RAC/M/48/2019
Final
28 May 2019

Minutes of the 48th Meeting of the Committee for Risk Assessment (RAC 48)

Wednesday 6 March starts at 09.00
Friday 8 March breaks at 13.00
Tuesday 12 March resumes at 14.00
Friday 15 March ends at 13.00

Part I Summary Record of the Proceedings

1. Welcome and apologies

The Chairman, Tim Bowmer, welcomed all the participants to the 48th meeting of the Committee for Risk Assessment (RAC 48). Apologies were received from six Members.

Chairman's address

The year 2019 will be a year of change for RAC and this has several reasons.

The Committee has grown steadily over the last five years and now has 57 members in total (this may become 58 after the March Management Board (MB) meeting. However, a bigger than usual exchange of members this year is anticipated, as a large group (some appointed at the start of the Committee in RAC 1) approach renewal in the second half of this year. We also expect an impact from the withdrawal of the United Kingdom from the European Union on our membership.

The MB will be asked for their MSCA's to please consult ECHA and the Committee Chairman before making nominations to RAC (and SEAC), in order to ensure the right expertise going forward. I would also like to ask you to please remind your CA's of this when the opportunity arises.

In our interviews through October 2018 and January 2019, I had the pleasure of discussing your work with you, how you see your contribution to RAC and still manage the expectations of your employers (not an easy task). My thanks as always for your time and your suggestions to me as to how we can manage things better. We discussed opportunities to contribute and various measures that we in the Agency have in mind. I collected a series of actions from the interviews and am working my way through them, starting with the most urgent, i.e. those involving ECHA and the respective MSCA's.

By 2014, The Committee's capacity had been expanded with a view to adopting about 80 opinions per year. We are now challenged with increasing the Committee's capacity to adopt up to 120 opinions per year. This will require wide-ranging changes. To give you an idea we adopted 102, 98 and 92 opinions in 2016, 2017 and 2018 respectively, a tribute to your hard work and that of the Secretariat; now we need to make that more easily achievable going forward.

Authorisation

As noted at the last two meetings, we intend to use working groups to take pressure off plenary. A revised draft mandate for a '**RAC-AfA working group**' is tabled at this meeting for adoption. With your agreement, it will commence its work by mid-April and again in October of this year. This also ties in with the following measures:

- A proposal to RAC and SEAC to lower the quorum from 60% to 50% of those having the right to vote, to be followed by agreement in the MB on 28/29 March. This is in order to allow members/rapporteurs more freedom to choose the sections of the meetings that they need to attend;
- The 'A-listing' procedure for AfA agreed at RAC 47, in which the WG would play a large part;

- A request to the MB also tabled for 28/29 March to request that RAC members involved in AfA be provided with advisors to support their work and to take part in the WG (through this peak).
- A proposal under development by the secretariat to further modify the opinion template, to shorten it and to work with groups of applications/uses and model opinions (for roll out at the first working group meeting.

Restrictions

There are six restrictions already in Committee and more on the way, so by September, we will have 8 in process. I expect the numbers to stabilise at between 5 and 8 through 2020, i.e. at a level at which The Commission and ECHA had designed this process over a decade ago. As I presented to you at the last meeting, conformity consists of a comparison of the components of the dossier with the regulation and is not an evaluation of the content - where possible we use the powers of REACH to fill any gaps. In more practical terms, to deal with the workload, we will use Working groups on an ad hoc basis where needed but intend to keep the work in plenary. Where possible, we will skip the 2nd meeting and wait for the PC to finish. The Secretariat is taking steps to reduce the length of opinions with character limits in the templates, to make them more readable and accessible and thereby to involve more members in commenting.

OELs

ECHA has signed a service level agreement with DG-Employment to develop OEL's on an ongoing basis. A first service request under this agreement has been received and acknowledged by ECHA. The first two health-based OEL's evaluated will be on lead and its inorganic compounds and diisocyanates, both under the Chemical Agents Directive. The turnaround time is 18 months to an adopted opinion. In the meantime, we have set up a process (also in our document management systems) in ECHA to manage OEL's, largely along the lines we used in 2017/18 for the pilot OEL project. I hope that now everything is in place to take on this serious challenge.

At the final meeting of the Scientific Committee on Occupational Exposure Limits (SCOEL) last month, the Director General of DG Employment and Social Inclusion, Mr Joost Korte expressed his hope that RAC would rise to the challenge and support the Commission with professional and timely opinions. The expectations of DG-Employment's Working party on Chemicals which I attended again in January to follow our OEL opinions on benzene, acrylonitrile and nickel and compounds are also high.

CLP

We will discuss with you later in the year how we can improve fast-track (A-listing), further reduce the length of some debates and reduce the length of opinions. The rapporteurs and the secretariat edited and proof read over 300 pages of text from the December meeting, so the efficiency gains from shorter opinions could be considerable. I am also considering some changes to how we structure CLP debates and the how the rapporteurs communicate the data to plenary.

The participants were informed that the meeting would not be recorded and that the recordings from the 47th meeting had already been destroyed. The Chairman noted that the minutes are adopted and they have been uploaded to S-CIRCABC and published on the ECHA website. The minutes include a full list of participants as given in Part III of these minutes.

2. Adoption of the Agenda

The Chairman reviewed the agenda for the meeting (RAC/A/48/2019).

The agenda and the list of all meeting documents, including conclusions and action points are attached to these minutes as Annexes I and II, respectively.

3. Declarations of conflicts of interests to the Agenda

The Chairman declared that he had no potential conflict of interest to any agenda points for the meeting.

The Chairman further requested all participants to declare any potential conflicts of interest to any of the agenda items. 14 Members and one invited expert declared potential conflicts of interest, each to specific agenda items, the majority related to concurrent employment of Members at agencies submitting dossiers to RAC but who had not been involved in the preparation. In the event of a vote, these Members were requested to refrain from voting on the respective agenda items, as stated in Article 9.2 of the RAC Rules of Procedure. Where Members declared that they had contributed to the preparation of a substance dossier for consideration by RAC, or similar potential conflict, they were asked to refrain from voting and the Chairman noted that he would consider additional mitigation measures. The list of persons declaring potential conflicts is attached to these minutes as Annex III.

4. Appointment of (co-) rapporteurs

a) Appointment of (co-)rapporteurs for CLH dossiers, restriction dossiers, authorisation applications, DNEL/dose-response relationships, Article 95 (3) requests and Article 77 (3) (c) requests (closed session).

The Secretariat collected the names of volunteers for rapporteurships for CLH dossiers and authorisation for applications, as stated in the restricted room document. The Committee agreed upon the proposed appointments of the Rapporteurs for the intentions and/or newly submitted CLH, as well as the forthcoming applications for Authorisation.

The Committee collected the names of volunteers for the Rapporteurs for the four restriction proposals, to be submitted in April/July 2019 and appointed them to the pool.

