

EXPERT PANEL FOR FRAGRANCE SAFETY MEETING

Minutes

January 22-24, 2024

San Diego

EXPERT PANEL MEMBERS	RIFM STAFF		Guests
Donald Belsito (Chair) Magnus Bruze Amanda Bryant-Friedrich G. Allen Burton, Jr. Maria Dagli (Vice-Chair) Wolfgang Dekant Allison Fryer Debra Laskin Trevor Penning I Glenn Sipes Yoshiki Tokura	Anne Marie Api Adrianna Bartlett Danielle Botelho (Virtual) Olive Chon (Virtual) Chaitra Deodhar Leah Jones Kaushal Joshi Aurelia Lapczynski (Virtual) Maura Lavelle (Virtual) Isabelle Lee (Virtual) Holger Moustakas	Jake Muldoon Gretchen Ritacco (Virtual) Nikaeta Sadekar (Virtual) Isabella Schember (Virtual) Faiz Siddiqi (Virtual) Gary Sullivan (Virtual) Yax Thakkar (Virtual)	Joseph Romano (1/22, pm) Jim McKim (1/23, virtual)

1) Discussion of the Meeting Schedule and Agenda Topics

- a) Completion/Signing of the Conflict-of-Interest Statement

Dr. Belsito opened the meeting. The Conflict-of-Interest Statement was signed.

2) Minutes

The minutes from the September 2023 meeting were approved with no changes.

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's recent publications.

- b) RIFM Safety Assessment Publications

The Panel reviewed the RIFM safety assessment publications list. This list is an ongoing list of all the published safety assessments.

5) RIFM Communication

a) Update on RIFM

Dr. Api provided an overview of RIFM activities (see Attachment 1).

b) Communications Update

Mr. Sullivan provided an update on the RIFM communication plans, safety assessment publications, and the Fragrance Resource Center website (see Attachment 2).

6) RIFM Safety Evaluation Process

a) **Presentation RIFM by D. Botelho Safety Assessment Update and Metrics**

Dr. Botelho gave a presentation on the progress of the safety assessment program including the safety assessment update and metrics on naturals (see Attachment 3)

b) Safety Assessment Overview

i) (37 Total Safety Assessments including 39 Total materials)

c) General Comments

i) Photoallergy statement

7) Presentation by Dr. Joseph D. Romano, Assistant Professor of Informatics and Pharmacology, Department of Biostatistics, Epidemiology, and Informatics, University of Pennsylvania (Monday afternoon)

Dr. Romano gave a presentation on the use of artificial intelligence approaches to fragrance ingredient risk assessments (see Attachment 4).

8) Endocrine Disruptors

a) **Presentation by K. Joshi, A. Bartlett, F. Siddiqi - Update on RIFM summary of all reproduction/fertility data**

Drs. Joshi and Barlett gave a presentation updating the Expert Panel on the project RIFM has undertaken to review all reproduction, fertility, and endocrine disruption data (see Attachment 5).

b) **Presentation by Prof. Wolfgang Dekant**

Dr. Dekant gave a presentation to review endocrine disruption framework in Europe (see Attachment 6). This will continue to be discussed at the May Expert Panel meeting.

9) Review Safety Assessments Batch 1

CAS #	Material Name	Tab	Status
15149-10-7	2-(4-Methylphenoxy)ethanol	Tab 16	Approved with changes
4359-47-1	2-(3-Heptyl)-1,3-dioxolane	Tab 17	Approved, MAC
39900-38-4	Cedryl formate	Tab 18	Approved, MAC
77-54-3	Cedryl acetate	Tab 19	Insufficient data, skin absorption, MAC
13567-39-0	Cedr-8-ene epoxide	Tab 20	Approved, MAC
26619-69-2	Isolongifolene oxide	Tab 21	Approved, MAC

10) Rose Ketones (Tab 22)

