EXPERT PANEL FOR FRAGRANCE SAFETY MEETING

Minutes

January 28-30, 2019

EXPERT PANEL MEMBERS		RIFM STAFF	GUESTS
Donald Belsito (Chair) Magnus Bruze G. Allen Burten, Jr. Jochen Buschmann Maria Dagli Wolfgang Dekant	Allison Fryer Daniel Liebler Trevor Penning Terry Schultz I Glenn Sipes (Vice Chair) Yoshiki Tokura	Anne Marie Api Sanket Gadhia Aurelia Lapczynski Gretchen Ritacco Jim Romine Danielle Botelho (1/28 morning via webinar) Mihir Date (1/29 morning via webinar) Sai Yee Tsang (1/29 afternoon via webinar) Nikaeta Sadekar (1/28 afternoon via webinar)	Allison Hilberer (IIVS) (1/28 afternoon) Tobey Marzouk (1/28) Jessica Palmer (Stemina, 1/29 afternoon via webinar)

1) Discussion of the Meeting Schedule and Agenda Topics

a)Completion/Signing of Conflict of Interest Statement

Dr. Belsito opened the meeting. The Conflict of Interest Statement was signed. The Elsevier Conflict of Interest form was also signed

2) Minutes

The August 2019 Expert Panel Meeting minutes were approved with changes.

3) Follow-Up and Informational Items

a) Follow-Up List

Dr. Api reviewed the status of the items on the follow-up list; all items are either in progress and will be discussed later in the meeting or have been completed.

4) Standing Items (For Expert Panel information only; per Panel's request)

a) RIFM Publications

Dr. Api reviewed the RIFM publication list with the Panel. This is a standing item on the agenda, which provides a summary of all RIFM recent publications.

5) RIFM Communication

a) RIFM communication

Dr. Romine gave a presentation on plans for communicating RIFM science program (see Attachment 1). He also discussed the strategy for RIFM in the future (see Attachment 2 and Attachment 3)

b) Update to safety assessment publication

G. Sullivan provided a summary of an update on the progress made in submitting the publications to Elsevier.

6) Legal review

Pursuant to Section 14.3 of the Expert Panel's Operating Procedures (http://fragrancesafetypanel.org/policies-and-guidelines/operating-procedures/), Mr. Tobey Marzouk (Legal Counsel) conducted an annual review of current legal issues affecting the Expert Panel, conflict of interest guidelines, and Expert Panel procedures and guidelines. Mr. Marzouk addressed any questions that the Panel had.

The procedure and timing of the Expert Panel self-assessment survey was discussed. With input from the Panel and the direct assistance of Dr. Sipes, Mr. Marzouk will propose to the Panel questions to be included in the survey. The survey process should take approximately one year.

In accordance with Section 2.0 of the Expert Panel's Operating Procedures, the Panel Chair, Dr. Belsito, is scheduled to address the RIFM Board of Directors at the June 2019 Board Meeting. The Panel made some suggestions of topics to bring to the Board's attention.

RIFM Board of Directors Chair, Mr. Shawn Blythe, will give an informational presentation to the Panel at the September 2019 Panel Meeting.

7) RIFM Safety Evaluation Process

a) **Presentation RIFM Safety Assessment Update and Metrics (webinar on Monday)**

Dr. Botelho presented an update the 2018 RIFM Safety Assessment project (see Attachment 4).

b) Low Exposure Materials Manuscript

Dr. Api presented another draft of the low exposure manuscript which incorporated the Expert Panel's comments on the previous draft. The final supplemental data were also presented. The Panel had additional comments and changes. The paper can be submitted to the journal for peer review after the final comments and changes are made.

c) Safety Assessment Overview

Ms. Ritacco presented the safety assessment overview for the materials being reviewed during the meeting. There are 26 Safety Assessments covering 36 materials.

d) General Comments

i) Inhalation template change – in cases where inhalation data exist in the repeat dose section, but are not complete to derive a NOEC for local respiratory effects, the data should be referred to in the local respiratory effect section. A statement should be included to state that the data are not sufficient to derive a NOAEC and then follow with the fact that the exposure falls below the TTC.

ii) Section VIII – the section should remain in the safety assessment, but it should be renamed to "conclusion" and either state that the material is safety under the conditions of use or add the maximum acceptable use levels.