The Chairman informed that parts of the OEL process were still under development and that the manner of appointing Rapporteurs had not yet been discussed with the Committee. He proposed that the same system of nomination to a pool by RAC, followed by appointment by the Chairman as employed in the Restriction process should be applied here also. RAC agreed to this and it will be included in the overall OEL procedure.

The Committee collected the names of the volunteers for the Rapporteurs on two scientific reports on evaluations of occupational exposure limits (OELs) and nominated them to the pools.

5. Report from other ECHA bodies and activities

a) Report on RAC-47 action points, written procedures and an update on other ECHA bodies

The Chairman informed the Committee that most of the action points from the previous meeting RAC-47, pending publications of three CLH opinions, had been completed. The summary of all substance-related written procedures, calls for expression of interests in (co-)rapporteurship

and written procedures for appointments of rapporteurs, and adopted opinions, is provided in the room document on administrative issues (RAC/48/2018/01) (see Annex IV).

The Chairman also informed the Committee that the final minutes of RAC-47 had been adopted via written procedure and were uploaded to S-CIRCABC and are published on the ECHA website, and thanked those Members who had provided comments on the draft.

b) RAC workplan for all processes

The Chairman informed the meeting participants about the updated RAC work plan for 2019, covering the four processes of Restriction, Authorisation, and Harmonised Classification and Labelling of substances and scientific evaluations of Occupational Exposure Limits. He informed Members that they could find the expected schedules for Restriction, Authorisation dossiers in the work plan. In addition, the scheduling to be considered for each Harmonised Classification and Labelling (CLH) dossier are given in the relevant section.

c) Revision of Rules of Procedure

The Chairman invited the meeting to agree on a proposed revision to the Rules of Procedure for RAC and SEAC.

As an efficiency measure and to enable RAC-members to handle the length of the plenary meetings through 2019 and 2020, RAC is asked to agree with the proposed lowering of the meeting quorum, achieved when at least fifty percent (instead of the current sixty percent) of all members having the right to vote are present at the meeting.

For reasons of consistency and as an efficiency measure for the Secretariat, the same change is proposed also for the opinions being adopted under written procedure, i.e. to lower the quorum from at least sixty percent to at least fifty percent.

RAC agreed with the proposed revisions to the Rules of Procedure (RAC/48/2019/02). After agreement on the same changes to their Rules of Procedure by SEAC, both are scheduled for approval[1] by the Management Board at their forthcoming meeting.

6. Requests under Article 77 (3)(c)

6.1 Copper compounds (M-factor)

The Chairman welcomed the expert accompanying the Eurometaux stakeholder observer and reported that based on a request from the Commission to ECHA of 8 October 2018, a mandate to RAC to develop and adopt an opinion on the M-factors for long-term aquatic hazard for the copper substances listed in Commission Regulation (EU) 2016/1179 has been given by the ECHA Executive Director[2].

At RAC 47 plenary, the Committee agreed in principle on the draft opinion (the calculations of the chronic M-factors based on the information in the opinion for granulated copper) and in line with the mandate, the Secretariat put the draft up for a short targeted public consultation.

The Rapporteur gave an oral presentation of the final opinion / chronic M-factors for the copper compounds in question. This resulted in agreement on the following : for 4 out of 10 copper

[1] REACH Art 85(9)

[2] Note for the attention of Tim Bowmer, Chairman of the Committee for Risk Assessment; https://echa.europa.eu/documents/10162/13580/rac_mandate_copper_compounds_m-factors_en.pdf/140120b5-0a92-04f1-728a-a1241cfe1583

compounds a 10-fold lower M-factor is proposed and for the remaining 6, there would be no change in M-factor), see Table 2 on page 58 of these minutes.

The Rapporteur further drew the attention of RAC to the impact of the updated copper ecotoxicity database on the acute ERVs (following re-calculation) and in particular on the acute M-factors. For seven out of nine copper salts the acute M-factors would remain the same, but for Copper (I) oxide (CAS 1317-39-1) and Copper (II) oxide (CAS 1317-38-0) the updated ERVs exceed 0.01 mg/L implying that the acute M-factors would need to be revised from the current M100 to M10. It was noted that this aspect exceeded the current mandate given to RAC and would from a procedural point of view require the submission of a new CLH proposal for revision of existing entries. However, as the change of acute M-factor(s) is in principle scientifically justified, the Committee agreed to draw these implied changes in acute M-factor(s) to the attention of the Commission for its consideration. The Secretariat will subject the final opinion to a short RAC consultation for checking before publication.

This case brought to light a potential discrepancy in the CLP-Guidance (as to the loading rate to be used for classification and for the M-factor calculation) which would need to be addressed the next time the Guidance is updated.

RAC adopted the opinion by consensus. The Chairman thanked the Rapporteur for the presentation of the arguments and the Committee Members for their comments.

7. Requests under Article 95(3)

None

8. Harmonised classification and labelling (CLH)

8.1 General CLH issues

A workshop on Modes of Action (MoAs) and human relevance in the context of classification and labelling (CLH) took place on the 5th of March 2019 at ECHA, ahead of the RAC-48 plenary meeting. Please see the short summary of the workshop in Annex V.

8.2 CLH dossiers

A. Hazard classes for agreement without plenary debate[3] (see section B below for hazard classes for the same substances debated in plenary)

RAC reviewed an 'A-listing' of hazard classes for a range of substances and being informed by the Secretariat of the appropriate scrutiny by Rapporteurs and commenting RAC Members in each case, agreed these without plenary debate. The details for each substance are given below in section B.

B. Substances with hazard classes for agreement in plenary session

1. 1,4-dioxane

[3] Following adequate scrutiny by the Rapporteur and commenting Members and taking the comments from the Public Consultation into account, selected hazard classes are proposed for agreement through a list ('fast-track') without further debate in the Committee.

The Chairman reported that 1,4-dioxane is used as a solvent in multiple chemical processes, e.g. in the production of lacquers, pulping of wood and insecticides. It has an existing entry in Annex VI to the CLP Regulation as Flam. Liq.2, Carc. 2, Eye Irrit. 2, STOT SE 3, EUH019, EUH066 and Note D. The legal deadline for the adoption of an opinion is 15 August 2019.

The DS (NL) proposes to modify 1,4-dioxane classification to Carc 1B; H350 and add classification as Muta 2; H341.

Regarding mutagenicity, RAC discussed the findings in *in vitro* and *in vivo* studies and noted that only negative results were found in test guideline compliant *in vitro* studies while the *in vivo* studies were mostly positive. RAC further noted that this apparent inconsistency with the *in* vivo studies could be justified as the *in vivo* positive results were not consistently described in all assays. Further, positive results were in most of the assays reported above the limit dose of 2000 mg/kg (and potentially influenced by cytotoxicity) or the studies where of unknown reliability.

