EXPERT PANEL FOR FRAGRANCE SAFETY MEETING

Minutes

January 20-22, 2020

EXPERT PANEL MEMBERS	RIFM STAFF	GUESTS
Donald Belsito (Chair) Magnus Bruze G. Allen Burten, Jr. Maria Dagli Wolfgang Dekant Allison Fryer Trevor Penning Terry Schultz I Glenn Sipes (Vice Chair) Yoshiki Tokura	Anne Marie Api Shannen Biserta Danielle Botelho Kaushal Joshi Jim Romine Nikaeta Sadekar	Kaushal Verma (2/20)

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. Drs. Buschmann and Liebler sent their regrets for not being able to attend the Panel meeting.

Dr. Api announced the formation of the Environmental Adjunct Panel - Scott D. Dyer, LeTourneau University, Paul C. DeLeo, Integral Consulting, Inc., Daniel Schlenk, Department of Environmental Sciences, University of California, Riverside, Dr. Mick Whelan, University of Leicester. Dr., Allen Burton and Terry Schultz are the Panel Liaisons.

A new member was added to the reproduction Adjunct Panel - John DeSesso, Exponent. He replaces Dr. Jodi Flaws, who had to leave the Adjunct Panel because of other obligations.

Dr. Api also announced the addition of two post-doctoral fellows to the RIFM Staff – Drs Holger Moustakas and Isabelle Bell. In addition, beginning on February 3, a new full-time computation chemist will join the RIFM Staff – Dr. Manoj Kumar.

2) Minutes

The minutes from the September 2019 meeting were approved.

3) Follow-Up and Informational Items

a) Follow-Up List

Dr. Api went through the follow-up list and provided updates on items and general comments where applicable.

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

a) RIFM Publications

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

5) RIFM Communication

a) RIFM communication update

Dr. Romine gave a presentation that provided an update on RIFM's communication plans (see Attachment 1).

b) Aromatherapy

Drs. Romine and Api gave presentations on aromatherapy (see Attachments 2 and 3).

c) Update to safety assessment publication

The Panel reviewed the progress of the publication of safety assessments in Food and Chemical Toxicology. The total number of published safety assessments in Food and Chemical Toxicology and on the Fragrance Material Safety Resource Center is 562 and a total 694 have been submitted. The total number of approved safety assessments is 1003.

6) RIFM Safety Evaluation Process

a) **Presentation RIFM Safety Assessment Update and Metrics**

Dr. Botelho gave a presentation that reviewed the last quarter of 2019 as well as the entire last year (see Attachment 4).

b) Safety Assessment Overview

The Panel reviewed 71 Total Safety Assessments including 87 Total materials.

c) General Comments

i) Read across – there is a need to streamline the process so that the changes in acceptable read across are minimized. All the read across should be reviewed prior to writing the safety assessment. In addition, for materials with a long write-up can be sent for a review of the read across materials. The exceptions to the rules are still being developed.

7) Update on QRA2 Implementation

a) **Dr. A.M. Api Presentation on QRA2**

Dr. Api gave a presentation on the what was learned from implementing the QRA2 in the IFRA 49th Amendment (see Attachment 5).

8) NCS Safety Assessments

a) Review general approach

The general approach that will be used to conduct a safety assessment on natural complex substances (NCSs) was reviewed with the Panel. The Panel recommended that all terms be clearly defined and standardized in a criteria document for NCSs.

b) Safety Assessment Review

The Panel reviewed the safety assessments for three NCSs and some general comments were made.

- Add plant taxonomy in the NCS definition on the first page
- For NCS Cramer Class III will be used; add templated text to the safety assessment to describe why CC III is used in the front of the document
- For each section: Table 1: Systemic exposure to the NCS for genotoxicity TTC; Table 2 Genotoxicity analysis for the component of the NCS
- Include RA in the abbreviation list
- Use CAS # not "#" only.

- Need to renumber all the Tables throughout the safety assessment
- Be consistent in the different way CAS Numbers and Material names are used in each section
- Repeat Dose Table add a footnote that the lowest MOE is X
- Phototoxicity/photoallergy: if there was no UV absorption on all the substances, then UV Absorption on the NCS will not be needed.
- Need a clarifying statement in the environmental section that the volume of use is derived and why the total amount of the individual material is not added together.

The following drafts were evaluated by the Panel. The Panel requested that updated drafts are provided at the next meeting after the recommended changes are made to the draft safety assessments.

i) 1042479 Petitgrain oil Terpeneless, Paraguay

ii) 1043739 Petitgrain oil terpenes, Paraguay

iii) 1046350 Petitgrain oil, Paraguay

c) NCS Safety Assessment publication

Change the bands to 1-10, 11-25, 26-50, >51

9) Presentation by Prof. Prof. (Dr.) Kaushal Verma, MD, FRCP, FAMS, FIMSA, Inspiring Physician - Royal College of Physicians Edinburgh, UK; Professor Department of Dermatology and Venereology, All India Institute of Medical Sciences, New Delhi - Monday January 20

Parthenium Allergy in India

Prof. Verma gave a presentation on parthenium allergy in India (see Attachment 6).