CAS #	Material Name	Tab	Status
23726-92-3 (RIFM ID: 1299)	(Z)-beta-1-(2,6,6-Trimethyl-1-cyclohexen-1-yl)-2-buten-1-one	Tab 23	Approved with changes; Need a statement on all Rose ketones
39872-57-6 (RIFM ID: 1215)	(E)-1-(2,4,4-Trimethyl-2-cyclohexen-1-yl)-2-buten-1-one	Tab 24	Approved with changes; Need a statement on all Rose ketones
43052-87-5 (RIFM ID: 1298)	alpha-1-(2,6,6-Trimethyl-2-cyclohexen-1-yl)-2-buten-1-one	Tab 25	Insufficient data; need additional Genotoxicity data from IOFI; Need a statement on sensitization all Rose ketones; need cross sensitization
57378-68-4 (RIFM ID: 1300)	delta-1-(2,6,6-Trimethyl-3-cyclohexen-1-yl)-2-buten-1-one	Tab 26	Approved with changes; Need revised uncertainty factor; Need a statement on all Rose ketones
23696-85-7 (RIFM ID: 1297)	1-(2,6,6-Trimethylcyclohexa-1,3-dienyl)-2-buten-1-one	Tab 27	Approved with changes; Need revised uncertainty factor; Need a statement on all Rose ketones
35087-49-1 (RIFM ID: 6402)	1-(2,2-Dimethyl-6-methylenecyclohexyl)but-2-en-1-one	Tab 28	Approved with changes; Need revised uncertainty factor; Need a statement on all Rose ketones

11) Presentation by Prof. Bruze “Preliminary results on MECs of fragrance substances, individually and combined.”

Prof. Bruze gave a presentation providing preliminary results on MECs of fragrance substances (See Attachment 7).

12) Review Safety Assessments Batch 2

CAS#	Material Name	Tab	Status
39255-32-8	Ethyl 2-methylpentanoate	Tab 29	Approved
2983-37-1	Ethyl 2-ethylhexanoate	Tab 30	Approved
6297-41-2	Butyl 2-methylvalerate	Tab 31	Approved
67707-75-9	Ethyl 3,5,5-trimethylhexanoate	Tab 32	Approved
100-86-7	alpha,alpha-Dimethylphenethyl alcohol	Tab 33	Approved
103-05-9	2-Methyl-4-phenyl-2-butanol	Tab 34	Approved
122-48-5	Zingerone	Tab 35	Approved with changes, MAC
96840-56-1	2-Ethoxy-4-[(1-methylethoxy)methyl] phenol	Tab 36	Approved with changes, MAC
60788-25-2	Citronellyl ethyl oxalate	Tab 37	Approved
57371-42-3	4-Allyl-2-methoxyphenyl benzyl ether	Tab 38	Approved
6413-26-9	cyclohexanone 1,3-butylene glycol ketal	Tab 39	Approved with changes
62406-73-9	6,10-Dioxaspiro[4.5]decane, 8,8-dimethyl-7-(1-methylethyl)-	Tab 40	Insufficient data: tier 3 search or need skin absorption
90-17-5	Trichloromethyl phenyl carbonyl acetate	Tab 41	Approved
63187-91-7	d,l-Menthone 1,2-glycerol ketal	Tab 42	Approved
89-83-8	Thymol	Tab 43	Approved
99-89-8	4-Isopropylphenol	Tab 44	Approved
103-50-4	Dibenzyl ether	Tab 45	Approved, MAC