8) RIFM Read Across Procedure

a) Draft manuscript on RIFM read across process

Dr. Date gave a presentation on the concepts used in the manuscript (see Attachment 5).

9) Review Safety Assessments Batch 1

CAS	Name	Tab	Comments	Status
71-23-8	Propyl alcohol	**Tab 28**		
71-36-3	Butyl alcohol	**Tab 29**		
71-41-0	Amyl alcohol	**Tab 30**		
78-83-1	Isobutyl alcohol	**Tab 31**		
65-85-0	Benzoic acid	**Tab 32**		
100-09-4	4-Methoxybenzoic acid	**Tab 33**		
5240-32-4	1-Ethynylcyclohexyl acetate	**Tab 34**		
5333-42-6	2-Octyldodecan-1-ol	**Tab 35**		
10340-23-5	*cis*-3-nonen-1-ol	**Tab 36**		
546-79-2	4-Thujanol	**Tab 37**		

10) 2,3-Butenedione – Review carcinogenicity manuscript

The Panel reviewed the NTP inhalation study and the genotoxicity data. They suggested that a benchmark dose analysis should be conducted on the chronic study. While local tumors were observed, significant local irritation was also observed. Carcinomas were reported at doses of 50-100 ppm with very high irritation. Local neoplasms might indicate result of inflammation and no other tumors were observed in the lung or in any in other organ. An in vivo COMET/MNT assay with demonstration of target organ exposure using duodenum and liver may be considered. If an intraperitoneal administration is used, then liver may be sufficient because the material will be metabolized by the liver.

11) Presentation by Dr. Fryer – "Bronchoconstriction: why it is so hard to measure in vitro"

Dr. Fryer gave a presentation on bronchoconstriction (see Attachment 6).

12) Review of gamma-terpinene, alpha-terpinene, and alpha-phellandrene

CAS	Name	Tab	Status	Comment
99-85-4	p-Mentha-1,4-diene, gamma-terpinene	**Tab 42 NOTE: Safety Assessment was approved by the Expert Panel for Fragrance Safety in 2016**	Approved with changes	The Panel wants to edit gamma-terpinene and use the read across to alpha-terpinene for both the reproduction and sensitization endpoints. The repro study on alpha-terpinene is the better study; details on the study on gamma-terpinene are insufficient.

99-86-5	*p*-Mentha-1,3-diene, alpha-terpinene	**Tab 43**	**Approved**	
4221-98-1, 99-83-2, 1329-99-3	(-)-(R)-alpha-Phellandrene, alpha-Phellandrene, Phellandrene	**Tab 44**	**Approved**	

13) Review Safety Assessments Batch 2

CAS	Name	Tab
127-91-3, 18172-67-3	beta-Pinene, *l*-beta-Pinene	**Tab 45**
79-92-5, 5794-04-7	Camphene, *l*-Camphene	**Tab 46**
80-56-8, 7785-26-4, 7785-70-8	alpha-Pinene, *l*-alpha-Pinene, *d*-alpha-Pinene	**Tab 47**
62518-65-4	3-(m-tert-Butylphenyl)-2-methylpropionaldehyde	**Tab 48**
80-54-6	*p-t*-Butyl-alpha-methylhydrocinnamic aldehyde	**Tab 49**
108-29-2	gamma-Valerolactone	**Tab 50**
105-21-5	gamma-Heptalactone	**Tab 51**
104-50-7	gamma-Octalactone	**Tab 52**
104-61-0	gamma-Nonalactone	**Tab 53**
706-14-9	gamma-Decalactone	**Tab 54**
2305-05-7	gamma-Dodecalactone	**Tab 55**

14) Update on QRA2 Implementation

Dr. Api reported on the implementation of the QRA2. The safety assessments are now being processed to include the maximum acceptable concentrations. The Panel recommended that the section should be titled Conclusion and list the either have the maximum acceptable concentrations or state that the material is safe under the declared levels of use.