10) Review Safety Assessments Batch 1

CAS	Name	Tab	Status
76649-16-6	Ethyl trans-4-decenoate	Tab 24	Approved
7367-88-6	Ethyl trans-2-decenoate	Tab 25	Approved
470-67-7	1,4-Cineole	Tab 26	Approved
526218-21-3	1-(2-Methylprop-2-enoloxy)-2,2,4-trimethylpentan-3-ol	Tab 27	Approved
141-79-7	4-Methyl-3-penten-2-one	Tab 28	Approved
2679-87-0	sec-Butyl ethyl ether	Tab 29	Approved
141773-73-1	2-(1-(3',3'-Dimethyl-1'-cyclohexyl)ethoxy)-2-methyl propyl propanoate	Tab 30	Approved
37172-02-4	2-(1-Methylpropyl)-1-vinylcyclohexyl acetate	Tab 31	Approved
6378-65-0	Hexyl hexanoate	Tab 32	Approved
4643-27-0	2-Octen-4-one	Tab 33	Approved
1669-44-9	3-Octen-2-one	Tab 34	Approved

CAS	Name	Tab	Status
10519-33-2	3-Decen-2-one	Tab 35	Approved
88-09-5	2-Ethylbutyric acid	Tab 36	Approved
646-07-1	4-Methylpentanoic acid	Tab 37	Approved
105-43-1	3-Methylpentanoic acid	Tab 38	Approved
105-85-1; 141-09-3	Citronellyl formate; Rhodinyl formate	Tab 39	Approved
141-16-2; 141-15-1	Citronellyl butyrate; Rhodinyl butyrate	Tab 40	Approved
150-84-5; 67601-05-2; 141-11-7	Citronellyl acetate; 3,7-Dimethyloct-6-enyl acetate; Rhodinyl acetate	Tab 41	Approved
141-14-0; 105-89-5	Citronellyl propionate; Rhodinyl propionate	Tab 42	Approved
7540-53-6	Citronellyl valerate	Tab 43	Approved
14374-92-6	4-Isopropyl-1-methyl-2-propenylbenzene	Tab 44	Approved with changes
94400-98-3	(1aalpha,4alpha,7aalpha)-1a,3,3,4,6,6-Hexamethyl-1a,2,3,4,5,6,7,7a-octahydronapth[3,3-b]oxirene	Tab 45	Insufficient data - sensitization
2810-04-0	2-Thiophenecarboxylic acid, ethyl ester	Tab 46	Approved with changes

11) RIFM Research Projects

a) Epidemiology Project Update

ROAT study report is being drafted and an abstract is being submitted at the ESCD. Eugenol study will be finished by Robert Ofenloch.

b) Final draft oral TTC manuscript

i) Presentation by K Joshi on TTC manuscript

Dr. Joshi gave a presentation on the oral TTC research project at RIFM in collaboration with scientists at P&G (see Attachment 7).

c) **Presentation by N. Sadekar on respiratory research program and the inhalation TTC project**

Dr. Sadekar gave a presentation on the inhalation TTC research project at RIFM in collaboration with scientists at P&G. She also gave an update on the respiratory research program. (see Attachment 8).

d) **Presentation by K Joshi on reproduction research program**

Dr. Joshi gave a presentation on the oral TTC research project at RIFM in collaboration with scientists at P&G (see Attachment 9).

12) Review Safety Assessments Batch 2

CAS	Name	Tab	Status
97-89-2; 138-23-8	Citronellyl isobutyrate; Rhodinyl isobutyrate	Tab 47	Approved

CAS	Name	Tab	Status
68922-10-1; 7778-96-3	Citronellyl isovalerate; Rhodinyl isovalerate	Tab 48	Approved
68901-22-4	2-Methyl-4-(camphenyl-8)-cyclohexanone	Tab 49	Approved
60405-50-7; 35151-11-2	5-Phenylhex-3-en-2-one; 5-Phenylhex-4-en-2-one	Tab 50	Approved
39067-80-6; 38237-00-2	Thiogeraniol; 2,6-Octadiene-1-thiol, 3,7-dimethyl-	Tab 51	Approved
75-18-3	Dimethyl sulfide	Tab 52	Approved
692-86-4	Ethyl 10-undecenoate	Tab 53	Approved
592-88-1	Allyl sulfide	Tab 54	Approved with changes
30168-23-1	4-Tricyclodecylidene butanal	Tab 55	Approved
821-55-6	2-Nonanone	Tab 56	Approved with changes
693-54-9	2-Decanone	Tab 57	Approved with changes
67634-08-6	Tetrahydro-.alpha.-pentylfurfuryl acetate	Tab 58	Approved with changes
611-13-2	Methyl 2-furoate	Tab 59	Insufficient data - genotoxicity
10031-90-0	Ethyl 3(2-furyl)propanoate	Tab 60	Approved
79-31-2	Isobutyric acid	Tab 61	Approved with changes
60308-76-1; 60308-75-0	2-Octenoic acid, 4-ethyl-, (2E)-; 2-Octenoic acid, 4-ethyl-, (2Z)-	Tab 62	Approved
542-55-2	Isobutyl formate	Tab 63	Approved
10588-10-0	2-Methylpropyl pentanoate	Tab 64	Approved
55590-83-5	Pentanoic acid, 2-methylbutyl ester	Tab 65	Approved
75-85-4	2-methyl-2-butanol	Tab 66	Approved
621-27-2	3-Propylphenol	Tab 67	Approved
82461-14-1; 99343-90-5	2,4-Dimethyl-4-phenyltetrahydrofuran; Furan, tetrahydro-2,4-dimethyl-4-phenyl-, (2R,4R)-rel-	Tab 68	Approved with changes
51755-66-9	3-(Methylthio)-1-hexanol	Tab 69	Approved
20489-53-6	Dihydronootkatone	Tab 70	Approved
4112-89-4	Guaiacyl phenylacetate	Tab 71	Approved with changes
851768-51-9	3-Hexanone, 5-mercapto-5-methyl-	Tab 72	Approved
41239-48-9	2,5-Diethyltetrahydrofuran	Tab 73	Approved with changes