13) Review Safety Assessments Batch 3

CAS #	Material Name	Tab	Status
24237-00-1; 24237-02-3	6-Butyl-2,4-dimethyldihydropyrane	Tab 46	Approved
120-57-0	Piperonal	Tab 47	Approved, MAC
142-19-8	Allyl heptanoate	Tab 48	Approved with changes
123-68-2	Allyl hexanoate	Tab 49	Approved
4230-97-1	Allyl octanoate	Tab 50	Approved
66-25-1	Hexanal	Tab 51	Approved, MAC
111-71-7	Heptanal	Tab 52	Approved, MAC
124-13-0	Octanal	Tab 53	Approved, MAC
124-19-6	Nonanal	Tab 54	Approved, MAC
112-31-2	Decanal	Tab 55	Approved, MAC
112-44-7	Undecanal	Tab 56	Approved, MAC
10486-19-8	Tridecanal	Tab 57	Approved, MAC
128-51-8; 35836-72-7	Nopyl acetate	Tab 58	Approved, MAC
51115-67-4	2-Isopropyl-N,2,3-trimethylbutyramide	Tab 59	Approved with changes

14) Review Safety Assessments Maintenance Batch

CAS#	Material Name	Tab	Status
5595-79-9	2-Ethoxy-4-(methoxymethyl)phenol	Tab 61	Approved, MAC
589-18-4	p-Tolyl alcohol	Tab 62	Approved
536-60-7	p-Isopropylbenzyl alcohol	Tab 63	Approved with changes gentox
67845-46-9	(4-Methylphenoxy)acetaldehyde	Tab 64	Approved with changes, MAC
72089-08-8	2-Methyl-4(2,2,3-trimethyl-3-cyclopentenyl)butanol	Tab 65	Approved, MAC
326-61-4	Piperonyl acetate	Tab 66	Approved
56172-46-4	Geranyl crotonate	Tab 67	Approved, MAC
88-09-5	2-Ethylbutyric acid	Tab 68	Approved
646-07-1	4-Methylpentanoic acid	Tab 69	Approved
105-43-1	3-Methylpentanoic acid	Tab 70	Approved
97-61-0	2-Methylvaleric acid	Tab 71	Approved
1561-11-1	Hexanoic acid, 4-methyl-	Tab 72	Approved
4536-23-6	2-Methylhexanoic acid	Tab 73	Approved
1188-02-9	2-Methylheptanoic acid	Tab 74	Approved
54947-74-9	4-Methyloctanoic acid	Tab 75	Approved
16493-80-4	4-Ethyloctanoic acid	Tab 76	Approved
45019-28-1	4-Methylnonanoic acid	Tab 77	Approved
78-37-5	Linalyl cinnamate	Tab 78	Approved
111-12-6	Methyl 2-octynoate	Tab 79	Approved, MAC
111-80-8	Methyl 2-nonynoate	Tab 80	Approved, MAC
7070-15-7	exo-2-[(1,7,7-Trimethylbicyclo[2.2.1]hept-2-yl)oxy]ethanol	Tab 81	Approved
112-72-1	1-Tetradecanol	Tab 82	Approved, MAC
59259-38-0; 61597-98-6; 17162-29-7	l-Menthyl lactate	Tab 83	Approved
93981-50-1	Ethyl 2,3,6-trimethylcyclohexyl carbonate	Tab 84	Approved
56836-93-2	Benzenepropanol, α,β -dimethyl-	Tab 85	Approved with changes, gentox
76649-25-7	3,6-Nonadien-1-ol	Tab 86	Approved
1322-17-4	1,3-Nonanediol acetate (mixed esters)	Tab 87	Approved
1569-60-4	2-Methyl-2-hepten-6-ol	Tab 88	Approved, MAC
40596-76-7; 379693-55-7	4,8-Dimethyl-7-nonen-2-ol	Tab 89	Approved, MAC

CAS#	Material Name	Tab	Status
472-97-9; 56747-96-7; 4586-22-5	beta-Caryophyllene alcohol	Tab 90	Approved, MAC
13466-78-9	delta-3-Carene	Tab 91	Approved with changes, MAC
125-12-2; 5655-61-8; 76-49-3	Isobornyl acetate	Tab 92	Approved

