuals be sidelined and denied places

on expert committees? Above all, Cropwatch is concerned that the low standards set out in many IFRA commercial standards may be rubber stamped & adopted by the EU Commission, as of course has happened previously, and which may come to be an increasing trend.

With a few minor punctuation changes, the reply from Catherine Gadras is set out below (we had asked for the exact botanical identification of the *Melissa* spp distilled for essential oil (since IFRA had failed to properly define it), and for its' geographic origin & compositional details. We had further asked the Robertet team for any views on the presented HRIPT & EC3 data. We also had an exchange of mails with Michel Meneuvrier of SAPAD who provided the oil for testing (see below) & who confirmed that the *Melissa* plants distilled for oil were produced organically from Diois region plants.

Catherine writes (remarks shaded in grey):

"As I mentioned below *Melissa* EO used for testing is *Melissa officinalis* subsp. *officinalis* L cultivated in the South East of France in the region of Di (Drôme). This genuine essential oil has been provided to us by the SAPAD (Société Anonyme des Plantes Aromatiques du Diois). The sample was taken from the crop 2008. 7 to 8 levels of fresh leaves plus the flower part are used for the distillation. Please find below the range of the main constituents provided to us by SAPAD and the composition of the sample used in the most recent tests. (See attached file: *Melissa*-EO Composition.pdf).

The crop results from the distillation of 3 "cuts: one at the end of May and the two others from the beginning of July and at the end of August/beginning of September. The producers finds that the citral content is maximum in the third cut (greater than 50%) and that citronellal is below 10%.

2) Comments regarding safety data (HRIPT and EC3)
The LLNA has been made to determine a level of concentration at which one begins to observe induction of sensitisation. In our case 4500µg/cm². Considering the high cost of this EO (5 to 7 tons of fresh plants to produce 1 Kg of essential oil) on one hand and the fact that we did not want to risk a positive reaction in the HRIPT, we have chosen this conservative 1470µg/cm²). This is more than adequate for perfumery use which is our business. It is quite possible that a higher safe limit for *Melissa* EO exists but in my opinion it must be verified by testing.

PS: I take advantage of our e-mail exchanges to make some comments concerning the Cropwatch report on *Melissa* (page 3) that I found on internet :

I have 2 comments on this sentence below: :

"Under the draft proposals for IFRA's 44th Amendment, *Melissa* oil (which they describe as 'genuine *Melissa officinalis* L.')

downgraded from an outright ban in fragrances, to a concentration restriction in the fragrance compound (as opposed to the finished cosmetic product). QRA data for melissa oil, which is categorised as a weak sensitiser, is presented by IFRA for the various established product categories, based on a No Expected Sensitization Induction Level (NESIL) of 1400µg/cm2."

1) Did you really mean "downgraded" ? My poor English would have expected "upgraded". (**Cropwatch comments:** downgraded from a negative position (a ban) but upgraded to more positive position (just a restriction) - it all depends on how you look at it!).

2) I confirm to you that the QRA limits are in finished consumer products and not in fragrance compounds." (**Cropwatch comments:** on this latter point we stand corrected. Thank you Catherine!).

Addenda – Analysis Data received from Robertet as attached file mentioned above 'Melissa-EO Composition.pdf.'

Analysis of Melissa EO sample used in HRIPT test.

Component	% FID CW
Myrcène	0,16
Limonène	0,37
Cis Ocimène	0,12
Trans Ocimène	1,14
Para cymène	0,15
Methylheptenone	1,76
Octène 1 ol 3	0,4
Citronellal	1,3
Alpha copaene	0,34
Beta bourbonene	0,4
Linalool	1,38
Cis + Trans Isocitral	1,6
Beta Caryophyllene	14,2
Neral	23,8
Methyl geraniate	0,32
Germacrene	4,3
Geranial	33
Geranyl acetate	2,2
Delta Cadinene or delta Amorphenone	0,7
Citronellol	0,2
Nerol	1,1
Isogeraniol (cis+trans)	0,24
Geraniol	1,7
Epoxydes de caryophyllene (cis+trans)	1,8
Germacradienol	0,3
Muurolol T	0,4
Thymol	2,1
Carvacrol	0,25
Alpha Cadinol	0,6
Neric acid	0,1

Geranic acid	0,3
TOTAL 96,73	

Information Stat. from SAPAD

	Mini %	Maxi%	Moyenne %	Escart Type %
Methyl heptenone	1.05	3.36	1.8	0.7
Limonene	0.04	0.48	0.18	0.13
Citronellal	0.6	19	4.9	4.4
Neral +citronellool	6.4	28	18.7	5.4
Geranial + Geraniol	9	38.3	25.6	7.4
Caryophyllene beta	10.1	29.6	18.3	4.4