CAS	Name	Tab	Status
2435-16-7	2-Heptyltetrahydrofuran	Tab 74	Approved with changes
38462-22-5	p-Mentha-8-thiol-3-one	Tab 75	Approved
125352-06-9	pyridine, 4-ethenyl-, reaction products with 3a,4,7,7a-tetrahydrodimethyl-4,7-methano-1H-indene	Tab 76	Approved with changes
3720-16-9	3-Methyl-5-propyl-2-cyclohexen-1-one	Tab 77	Approved
632-15-5	3,4-Dimethylthiophene	Tab 78	Approved with changes
1708-81-2	3-hepten-1-ol, (3z)-	Tab 79	Approved
57074-37-0	cis-4-Decenol	Tab 80	Approved
478695-70-4	Propanedioic acid, 1-(3,3-dimethylcyclohexyl) ethyl, ethyl ester	Tab 81	Approved
3208-40-0	2-(3-Phenylpropyl)tetrahydrofuran	Tab 82	Approved
13215-88-8; 163440-97-9	4-(2-Butenylidene)-3,5,5-trimethylcyclohex-2-en-1-one	Tab 83	Approved
155514-23-1	Butanoic acid, 2-methyl-, 5-hexen-?1-yl ester	Tab 84	Approved
17369-59-4	3-Propylidenephthalide	Tab 85	Approved with changes
59020-90-5	2-Furanmethanethiol formate	Tab 86	Approved
13678-68-7	Furfuryl thioacetate	Tab 87	Approved
144-62-7	Ethanedioic acid	Tab 88	Approved with changes
224031-70-3; 224031-71-4	4-Penten-1-one, 1-spiro[4.5]dec-7-en-7-yl-; 4-Penten-1-one, 1-spiro[4.5]dec-6-en-7-yl-	Tab 89	Approved
123-63-7	Paraldehyde	Tab 90	Approved with changes
110-93-0; 409-02-9	6-Methyl-5-hepten-2-one	Tab 91	Approved
2550-11-0	4,7-Dimethyloct-6-en-3-one	Tab 92	Approved
16587-71-6	4-t-Amylcyclohexanone	Tab 93	Approved
29895-73-6; 4740-79-8; 5694-72-4	Phenylacetaldehyde glyceryl acetal	Tab 94	Approved

13) Presentation by Alok Dhawan, Director, CSIR-Indian Institute of Toxicology Research on CSIR

Dr. Dhawan was unable to attend the Panel meeting.

14) Expert Panel Operating Procedures

a) Review Tenure

The Panel is aware their operating procedures has a term limit. They decided to suspend term limits until the safety assessment workload is completed.

b) Elect Chair/Co-Chair

Dr. Belsito was voted in for a second term as Chair of the Expert Panel for Fragrance Safety. The vote for Vice-Chair was postponed until the next meeting.

15) Expert Panel Executive Session

The Expert Panel held an executive session.

16) Future Meeting Dates

• Monday – Wednesday	May 18-20, 2020	Chicago
• Monday – Wednesday	Sept. 21-23, 2020	New Jersey
• Wednesday – Friday	Jan. 20-22, 2021	Puerto Rico
• Monday – Wednesday	May 30-June 2, 2021	Lisbon
• Monday – Wednesday	Sept. 20-22, 2021	New Jersey
• Monday-Wednesday	Jan. 24-26, 2022	Miami

Respectfully submitted,

Anne Marie Api

Anne Marie Api, PhD
Vice President

Attachment 1:	Presentation: Dr. James Romine
Attachment 2	Presentation: Dr. James Romine
Attachment 3:	Presentation: Dr. Anne Marie Api
Attachment 4:	Presentation: Dr. Danielle Botelho
Attachment 5:	Presentation: Dr. Anne Marie Api
Attachment 6:	Presentation: Dr. Kaushal Verma
Attachment 7:	Presentation: Dr. Kaushal Joshi
Attachment 8:	Presentation: Dr. Nikaeta Sadekar
Attachment 9:	Presentation: Dr. Kaushal Joshi