RAC noted that since *in vitro* findings were all negative it suggested that 1,4-dioxane is non-genotoxic and, in addition, substances with this profile of *in vivo* results are rarely *de facto* genotoxic *in vivo*. One member added that the mixed results from the *in vivo* studies could be the result of 1,4-dioxane inducing replicative DNA synthesis. Therefore it would seem credible that this substance could induce the production of micronuclei but by an indirect, non-genotoxic route. In addition, considering that a non-genotoxic regenerative hyperplasia mode of action (MoA) for the induction of liver tumours cannot be excluded for the current carcinogenicity classification proposal, and that no robust data supported classifying 1,4-dioxane as mutagen, RAC concluded no classification is warranted for mutagenicity in contrary to DS proposal.

The DS informed the Committee that after public consultation it became aware of two new *in vivo* studies. As no public consultation was conducted on the studies and RAC had not been consulted, it was agreed that the opinion of RAC will be based on the currently available studies in the dossier. The DS noted that the dossier might be resubmitted at a later stage for mutagenicity hazard.

RAC agreed with DS proposal to modify the current carcinogenicity classification of Cat 2 to Cat 1B based on clear evidence of carcinogenicity in different tissues observed in two species at reasonable dose levels. RAC considered the new available data and the change in classification criteria from DSD to CLP as sufficient to warrant the classification as Cat 1B. No mechanism was provided to conclusively dismiss the human relevance of these tumour findings in rats and mice. RAC concluded that considering the calculations to the T25 concept, 1,4-dioxane is of medium potency and no SCL is warranted which is in accordance with the DS proposal.

RAC adopted the opinion by consensus. The Chairman thanked the Rapporteurs for the presentation of the arguments and the Committee Members for their comments.

2. flumioxazin (ISO)

The Chairman welcomed the expert accompanying the ECPA stakeholder observer and reported that flumioxazin (ISO) is an active substance used in plant protection products as a herbicide.

Flumioxazin (ISO) has an existing entry in Annex VI to the CLP Regulation as Repr. 1B; H360D and for hazards to aquatic environment (Aquatic Acute 1; H400 and Aquatic Chronic 1; H410 with M-factors of 1000 for both endpoints). The legal deadline for the adoption of an opinion is 3 August 2019.

The dossier submitter (CZ) proposed to modify the classification for toxicity to reproduction as Repr. 2; H361d.

RAC discussed and adopted an opinion on toxicity to reproduction of the substance at RAC 29; disagreeing with the DS contention at that time that the developmental toxicity findings were not relevant to humans and noting that this had not been sufficiently demonstrated. The classification was based on reduced number of live foetuses, reduced foetal body weights, increased incidence of cardiac ventricular septal defects, wavy ribs, and reduced ossification of sacrococcygeal vertebral bodies in two studies in rats. In 2014, RAC concluded that the proposed mode of action (MoA) was plausible but not convincingly demonstrated and that relevance for humans could not be excluded, although there may be quantitative differences between rats and humans.

In the current CLH report, the manufacturer provided new mechanistic information with the aim to further demonstrate the inhibition of the enzyme protoporphyrinogen oxidase, PPO, clarify the cause of developmental effects (ventral septal defects) observed in the low doses, explore other MoAs and to further investigate the differences in haem synthesis among different species.

In line with the previous RAC opinion, RAC Members agreed not to classify for adverse effects on sexual function and fertility.

Some RAC members considered that the new studies (*in vitro* / *in silico* / *in vivo*) provide evidence for quantitative species differences in PPO-inhibition and a qualitative difference in haem synthesis inhibition in rats and humans. RAC members expressed that uncertainties still exist including unresolved questions related to the suggested link between anaemia and developmental toxicity; and why there were no effects on haem production in human cell lines although PPIX was increased after flumioxazin treatment. RAC members also commented that the positive control DHA was not relevant for the interpretation of data on flumioxazin as it did not act on PPIX. IND replied that DHA also interferes with haem synthesis but at a different step than flumioxazin and therefore it does not increase PPIX but causes a decrease in haem production that leads to the same effects as flumioxazin, i.e. anaemia, heart defects and fetal death. Therefore, DHA and flumioxazin have similarities in their MoA, both produce the same developmental effects by targeting haem production, but because they act on a different step of the haem synthetic pathway, effects linked to different key events were not identical. IND mentioned the studies that have shown that PPO binding by flumioxazin was stronger in rats than in humans and that was assumed to explain the difference in the effect on haem production between the species. IND had also looked at literature on several other chemicals that caused similar effects in the developing heart as flumioxazin but by different modes of action, and the critical window was suggested to be during gestation days 9-10 in the rat, whereas the critical window for flumioxazin was later, gestation day 12, which coincides with the peak production of polychromatic erythrocytes in the rat embryo.

RAC agreed that the data presented were sufficient to reassess the existing classification. RAC members were of the view that although several uncertainties remained there were some quantitative and qualitative differences between the responses to flumioxazin in human and rat cell lines. The MoA described in the CLH report was considered plausible and of no or low relevance for humans. As some doubts remained, however, no classification was not considered relevant.

However, overall, based on the observed effects, the proposed MoA, and its remaining uncertainties, RAC agreed to re-classify flumioxazin (ISO) as a substance suspected of damaging the unborn child (Repr. 2; H361d).

RAC adopted the opinion by consensus. The Chairman thanked the Rapporteur for the presentation of the arguments and the Committee Members for their comments.

3. prothioconazole (ISO)

The Chairman welcomed the expert accompanying the ECPA stakeholder observer and reported that prothioconazole (ISO) is an active substance used in plant protection products as a fungicide.

The substance has no existing entry in Annex VI to the CLP Regulation.

The legal deadline for the adoption of an opinion is 21 September 2019.

The DS (UK) proposed to classify prothioconazole (ISO) for hazards to aquatic environment as Aquatic Acute 1, H400 (M=10) and Aquatic Chronic 1, H410 (M=1).

RAC agreed the following via the fast-track procedure, i.e. with scrutiny but without plenary debate: no classifications for physical hazards, acute toxicity (all routes of exposure), skin irritation/corrosion, eye irritation/damage, skin sensitisation, germ cell mutagenicity, carcinogenicity, STOT SE and STOT RE, and classification for hazards to aquatic environment as Aquatic Acute 1; H400, M=10 and Aquatic Chronic 1; H410, M=1.

The Committee agreed that there were no effects in the 2-generation reproduction toxicity study in rats that would warrant classification for fertility. No classification was also agreed for effects on or via lactation.

