

EXPERT PANEL FOR FRAGRANCE SAFETY MEETING

DRAFT AGENDA

May 20-22, 2019

Rome, Italy

Start 9:00 AM

- | | |
|---|-------------------|
| 1) Discussion of the Meeting Schedule and Agenda Topics | DVB |
| a) Completion/Signing of Conflict of Interest Statement | AMA |
| b) Completion/Signing of Elsevier Conflict of Interest Form | AMA |
| 2) Minutes (Tab 01) (Tab 02) (Tab 03) (Tab 04) (Tab 05) (Tab 06) (Tab 07) (Tab 08) (Tab 09) (Tab 10) (Tab 11) (Tab 12) AMA | |
| 3) Follow-Up and Informational Items | |
| a) Follow-Up List (13) | AMA |
| 4) Standing Items (For Expert Panel information only; per Panel's request) | |
| a) RIFM Publications (Tab 14) | AMA |
| 5) RIFM Communication | |
| a) RIFM communication update | JR |
| b) Update to safety assessment publication (Tab 15) | DB |
| 6) Prof. dr. Maurice Whelan, head of the Chemical Safety and Alternative Methods Unit of the Directorate for Health, Consumers and Reference Materials of the European Commission's Joint Research Centre (JRC) Presentation (Monday May 20) | |
| 7) Prof. Dr. Brunhilde Blömeke, Umwelttoxikologie/Head of the Department of Environmental Toxicology Presentation: COCAT – A HaCaT/THP-1 coculture model to estimate skin sensitization potential and potency in vitro. (Tuesday morning May 21) | |
| 8) Dr. Jochen Buschmann Presentation Testing for Endocrine Disruptors | |
| 9) RIFM Safety Evaluation Process | |
| a) Presentation RIFM Safety Assessment Update and Metrics | DB |
| b) Update on Low Exposure Materials manuscript | AMA |
| c) Safety Assessment Overview (Tab 16) | (DB/Staff) |
| i) (119 Safety Assessments covering 148 materials) | |

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d) General Comments

10) Maria Dagli Presentation on carcinogenesis, thresholds, modes of action

11) Sensitization summary on cinnamyl acetate and related esters (Tab 17)

DOB

12) Review Safety Assessments Batch 1

CAS	Name	Tab
81925-81-7 and 102322-83-8	5-Methyl-2-hepten-4-one	Tab 18
13877-91-3 and 3338-55-4	3,7-Dimethyl-1,3,6-octatriene	Tab 19
123-35-3	Myrcene	Tab 20
2436-90-0	Dihydromyrcene	Tab 21
1139-30-6	Caryophyllene oxide	Tab 22
2563-07-7	2-Ethoxy-4-methylphenol	Tab 23
13257-44-8	2-Nonyn-1-yl dimethylacetal	Tab 24
13019-22-2	9-Decen-1-ol	Tab 25
112-43-6	Undecen-1-ol	Tab 26
118562-73-5	Cyclododecaneethanol, .beta.-methyl-	Tab 27
929625-08-1	2-(2,2,7,7-Tetramethyltricyclo[6.2.1.0 ^{1,6}]undec-5-en-5-yl)propan-1-ol	Tab 28
55066-48-3	3-Methyl-5-phenylpentanol	Tab 29
93-28-7	eugenyl acetate	Tab 30
100-42-5	Styrene	Tab 31
28664-35-9	4,5-Dimethyl-3-hydroxy-2,5-dihydrofuran-2-one	Tab 32
3658-77-3	4-Hydroxy-2,5-dimethyl-3(2H)-furanone	Tab 33
27538-09-6 and 27538-10-9	2-Ethyl-4-hydroxy-5-methyl-3(2H)-furanone	Tab 34
2785-89-9	4-Ethylguaiacol	Tab 35
13794-73-5	Isocedranone	Tab 36
25966-79-4	3-Thujopsanone	Tab 37