15) Review Safety Assessments – Batch 3

CAS	Name	Tab
470-82-6	Eucalyptol	**Tab 56**
30310-41-9, 68039-40-7, 68039-41-8	Tetrahydro-2-methyl-4-methylene-6-phenyl-2H-pyrane, 3,6-Dihydro-2,4-dimethyl-6-phenyl-2H-pyran, 3,6-Dihydro-4,6-dimethyl-2-phenyl-2H-pyran	**Tab 57**

CAS	Name	Tab
93893-89-1, 53243-60-0, 53243-59-7	3-Methyl-5-phenylpent-2-enenitrile, (E)-3-Methyl-5-phenylpent-2-enenitrile, (Z)-3-Methyl-5-phenylpent-2-enenitrile	Tab 58

16) Human Health Research Projects

a) Epidemiology

i) Validation of Clinical Relevance Algorithm

Prof. Bruze reported that the manuscript has been submitted to the British Journal of Dermatology and a second paper is being drafted. The EDEN group will meet in late March and there will be an update

b) Eugenol Elicitation Threshold draft report

We are still awaiting another draft report. Dr. Api will follow-up with a conference call

c) Presentation by Allison Hilberer – In Vitro Phototoxicity and Photoallergy Research Project (Monday afternoon)

Ms. Hilberer gave a presentation on the collaborative work between IIVS and RIFM (see Attachment 7).

d) Presentation by SY Tsang on in vitro developmental toxicity pilot study (via webinar Tuesday afternoon)

Ms. Jessica Palmer gave a presentation on an in vitro developmental toxicity model (devTOX^{qp}) (see Attachment 8).

e) Update on RIFM oral TTC research

Dr. Api provided an update on the RIFM oral TTC project, which is almost completed. A manuscript is in its final stages of development.

f) Presentation by S. Gadhia - Update on internal TTC research project and RIFM collaboration in the ILSI EU uncertainty in risk assessment project

Dr. Gadhia gave a presentation on RIFM collaboration with Cosmetic Europe on the internal TTC research project and RIFM collaboration in the ILSI EU uncertainty in risk assessment project (see Attachment 9).

g) Presentation by N. Sadekar - Update on RIFM inhalation TTC research (Monday afternoon webinar)

Dr. Sadekar gave a presentation to update the Panel on the RIFM inhalation TTC research project (see Attachment 10).

17) Presentation by A. Lapczynski on Environmental Safety Assessment and Research Projects

Ms. Lapczynski gave a presentation on the environmental safety assessment and research projects with some specific examples (see Attachment 11). It was agreed that RIFM should be involved in additional testing on OTNE.

18) IFRA Standards

a) Photosensitization Standards

The Panel recommended that products in Category 12 (products not intended for direct skin contact, minimal or insignificant transfer to skin) should be included for phototoxicity effects.

19) Future Meeting Dates

- Monday – Wednesday May 20-22, 2019 Rome

• Monday – Wednesday	Sept. 23-25, 2019	New Jersey
• Monday – Wednesday	Jan. 20-22, 2020	Delhi, India
• Thursday	Jan. 23, 2020	INFOX India - Delhi, India
• Monday – Wednesday	May 18-20, 2020	Chicago
• Monday – Wednesday	Sept. 21-23, 2020	New Jersey
• Wednesday – Friday	Jan. 20-22, 2021	Puerto Rico?

Respectfully submitted,

Anne Marie Api, PhD
Vice President, Human Health Sciences
(date finalized)

Attachment 1:	Dr. Romine presentation on the RIFM d communication
Attachment 2 and 3:	Dr. Romine presentation on strategy for the future of RIFM
Attachment 4:	Dr. Botelho presentation on the safety assessment process
Attachment 5:	Dr. Date presentation on the concepts used in the manuscript
Attachment 6:	Dr. Fryer presentation on bronchoconstriction
Attachment 7:	Ms. Hilberer presentation on the collaborative work between IIVS and RIFM
Attachment 8:	Ms. Jessica Palmer presentation on an in vitro developmental toxicity model (devTOX^{qp})
Attachment 9:	Dr. Gadhia presentation on RIFM collaboration with Cosmetic Europe on the internal TTC research project and RIFM collaboration in the ILSI EU uncertainty in risk assessment
Attachment 10:	Dr. Sadekar gave a presentation to update the Panel on the RIFM inhalation TTC research project
Attachment 11:	Ms. Lapczynski presentation on the environmental safety assessment and research projects