RAC discussed developmental effects observed in rats and rabbits and noted increased incidences of microphthalmia (mostly unilateral, but bilateral in two cases) compared to control in a rat developmental toxicity study (GLP and OECD–compliant) in all dose-groups (although not dose-related in the low- and mid-dose groups), above the historical control data (HCD) in the highest dose group, which was conducted at the limit dose of 1000 mg/kg bw and was maternally toxic. On the other hand, it was noted that the rat strain used in the study (Hsd Cpb:WU Wistar rats) had a high spontaneous background incidence of this type of malformations. This is supported by the absence of microphthalmia in studies with another rat strain. In the study on rabbits a single case of microphthalmia was observed, but this foetus had multiple malformations. Other developmental effects observed in rats (rudimentary supernumerary 14th rib (dose-related), dilated renal pelvis in the top dose) were considered not sufficient for classification.

Microphthalmia is considered a rare malformation that would potentially lead to classification, also because the relationship between maternal toxicity and microphthalmia is not obvious. Several RAC Members asked if further details on HCD were available. The IND expert clarified that the HCD includes both unilateral and bilateral microphthalmia cases (max. incidence 4 fetuses with bilateral microphthalmia out of 5 total (uni- & bilateral microphthalmia); range: 0-1.6% foetal incidence, 0-8.7% litter incidence). Although cases of unilateral microphthalmia may be spontaneous, it is unlikely for bilateral microphthalmia. Weighing the evidence, consisting of: microphthalmia found outside HCD at the limit dose 1000 mg/kg bw/day, in the presence of maternal toxicity, in a known susceptible strain of rats, and the absence of microphthalmia in another rat strain, the Committee agreed that no classification was warranted for developmental toxicity of prothioconazole (ISO).

RAC adopted the opinion by consensus. The Chairman thanked the Rapporteurs for the presentation of the arguments and the Committee Members for their comments.

4. thiophanate-methyl (ISO)

The Chairman welcomed the expert accompanying the ECPA stakeholder observer and reported that thiophanate-methyl is an active substance used in plant protection products. The substance has an existing entry in Annex VI of the CLP Regulation: Acute Tox. 4*; H332, Skin Sens. 1;

H317, Muta. 2; H341, Aquatic Acute 1; H400, Aquatic Chronic 1; H410. The legal deadline for the adoption of an opinion was 3 October 2019.

The DS (SE) proposed to retain Skin Sens. 1; H317, Aquatic Acute 1; H400, Aquatic Chronic 1; H410, to modify Acute Tox. 4; H332, Muta. 1B; H340 and to add Carc. 2; H351, STOT RE 2; H373, and M-factor 10 for Aquatic Acute and M-factor 10 for Aquatic Chronic hazard classes. In response to comments received during public consultation the DS revised their position to Muta. 2; H341 and no classification for Carc, and proposed to include thyroid as target organ for STOT RE 2 and an ATE of 1.7 mg/L for acute inhalation.

RAC agreed the following via the fast-track procedure (i.e. with scrutiny but without plenary debate): no classification for physical hazards, acute toxicity (oral and dermal routes of exposure), skin corrosion / irritation, serious eye damage / irritation, and classification for Acute Tox. 4; H332 (ATE = 1.7 mg/L (dusts and mists)).

RAC discussed effects on fertility. Results of two studies were available: a 2-generation reproduction study according to the testing guideline OECD 416 and a 3-generation study predating the OECD 416 guidelines, both on rats. The 3-generation reproduction study was considered by the DS and RAC as non-compliant by current standards. No adverse effects were seen that would warrant classification. During the discussion RAC members noted that the dosing used in the OECD TG 416 study was too low (173 mg/kg bw/day) and sufficient toxicity was not reached. RAC agreed on no classification for the effects on fertility due to inconclusive data.

Regarding the effects on development, no such effects were observed in studies with rats and mice. For rabbits, which was considered the most sensitive species, the results of two studies PNDT studies according to the testing guideline OECD 414, including range-finding studies were available. RAC agreed that in the highest dose the animals clearly showed signs of severe maternal toxicity. The effects observed at this dose level was thus disregarded. At the lower dose levels there were some effects on pup weight and increased number of supernumerary ribs. , but this effect is not severe enough to lead to classification. RAC members agreed on no classification for the developmental toxicity effects.

During the discussion on mutagenicity, the rapporteur presented results from number of the available *in vitro* and *in vivo* studies. One micronucleus study according to OECD TG 487 on human peripheral lymphocytes showing positive results without S9 provided evidence for aneuploidy. The results of an *in vivo* Micronucleus test according to OECD 474 in mice in somatic cells (single dose of administration via oral gavage of 500, 1 000 and 2 000 mg/kg bw) demonstrated 4-fold increase in aneuploidy over the control population data. The three available *in vivo* studies in germ cells (one of them a Spermatogonial chromosomal aberration test according to OECD 483 in mice) showed negative results. The expert accompanying the ECPA stakeholder representative noted several deficiencies in the available *in vitro* studies and noted that *in vivo* data very clearly indicate that even at very high doses there is no effect observed. Considering the weight of evidence from the available studies RAC agreed that the available data do not warrant a classification as 1B, but concluded that the substance should be classified as Muta 2; H341.

The rapporteur then presented the results from five long-term carcinogenicity studies. Three of them were not GLP-compliant, and showed major deviations from the OECD recommendations and were therefore only considered by the DS as supportive information. The other two studies were considered acceptable for the assessment of carcinogenicity: one in the rat (OECD TG 453) and one in mice (OECD TG 452). The first study demonstrated statistically significant increase of thyroid tumours only above the maximum tolerated dose. Hepatocellular adenomas reported below the maximum tolerated dose were among the significant findings from the second study. The observed hepatocellular carcinomas were not clearly dose-dependent. It was noted that the

mode of action is not clear. RAC concluded that the substance should be classified as Carc. 2; H351 based on the observed hepatocellular adenomas with the supporting information from the identified thyroid follicular cell changes in rats with statistical significance at the two top-level doses of 1 200 ppm and 6 000 ppm.

RAC noted in the context of STOT-RE that the results of the available repeated dose studies clearly show thyroid as the target organ. However, the findings in thyroid, such as weight increase, hypertrophy, slight hyperplasia in limited number of animals and decrease in T3 and T4 hormones concentration are not of sufficient severity to meet the classification criteria. Hence the RAC members agreed not to classify the substance for STOT RE.

After the presentation of the STOT SE hazard class the RAC members agreed that the substance does not meet the classification criteria.

During the discussion on the skin sensitisation, the RAC rapporteur acknowledged that despite the high response rate, sub-categorisation in 1A would not be appropriate. The concentration used was higher than the criteria for 1A stipulates. As it cannot be excluded that test lower concentrations could support 1A it was agreed that Skin Sens. 1 without sub-categorisation would be appropriate.

During the discussion on the environmental hazards the Committee agreed to classify based on data for the degradation product Carbendazim, which is more toxic than thiophanate-methyl. RAC agreed to classify the substance as Aquatic Acute 1; H400 (M-factor of 10) based on the lowest value corresponding to the fish species *Ictalurus punctatus* (96h LC_{50} = 0.019 mg/L), which was obtained following a standard test comparable to OECD 203, and Aquatic Chronic 1; H410 (M-factor of 10) based on the lowest value corresponding to a 21d NOEC of 0.0015 mg/L with *Daphnia magna*; the substance is not rapidly degradable.