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629-19-6	Dipropyl disulfide	Tab 38
37677-14-8 and 52475-89-5	Isohexenyl cyclohexenyl carboxaldehyde	Tab 39
56107-04-1	3-(p-tert-Butylphenyl)-2-methyl propanol (Lysmerol)	Tab 40
2035-93-0	4-methyl-4-phenylpentan-2-ol;b enzenepropanol, α,γ,γ -trimethyl-;2-pentanol, 4-methyl-4-phenyl-;benzenepro panol, α, γ,γ -trimethyl-	Tab 41
123-76-2	Levulinic acid	Tab 42
28043-10-9	Methyl 2,6,6-trimethylcyclohex-2-ene- 1-carboxylate	Tab 43
815580-59-7; 540734-22-3	3-Cyclohexene-1-carboxylic acid, 2,6,6-trimethyl-, methyl ester	Tab 44
57934-97-1 and 77851-07-1	Ethyl 2-ethyl-6,6-dimethylcyclohex-2- ene-1-carboxylate	Tab 45
94333-50-3	Ethyl 2-ethyl-3,6,6-trimethylcyclohex enecarboxylate	Tab 46
138-22-7	Butyl lactate	Tab 47
65405-69-8	Cyclohexyl cyclopent-2-ene-1-acetate	Tab 48
87-91-2	Diethyl tartrate	Tab 49
33885-51-7	6,6-Dimethylbicyclo[3.1.1]hept- 2-ene-2-propionaldehyde	Tab 50
68527-82-2	Octane, 1,1-bis(octyloxy)-	Tab 51
7779-94-4	Hydroxycitronellal diethyl acetal	Tab 52
1708-34-5	2-Hexyl-1,3-dioxolane	Tab 53
358331-95-0; 357650-26-1; 847144-75-6	5,6,7-Trimethylocta-2,5-dien-4- one	Tab 54
68922-12-3 and 68141-16-2	10-Dodecen-3-one, 5-hydroxy-7,11-dimethyl-	Tab 55
108-94-1	Cyclohexanone	Tab 56

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28940-11-6	7-Methyl-2H-benzo-1,5-dioxepin-3(4H)-one	Tab 57
34131-98-1	6-Isopropyl-2(1H)-octahydrophthalenone	Tab 58
30640-46-1; 1489-56-1; 1888-90-0; 1489-57-2	Methyl cyclohexadiene (mixture of isomers)	Tab 59
39212-23-2	4-Hydroxy-3-methyloctanoic acid lactone	Tab 60
33673-62-0	Dihydro-4-methyl-5-pentylfuran-2(3H)-one	Tab 61
67663-01-8	(+/-) 3-Methyl-gamma-decalactone	Tab 62
7011-83-8	gamma-Methyldecalactone	Tab 63

13) Review Safety Assessments Batch 2

CAS	Name	Tab
3391-86-4; 3687-48-7	1-Octen-3-ol ; (R)-(-)-1-Octen-3-ol	Tab 64
1322-17-4	1,3-Nonanediol acetate (mixed esters)	Tab 65
141-92-4	Hydroxycitronellal dimethyl acetal	Tab 66
5182-36-5	2,4,6-Trimethyl-4-phenyl-1,3-dioxane	Tab 67
1373821-23-8	4H-1,3-Benzodioxin, hexahydro-4-methyl-2-(phenyl methyl)-	Tab 68
326-61-4	Piperonyl acetate	Tab 69
617-35-6	Ethyl pyruvate	Tab 70
1447712-18-6	2-Cyclohexen-1-one, 2-methyl-5-propyl-	Tab 71
83863-64-3	7,9-Dimethylspiro[5.5]undecan-3-one	Tab 72

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92015-65-1	2(3H)-Benzofuranone, hexahydro-3,6-dimethyl-	Tab 73
68228-06-8	4-Methyl-1-oxaspiro[5.5]undecene	Tab 74
13679-86-2	5-Isopropenyl-2-methyl-2-vinyltetrahydrofuran	Tab 75
22047-25-2	Acetylpyrazine	Tab 76
19096-86-7	Cyclohexanone,5-methyl-2-(1-methylethyl)-,oxime	Tab 77
847565-09-7	N-(2-(Pyridin-2-yl)ethyl)-3-p-methanecarboxamide	Tab 78
1643-20-5	Dodecyldimethylamine oxide	Tab 79
1392276-61-7	Acetonitrile, 2-(2,4,4-trimethylcyclopentylidene)-	Tab 80
42075-45-6	Methyl 2-methylthiobutyrate	Tab 81
68398-18-5; 68921-26-6	4,7,7-Trimethyl-6-thiabicyclo[3.2.1]octane ; Cyclohexene, 1-methyl-4-(1-methylethenyl)-, sulfurized	Tab 82