15) RIFM Research Projects

a) Overview of research programs

Dr. Api proposed to have an orientation for new Panel members to the RIFM safety assessment process as well as the RIFM Research Program. In addition, it was proposed that all RIFM research programs be reviewed at the September meeting and therefore limit external speakers and focus on the RIFM staff. The Panel agreed to both proposals.

b) Epidemiology

Prof Bruze reported that EDEN is planning to submit another paper on psoriasis. As part of IDEA an extended surveillance study is planned.

c) Chemistry

i) Chemical Signature paper

Dr. Muldoon gave a presentation on the RIFM chemical structure signature project and the progress of the paper (see Attachment 8).

d) Environmental Research Program Update

Ms. Laczynski gave an update on the Koc testing and the biodegradation summary (see Attachment 9).

e) Skin Sensitization Research Projects

i) **Presentation by I. Lee/H. Moustakas on epoxide research update**

Drs. Lee and Moustakas gave an update on skin sensitization chemistry research (see Attachment 10).

f) Phototoxicity and Photoallergy

i) **Presentation by C. Deodhar on the ROS Assay**

Dr. Deodhar presented the preliminary results from the ROS Assay (see Attachment 11). A list of proposed materials for the next phase will be circulated focusing on materials that absorb but are not photoallergens.

ii) **Presentation by G. Ritacco on Proposed Project**

Ms. Ritacco gave a presentation on a proposed research project from Dr. Elena Gimenez (U. Strasbourg) (see Attachment 12). Ms. Ritacco will circulate the proposal and gather comments by the end of February. Dr. Gimenez will be invited to the May Expert Panel meeting.

g) Repeat Dose Toxicity

i) **Presentation by J. McKim, IONTOX, Tuesday 9AM**

Dr. McKim gave a presentation on the research project which was a pilot study to evaluate the kinetics and metabolism of test compounds in a three-organ integrated model (see Attachment 13).

16) IFRA Standards Proposal

The Panel reviewed the draft IFRA Standards on Furocoumarins and agreed with the proposed Standard.

17) New Expert Panel Members

The January 2024 meeting will be Dr. Tokura's last meeting; he will be retiring from the Panel. The Panel wished him well and expressed their gratitude for his ten years of service. Dr. Terry Schultz has announced his intention to retire from the Panel at the end of 2024.

18) Panel Executive Session

The Expert Panel held an Executive Session.

19) Future Meeting Dates

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|---------------------|------------------------------|----------------|
| • Monday-Wednesday, | May 20-22, 2024 | Edinburgh |
| • Wednesday-Friday, | September 25-27, 2024 | New Jersey |
| • Monday-Wednesday, | January 27-29, 2025 | Puerto Rico |
| • Wednesday-Friday, | May 28-30, 2025 | Krakow, Poland |
| • Monday-Wednesday, | September 29-October 1, 2025 | NY/NJ |
| • Monday-Wednesday, | January 26-28, 2026 | TBD |

Respectfully submitted,



Anne Marie Api, Ph.D., ATS
President

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| Attachment 1: | Presentation: Dr. Anne Marie Api |
| Attachment 2: | Presentation: Mr. Gary Sullivan |
| Attachment 3: | Presentation: Dr. Danielle Botelho |
| Attachment 4: | Presentation: Dr. Joseph Romano |
| Attachment 5: | Presentation: Drs. Kaushal Joshi and Arianna Bartlett |
| Attachment 6: | Presentation: Prof. Wolfgang Dekant |
| Attachment 7: | Presentation: Prof. Magnus Bruze |
| Attachment 8: | Presentation: Dr. Jake Muldoon |
| Attachment 9: | Presentation: Ms. Aurelia Lapczynski |
| Attachment 10: | Presentation: Drs. Isabelle Lee and Holger Moustakas |
| Attachment 11: | Presentation: Dr. Chaitra Deodhar |
| Attachment 12: | Presentation: Ms. Gretchen Ritacco |
| Attachment 13: | Presentation: Dr. James McKim |