RAC adopted the opinion by consensus. The Chairman thanked the Rapporteurs for the presentation of the arguments and the Committee Members for their comments.

5. tolpyralate

The Chairman welcomed the expert accompanying the ECPA stakeholder observer and reported that tolpyralate is a new active substance used in plant protection products as a broad spectrum herbicide, effective against broad leaf weeds in maize crops.

It has no existing entry in Annex VI to the CLP Regulation.

The legal deadline for the adoption of an opinion is 10 October 2019.

The DS (UK) proposed to classify tolpyralate for carcinogenicity (Carc. 2; H351), repeated dose toxicity (STOT RE 2; H373 (eyes, kidney) and for hazards to aquatic environment as Aquatic Acute 1; H400, with and M-factor of 10 and Aquatic Chronic 1; H410, with an M-factor of 100. RAC agreed the following via the fast-track procedure, i.e. with scrutiny but without plenary debate: no classifications for physical hazards, acute toxicity (all routes of exposure), skin irritation/corrosion, serious eye damage/irritation, respiratory sensitisation, skin sensitisation, and STOT SE, and classification for hazards to aquatic environment: Aquatic Acute 1; H400 (M=10) and Aquatic Chronic 1; H410 (M-100).

As regards mutagenicity, the Committee considered the three available *in vivo* studies, all negative (one micronucleus test in the mouse and two Comet assays in the rat) as a sufficient evidence to remove the concern raised by the positive *in vitro* test (mouse lymphoma assay) and agreed on no classification for germ cell mutagenicity.

As regards repeated dose toxicity, RAC agreed that the effects in the eye (keratitis and ocular opacity) occurring below the guidance value in the available rat studies warrant classification in category 2. Renal effects observed in the 2-generation study show that kidney is target organ for tolpyralate. RAC Members concurred that given the toxic effects were observed in animals exposed as foetuses and/or juveniles but not in animals exposed only as adults these are more relevant as evidence for developmental toxicity and not for STOT RE. RAC further agreed that the effects observed in other organs (thyroid, liver, gall bladder, pancreas and nervous system) were weak and did not warrant classification.

As regards carcinogenicity, it was noted that tolpyralate acts through HPPD inhibition. The IND expert contended that there was a strong evidence that HPPD inhibition MoA was not relevant to humans. He further elaborated that ocular lesions causing corneal tumours observed in male rats were mediated by high level of tyrosine caused by low activity of tyrosine aminotransferase (TAT) enzyme in rats and pointed to difference compare to mice, which have a higher TAT activity and where no ocular lesion have been observed. IND stated that as humans have TAT activity similar to mice it is unlikely that the lesion would occur in human; this is supported by absence of ocular tumours in patients treated with the drug nitisinone (NTBC, used for tyrosinemia type I genetic disorder), which is a HPPD inhibitor. The IND expert concluded that according to him, the ocular tumours reported in male rats do not occur in humans and are specific to the male rat[4].

The Committee concurred with the DS proposal that Carc. 2 is warranted based on significant dose-dependent increase in incidences of malignant squamous cell carcinoma in the eye of male rats in a 2-year repeated dose study. The occurrence of tumours in males only is consistent with a higher severity of keratitis in this sex. It was further noted that TAT activity alone could not explain the interspecies differences in susceptibility to tyrosinemia and ocular effects from exposure to HPPD inhibitors. As ocular lesions were also observed in animals with high TAT activity (dogs), but not in others with lower TAT (rabbit, Locke *et al.,* 2006).This is also in line with previous RAC recommendations on other HPPD inhibitors.

In the discussion on toxicity to reproduction, several RAC Members considered the delayed preputial separation and vaginal opening (both by 4 days) as significant adverse effects warranting classification for fertility, noting that the observed reduced body weight would not be sufficient to explain the delay in attaining puberty. The Committee concurred that the effects warrant classification in category 2 for fertility.

RAC agreed to classify the substance in category 2 for developmental effects based on increased pup mortality on PND 1-4 in the 1-generation range finding study and on PND 0 in the main 2-generation study, and on renal effects in the offspring in the 2-generation study.

RAC agreed on no classification for effects on or via lactation.

RAC adopted the opinion by consensus. The Chairman thanked the Rapporteurs for the presentation of the arguments and the Committee Members for their comments.

6. *p*-cymene

The Chairman welcomed the expert accompanying the ECPA and IFRA stakeholder observers and reported that *p*-cymene is an ingredient of terpenoid blend QRD 460, which is accepted as

[4] The industry expert clarified the absence of ocular tumours in humans suffering tyrosinemia from lifetime deficiency of HPPD or indeed with a lifetime deficiency of TAT, where ocular lesions have been reported. Likewise ocular lesions have been reported in 5% of patients treated with nitisinone and treatment of these patients has continued for almost 30 years and no ocular tumours have been reported.

an active substance for plant protection products. The substance has no existing entry in Annex VI of the CLP Regulation. The legal deadline for the adoption of an opinion was 17 October 2019.

The DS (NL) proposed to classify the substance Flam. Liq. 3; H226, Acute Tox. 3; H331 (with ATE = 3 mg/L (vapour), as proposed following public consultation), Asp. Tox. 1; H304, Aquatic Acute 1; H400 (M = 1) and Aquatic Chronic 3; H412.

RAC agreed the following via the fast-track procedure (i.e. with scrutiny but without plenary debate): no classification for acute toxicity (oral and dermal routes of exposure), skin corrosion / irritation, STOT SE, STOT RE and germ cell mutagenicity, and classification for Flam. Liq. 3; H226, Asp. Tox. 1; H304, and Acute Tox. 3; H331 (ATE = 3 mg/L (vapour)).

The Committee agreed with the rapporteurs' proposal not to classify the substance for skin sensitisation due to inconclusive data.

The Committee agreed with the rapporteurs' proposal to classify *p*-cymene as Aquatic Chronic 2; H411. This is based on the data from the 48-h aquatic acute toxicity test on *Daphnia magna* with an EC_{50} value of 3.7 mg/L, together with the conclusion that *p*-cymene has a potential for bioaccumulation, through the surrogate method in the absence of chronic data for Daphnia.

RAC adopted the opinion by consensus. The Chairman thanked the Rapporteurs for the presentation of the arguments and the Committee Members for their comments.

7. *d*-limonene

The Chairman welcomed the expert accompanying the ECPA and IFRA stakeholder observers and reported that *d*-limonene is an ingredient of terpenoid blend QRD 460, which is accepted as an active substance for plant protection products. *d*-Limonene is part of an existing group entry in Annex VI of the CLP Regulation: Flam. Liq. 3; H226, Skin Irrit. 2; H315, Skin Sens. 1; H317, Aquatic Acute 1; H400 and Aquatic Chronic 1; H410, Note C. The legal deadline for the adoption of an opinion was 19 October 2019.