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<p>943723-15-7; 93939-86-7; 85633-07-4; 85700-01-2; 85700-02-3; 85633-08-5</p>	<p>5,8-Methano-2H-1-benzopyran, 6(or 7)-ethylideneoctahydro-, [4aR,5S,8S,8aS(or 4aR,5R,8S,8aR)]-rel-; 6-Ethylideneoctahydro-5,8-methan o-2H-benzo-1-pyran; 5,8-Methano-2H-1-benzopyran, 6-ethylideneoctahydro-, (4aalpha,5beta,7Z,8beta,8aalpha)- 5,8-Methano-2H-1-benzopyran, 6-ethylideneoctahydro-, (4aalpha,5beta,7E,8beta,8aalpha) -; 5,?8-?Methano-?2H-?1-?benzopyr an, 6-?ethylideneoctahydro-?, (4aα,?5β,?6E,?8β,?8α)?-; 5,8-Methano-2H-1-benzopyran, 6-ethylideneoctahydro-, (4aalpha,5beta,6Z,8beta,8aalpha)-</p>	<p>Tab 83</p>
<p>1245725-35-2</p>	<p>Cyclopentanol, 2-?methyl-?5-?(1-?methylethyl)?-? , 1-?propanoate</p>	<p>Tab 84</p>
<p>2230-87-7</p>	<p>Cyclohexanol, 5-methyl-2-(1-methylethyl)-, acetate, (1a,2a,5b)-</p>	<p>Tab 85</p>
<p>1266606-26-1</p>	<p>Butanoic acid, 2-?methyl-?5-?(1-?methylethyl)?cy clopenty ester</p>	<p>Tab 86</p>
<p>52557-97-8</p>	<p>Methyl 3,3-dimethylbicyclo[221]heptan e-2-carboxylate</p>	<p>Tab 87</p>
<p>67845-30-1</p>	<p>8-Isopropyl-6-methylbicyclo[2.2 .2]oct-5-ene-2-carbaldehyde</p>	<p>Tab 88</p>
<p>68259-31-4</p>	<p>5(Or 6)-Methyl-7(or 8)-(1-methylethyl)bicyclo[2.2.2] oct-5-ene-2-carbaldehyde</p>	<p>Tab 89</p>

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120-72-9	Indole	Tab 90
93963-23-6	Ethanone, 1-(1,2,3,4,5,6,7,8-octahydro-2,3,8-tetramethyl-2-naphthalenyl)-	Tab 91
54464-57-2; 68155-66-8; 68155-67-9	1-(1,2,3,4,5,6,7,8-Octahydro-2,3,8,8-tetramethyl-2-naphthalenyl)ethanone; 1-(1,2,3,5,6,7,8,8a-Octahydro-2,3,8,8-tetramethyl-2-naphthyl)ethan-1-one; 1-(1,2,3,4,6,7,8,8a-Octahydro-2,3,8,8-tetramethyl-2-naphthyl)ethan-1-one	Tab 92
188570-78-7	Cyclopropanecarboxylic acid, (3Z)-3-hexenyl ester	Tab 93
93-29-8	isoeugenyl acetate	Tab 94
63767-86-2	alpha-Methyl-4-(1-methylethyl)-cyclohexanemethanol	Tab 95
60241-52-3	cyclohexanepropanol, alpha-ethyl-2,2,6-trimethyl-	Tab 96
139504-68-0	1-(2-tert.-Butyl cyclohexyloxy)-2-butanol	Tab 97
32974-92-8	2-Acetyl-3-ethylpyrazine	Tab 98
23787-80-6	2-Acetyl-3-methylpyrazine	Tab 99
13678-59-6	2-Methyl-5-(methylthio)furan	Tab 100
3526-75-8	1.alpha.,5.alpha.-Dihydroguaialol	Tab 101
57-10-3	Palmitic acid	Tab 102
64-18-6	Formic acid	Tab 103
5421-17-0	Hexyl phenylacetate	Tab 104
63449-68-3	beta-Naphthyl anthranilate	Tab 105
4312-99-6	1-Octen-3-one	Tab 106