For an individual entry, the DS (NL) proposed to retain the existing classifications for d-limonene as Flam. Liq. 3; H226 and Aquatic Acute 1; H400, to modify existing classifications to Skin Sens. 1B; H317 and Aquatic Chronic 3; H412, and to add Asp. Tox. 1; H304 and M-factor 1 for the Aquatic Acute hazard class.

RAC agreed the following via the fast-track procedure (i.e. with scrutiny but without plenary debate): classification for Flam. Liq. 3; H226[5] and Asp. Tox. 1; H304.

RAC discussed whether or not Skin Sens.1, H317 without sub-categorisation should be retained. The results from the two available Local Lymph Node Assays (from 2004 and 2001, both conducted according to OECD TG 429) supported classification of the substance as Skin Sens. 1B and human data from eight clinical studies indicated that some oxidation products of *d*-limonene formed after forced exposure to air are more potent skin sensitisers than the substance itself. It was noted that oxidised *d*-limonene is a potent skin sensitiser, but it was unclear whether in this case this could be the basis for classification of the substance itself according to the CLP Regulation. A number of RAC members and an expert from IFRA acknowledged that the clinical patch tests do not provide reliable information about the potency of *d*-limonene. It is unclear how the dermatitis patients testing positive were first sensitised. They may have been exposed to oxidised forms of this substance and this may have contributed to their sensitivity to sensitisation by *d*-limonene. RAC agreed that for *d*-limonene the harmonised classification

[5] Physical hazards were not opened for comments during the public consultation, therefore this part was removed prior to publication of the final opinion.

should apply to the substance itself rather than any impurities or substances that result from chemical reactions by incidental contact with e.g. air or water, and that the substance should therefore be classified as Skin Sens. 1B; H317.

RAC members generally supported the rapporteurs' proposal for classification as hazardous to the aquatic environment. After a detailed discussion on the key biodegradation study, RAC concluded that *d*-limonene is readily biodegradable and therefore rapidly degradable. RAC consequently agreed to classify *d*-limonene with Aquatic Acute 1; H400 with and M-factor of 1, based on the lowest E_rC_{50} of 0.25 mg/L for algae and with Aquatic Chronic 3; H412 based on the lowest chronic toxicity value for algae, an EC_{10} of 0.14 mg/L for a rapidly degradable substance.

RAC adopted the opinion by consensus. The Chairman thanked the Rapporteurs for the presentation of the arguments and the Committee Members for their comments.

8. alpha-terpinene

The Chairman welcomed the expert accompanying the ECPA and IFRA stakeholder observers and reported that alpha-terpinene is an ingredient of the plant protection product terpenoid blend QRD 460, which is accepted as an active substance for plant protection products. Alpha-terpinene has no existing entry in Annex VI of the CLP Regulation. The legal deadline for the adoption of an opinion was 17 October 2019.

The DS (NL) proposed to classify the substance as Flam. Liq. 3; H226, Skin Sens. 1A; H317, Repr. 2; H361, Asp. Tox. 1; H304, Aquatic Acute 1; H400 (M = 1) and Aquatic Chronic 3; H412. The DS changed the proposal during PC to Aquatic Chronic 2; H411 only for hazards to the aquatic environment, and agreed to add Acute Tox. 4; H302.

RAC agreed the following via the fast-track procedure (i.e. with scrutiny but without plenary debate): no classification for germ cell mutagenicity, and classification for Flam. Liq. 3; H226, Acute Tox. 4; H302 (ATE = 1 680 mg/kg bw) and Asp. Tox. 1; H304.

During the plenary discussion on skin sensitisation the discussion was focussed on whether Skin Sens. 1A, 1B or 1 would be more appropriate. The data on non-oxidised alpha-terpinene would justify Skin Sens. 1B. However, the DS had proposed Skin Sens. 1A based on data from a study on autooxidised alpha-terpinene, which was more sensitising than the non-oxidised substance. The Rapporteur proposed to classify in Category 1, primarily due to the uncertainties as to whether alpha-terpinene would oxidise to the same extent under natural conditions (as opposed to simulated conditions). The RAC discussion questioned whether it would be consistent with the CLP criteria to use data on an autooxidised substance or whether the data on the non-oxidised substance alone would be more appropriate. It was noted that using data on the autooxidised substance could be considered as risk rather than hazard assessment since it would consider the use as such rather than the intrinsic properties of the substance. Classification in Category 1B would be appropriate based on the data from the non-oxidised substance. Other members however commented that as the substance is an antioxidant and since its purpose is to oxidise in order to prevent other substances in a mixture from oxidisation, it is clear that the substance will oxidise under natural conditions. Thus, taking into account data from the study with the autooxidised forms could be appropriate. However, due to uncertainties as to what extent and at what rate the substance would oxidise under natural conditions, RAC concluded on classification as Skin Sens. 1 for alpha-terpinene.

For reproductive toxicity the dossier submitter proposed Repr. 2; H361 (without specifying whether the classification was for fertility or developmental toxicity), based on a published study (Araujo et al., 1996). In the study there was a higher incidence of sperm positive dams with an absence of implantation sites at the highest dose, which was considered by the dossier submitter

to be due to total litter loss pre-implantation. However, the Rapporteur proposed no classification as there were several uncertainties in the study, which is not performed according to internationally recognised guidelines and not under GLP conditions, and as the highest dose - where the effects were seen - was considered to have exceeded the maximum tolerable dose (MTD). Dams at the two highest doses had significantly lower body weights, both absolute and when corrected for uterus weight, consistent with a reduced body weight gain. It was confirmed by the industry stakeholder (ECPA) that the corrected body weight was approximately 20 grams (corresponding to around 20 %) lower in high dose dams compared to controls at the end of the study. It was noted that the mating conditions were not according to normal test guidelines and it was unclear whether mating had occurred at all in some dams, making it difficult to evaluate the data. RAC also noted that since dosing of the dams started on gestation day 6, the study might not be suitable for evaluation of fertility effects. One member suggested that an absence of implantation sites should have been seen in all dose groups if it was due to the mating procedure alone. Overall, it was agreed that the study could not be used to assess fertility, leading to a conclusion of 'no classification' for fertility due to lack of data. For development, there was overall agreement that 'no classification' was appropriate.

During the discussion on the aquatic hazard classes the RAC rapporteurs disagreed with the proposal presented in the CLH Report but agreed with the DS proposal made in the response to PC comment document. The Co-rapporteur agrees to classify alpha-terpinene as Aquatic Chronic 2; H411, using the surrogate method with the acute fish and Daphnia data as the substance is considered not rapidly degradable. The RAC agreed with the approach taken by the rapporteurs and supported the above classification.

RAC adopted the opinion by consensus. The Chairman thanked the Rapporteurs for the presentation of the arguments and the Committee Members for their comments.

9. 1,2,4-triazole

The Chairman welcomed the expert accompanying the ECPA stakeholder observer and reported that 1,2,4-triazole is used as an intermediate and as a fertilizer.

The substance has an existing entry in Annex VI to the CLP Regulation for Acute Tox. 4*; H302, Eye Irrit. 2; H319, Repr. 2, H361d***.

The legal deadline for the adoption of an opinion is 14 September 2019.

The DS (BE) proposed to modify the existing classification for acute oral toxicity (Acute Tox. 4; H302 – to confirm the minimum classification) and for toxicity to reproduction (Repr. 1B; H360FD).

RAC agreed to classify the substance for acute oral toxicity in category 4 (to confirm the minimum classification) and to assign the acute toxicity estimate of 1320 mg/kg bw to classify and label mixtures containing the substance via the fast-track procedure, i.e. with scrutiny but without plenary debate.

RAC supported the proposal by the DS to classify 1,2,4-triazole for toxicity to reproduction (effects on fertility and development) based on the effects observed in rats and/or mice. The Committee supported classification in category 1B for treatment-related effects on fertility, namely almost complete infertility, increased incidence of uterus dilatation, reductions in sperm count and reductions in the number of sperm with normal morphology in the rat two-generation study supported by increased incidence of spermatid degeneration/depletion/asynchrony in mice and decreased uterus weight and increased corpora lutea in rats. Category 1B for developmental effects was supported based on increased incidence of cleft palates (above HCD), undescended

testicle, hydronephrosis, a significant increase in post-implantation losses and decreased number of foetuses per dam in the highest dose in the main rat study. It was also noted that a high rate of resorptions may have masked some malformations in the main study. A significantly increased number of runts and decreased mean foetal weight was considered as supporting evidence for classification. RAC investigated the issue of impurities in the test substance but concluded that the developmental effects observed were substantially caused by 1,2,4-triazole.

RAC adopted the opinion by consensus. The Chairman thanked the Rapporteur for the presentation of the arguments and the Committee Members for their comments.

10. Sedaxane

The Chairman reported that sedaxane is used as a broad-spectrum, seed treatment fungicide. It is an active substance and subject to harmonised classification and labelling. Currently, there is no entry in Annex VI of CLP regulation for sedaxane. The legal deadline for adoption of the opinion is 25 October 2019.

The DS (FR) proposes to classify sedaxane as Carc 2; H351, Aquatic Acute 1; H400 (M=1) and Aquatic Chronic 2; H411.

RAC agreed the following hazard classes via the fast-track procedure, i.e. with scrutiny but without plenary debate: no classification for physical hazards, acute toxicity (all routes of exposure), skin corrosion/ irritation, serious eye damage / eye irritation, respiratory / skin sensitisation, germ cell mutagenicity, STOT SE, STOT RE and aspiration hazard.

Considering that the effects on female reproductive organs and offspring development in a 2-generation study with rats were seen only at top doses and reproductive performance was not affected at any dose level, RAC considers classification for fertility not warranted, noting however uncertainties on the informative value of the chosen dosing regime for the available 2-generation study. Regarding development, RAC concluded based on two developmental toxicity studies, one in rats and one in rabbits. No adverse effects such as death of the developing organism, structural abnormalities, altered growth, or functional deficiency was associated with sedaxane exposure during pregnancy or as a result of parental exposure in developing rats and rabbits that would require classification and therefore no classification is warranted.

RAC discussed the plausibility of the mode of action proposed by the DS for carcinogenicity and the incidences of tumours at multiple sites in two species. RAC also discussed the adequacy of the data provided to assess human relevance. With regard to liver tumours in rats and mice, RAC agreed that a CAR-mediated MoA seems the most plausible mechanism. However, evidence for non-human relevance consisted only of one human hepatocytes assay with cells from only one donor and no confirmatory studies e.g. with CAR-Knock-Out mice had been performed. RAC therefore agreed to consider the liver tumours in the overall weight-of-evidence assessment. With regard to thyroid tumours in rats, RAC agreed that the CAR-mediated induction of hepatic UGT activity is the most plausible mechanism and thyroid tumours induced via this MoA are considered of limited relevance to humans. In the same line with regard to liver tumours in both rats and mice, RAC agreed that the CAR/PXR mode of action is the most plausible mechanism. RAC considered the proposed MoA for uterine tumours not sufficiently demonstrated and thus not adequate to assess human relevance. The observed uterine adenocarcinomas although seen in high dose are considered treatment related and relevant for classification. Therefore, human relevance of the uterine neoplastic lesions associated with sedaxane in rats need to be considered. RAC considers these effects together with the remaining uncertainty related to the missing or insufficient mechanistic data package for the liver carcinoma in mice. Uterine adenocarcinoma were reported only in the top dose of one species, accompanied by marked

decrease in body weight gain. In addition, sedaxane is unlikely to be genotoxic. RAC considers therefore that classification in category 1B is not justified and overall pattern of effects justifies downgrading classification. Therefore, on balance, RAC considered classification as Carc. 2; H351 warranted based primarily on concern for the uterine tumours in rats but weighing in also the liver tumours.

With regard to ozone depletion, RAC agreed that no classification is warranted for sedaxane as local and global effects are expected to be negligible due to its very low vapour pressure and Henry's constant, whilst its photochemical oxidative degradation in air is expected to be rapid.

RAC discussed the environmental hazards of sedaxane and concluded that the substance is not rapidly degradable and is unlikely to bioaccumulate. RAC agreed the classification as Aquatic Acute 1; H400 (M=1) is warranted based on the lowest value LC50 = 0.62 mg/L for *Cyprinus carpio*. The DS proposed Aquatic Chronic 2 (M=1) based on *Pimephales promelas* chronic data.

For chronic aquatic toxicity RAC discussed two options: one considering chronic classification based on the above-mentioned chronic study (as well as all other available chronic data on the other trophic levels) and one based on the use of both acute and chronic data. The latter could be applied in case of a conclusion that the substance is data poor and there are strong indications that the most sensitive species from the acute tests was not tested in the respective chronic ones. RAC concluded that the available information "package" for sedaxane cannot be regarded as data poor and the sensitivity differences between *Cyprinus carpio* and *Pimephales promelas* (in the same phylum) are not significant, such that there is no reason to expect a difference in chronic testing. RAC agreed on the use of the reliable available chronic toxicity study for *Pimephales promelas* that derived a NOEC value of 0.165 mg/L and lead to Aquatic Chronic 2; H411.

RAC adopted the opinion by consensus. The Chairman thanked the Rapporteurs for the presentation of the arguments and the Committee Members for their comments.