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36267-71-7	5,7-Dihydro-2-methylthieno(3,4-d)pyrimidine	Tab 107
140-39-6	<i>p</i> -Tolyl acetate	Tab 108

14) Update on QRA2 Implementation

a) A.M Api Presentation on QRA2

AMA

15) Review Safety Assessments – Batch 3

CAS	Name	Tab
93-15-2	Eugenyl methyl ether	Tab 109
7784-67-0	Isoeugenyl ethyl ether	Tab 110
6032-29-7	2-pentanol	Tab 111
14765-30-1	2-sec-Butylcyclohexanone	Tab 112
10461-98-0	alpha-Cyclohexylidene benzeneacetonitrile	Tab 113
916887-53-1	2-Cyclohexylidene-2-o-tolylacetonitrile	Tab 114
5405-41-4	Ethyl 3-hydroxybutyrate	Tab 115
21188-58-9	Methyl 3-hydroxyhexanoate	Tab 116
2305-25-1	Ethyl 3-hydroxyhexanoate	Tab 117
2555-49-9	Ethyl phenoxyacetate	Tab 118
67633-94-7	Phenylacetaldehyde 2,4-dihydroxy-2-methylpentane acetal	Tab 119
33941-99-0	2-Methyl-4-phenyl-1,3-dioxolane	Tab 120
104-67-6	gamma-Undecalactone	Tab 121
99-48-9; 2102-59-2; 1197-07-5	Carveol	Tab 122
40203-73-4	Methyl cyclopentylideneacetate	Tab 123
94-46-2	Isoamyl benzoate	Tab 124
947-05-7	Oxacyclotridecan-2-one	Tab 125

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51755-83-0	3-Mercaptohexanol	Tab 126
96-48-0	4-Hydroxybutanoic acid lactone	Tab 127
614-34-6	p-Cresyl benzoate	Tab 128
2206-94-2	Benzenemethanol, alpha-methylene-, acetate	Tab 129
118-93-4	2-Hydroxyacetophenone	Tab 130
13477-62-8	Tetrahydro-2-isobutyl-4-methyl-2 H-pyran	Tab 131
78-93-3	2-Butanone	Tab 132
140-67-0	Estragole	Tab 133
104-46-1; 25679-28-1; 4180-23-8	Anethole (isomer unspecified)	Tab 134
501-92-8	4-Allylphenol	Tab 135
1122-62-9	2-Acetylpyridine	Tab 136

16) Human Health Research Projects

- a) Epidemiology
 - i) Validation of Clinical Relevance Algorithm **MB**
- b) Eugenol Elicitation Threshold draft report (**Tab 137**)
- c) **Presentation by D. O'Brien on RIFM Dermal Sensitization Research Project Update**
- d) **Presentation by Prof. Jean-Pierre Lepoittevin, Laboratoire de Dermatochimie, Institut Le Bel - Development of HRMAS NMR spectroscopy in association with RHE to follow and characterize the metabolic transformation/activation of pro-haptens Research Project (Tuesday afternoon May 21)**
- e) **Presentation by K. Joshi - Use of the EpiDerm™ 3D reconstructed skin micronucleus assay to address misleading positive results from in vitro genotoxicity assays for fragrance materials**

17) 2,3-Butanedione (Tab 138) (Tab 139) Tab 140)

18) Expert Panel Executive Session

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19) Future Meeting Dates

- | | | |
|----------------------|-------------------|-------------------------------|
| • Monday – Wednesday | Sept. 23-25, 2019 | New Jersey |
| • Monday – Wednesday | Jan. 20-22, 2020 | Delhi, India |
| • Thursday | Jan. 23, 2020 | INFOX in 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? |