11. tolclofos-methyl (ISO)

The Chairman reported that tolclofos-methyl (ISO) is used as a contact fungicide for the control of Rhizoctonia. Tolclofos-methyl (ISO) has an existing entry in Annex VI to the CLP Regulation as Skin Sens. 1; H317, Aquatic Acute 1; H400 and Aquatic Chronic 1; H410. The legal deadline for adoption of the opinion is 25 October 2019.

The DS (UK) proposed to modify the existing classification to Skin Sens. 1B; H317, to add M-factors of 1 for Aquatic Acute and Aquatic Chronic hazard classes, and to establish no classification for physical hazards and all remaining human health endpoints.

RAC agreed in the following hazard classes via the fast-track procedure, i.e. with scrutiny but without plenary debate: no classification for physical hazards, acute toxicity (all routes of exposure), carcinogenicity, eye irritation/damage, skin irritation/corrosion, STOT SE, germ cell mutagenicity, reproductive toxicity and modifying classification to Skin Sens. 1B; H317 and adding M=1 to both aquatic acute and chronic hazards.

In regards to a comment received in the public consultation, RAC discussed STOT RE and the effects on acetylcholinesterase (AChE). The Rapporteur explained that there was no inhibition in brain or erythrocyte AChE activity above 20% at dose levels relevant for classification in any of the studies, except for one, in male mice. There, erythrocyte AChE activity was reduced by 20%, which is at cut-off for adversity; brain AChE activity was however not affected. RAC proposes no classification in agreement with DS proposal.

RAC adopted the opinion by consensus. The Chairman thanked the Rapporteurs for the presentation of the arguments and the Committee Members for their comments.

12.mancozeb (ISO)

The Chairman welcomed the expert accompanying the ECPA stakeholder attending the meeting. It was noted that mancozeb is an active substance used in plant protection products authorised in the EU as a fungicide.

At RAC-47 the Committee agreed on classification of mancozeb as Repr. 1B; H360D, Skin Sens. 1; H317, STOT RE 2; H373 (thyroid, nervous system), Aquatic Acute 1; H400 M=10 and Aquatic Chronic 1; H410 M=10.

At this plenary, RAC agreed on no classification of mancozeb for germ cell mutagenicity via the fast-track procedure, with scrutiny by RAC but without plenary debate.

Contrary to the DS proposal (no classification for carcinogenicity) the Rapporteur proposed to classify mancozeb for carcinogenicity based on a weight of evidence analysis of the thyroid tumours observed in rats (both sexes) in two independent studies. RAC noted that the findings would warrant a classification in category 1B according to the CLP criteria since sufficient evidence of carcinogenicity has been observed; however, as pointed out by the Rapporteur and supported by several RAC members, several factors contributed to decrease the concern of carcinogenicity e.g. the compound is non-genotoxic, thyroid tumours occur via perturbation of thyroid homeostasis (thyroperoxidase (TPO) inhibition and subsequent disturbance of the hypothalamic–pituitary–thyroid (HPT) axis) which has a threshold and there are substantial differences in sensitivity to thyroid effects in different species where humans are likely less sensitive. RAC members were also of the opinion that the current knowledge on the non-genotoxic MoA of thyroid cancer is incomplete and as such cannot justify upgrade the classification to category 1B.

On the other hand, RAC stressed that the absence of thyroid tumours in mice in two independent mouse dietary carcinogenicity studies, was associated with very limited general toxicity, decreasing the likelihood to elicit these effects in that species. Furthermore, other MoAs potentially relevant to humans were not investigated and thus cannot be completely ruled out. The concern about malignant liver tumours, which were seen in studies with ETU, was also discussed but not taken into account in the proposed classification. Overall, RAC members supported the Rapporteur's view to classify mancozeb based on the weight of evidence of the results from the rat studies.

The expert accompanying the ECPA stakeholder stressed that the doses of mancozeb in their studies were selected according to the recommendations of the OECD guidelines at the time they were conducted, pointing out that 750 ppm is a maximum tolerated dose (MTD) in rats. Moreover, higher doses in mouse studies would not have had an impact as the ETU doses tumorigenic in this species (as identified in the study by NTP, 1992) correspond to very high doses of mancozeb (1500 mg/kg bw/d and higher when using a conversion factor of 3.5%). Regarding the top dose selected for the long-term studies in rodents, RAC members pointed out that only minor reductions in body weight gains associated with disruption of the HPT axis do not constitute adequate hazard identification to fulfil the regulatory requirements prescribed by the OECD guidelines. Dose levels should generally be based on the results of shorter-term repeated dose studies. In the case of mancozeb, the top doses selected for the mouse carcinogenicity studies were 10 times lower than a relatively well tolerated top dose in a 90-day study. Furthermore, RAC considered that the toxicity of mancozeb can also be attributed to other metabolites than ETU.

The expert accompanying the ECPA stakeholder also pointed out differences in thyroid cancers mechanisms between rats, mouse and humans. RAC acknowledged that humans appear to be quantitatively less sensitive than rats to the induction of malignant thyroid tumours and that a non-genotoxic, threshold MoA is probably operative. RAC also agreed with the expert, the DS and the commenting MSCAs that TPO inhibition is likely to be the main mode of action (MoA) of the mancozeb-induced thyroid tumours. However, RAC notes that some additional non-genotoxic MoAs which have not been investigated, may potentially contribute to the effects. In addition, there is currently insufficient information on the carcinogenic potential of mancozeb in the mouse and potential liver tumours at doses higher than those tested could trigger a more stringent classification.

RAC concluded to classify mancozeb as Carc. 2; H351.

Regarding the classification for reproductive toxicity agreed at RAC-47 (Repr. 1B), the RAC Chairman invited the expert accompanying the ECPA stakeholder to present their additional concerns through a brief oral statement. The industry expressed their surprise and disappointment upon the agreed, more severe classification by RAC since the original dossier submitter's proposal was to remove the existing classification for developmental toxicity (Repr. 2, H361d). Industry provided a brief overview of the history of the classification of mancozeb under DSD by the Technical Committee for classification and labelling (TC C&L), in 1993 (no classification) and 2005 (Repr. 2, H361d). According to industry, the less severe classification was set by the TC C&L on the condition that developmental neurotoxicity (DNT) studies be conducted. Since then, three DNT studies were conducted and, all three being negative, the outcome at RAC-47 (Repr. 1B, H360D) was not in line with their expectations from the previous (DSD) discussions on the classification of mancozeb. On the basis of the draft minutes of RAC-47, it was also not clear to industry why RAC considered some studies as having too low doses and other shortcomings, including the non-GLP PNDT study. They also stressed a possible confusion of studies conducted with ETU instead of mancozeb or speculation by RAC on what would have happened at higher dose levels. Industry felt that more in depth discussion on kinetics of conversion of mancozeb to ETU was needed. RAC noted that the malformations are likely due to the main metabolite of mancozeb, ETU, which is a developmental toxicant with a harmonised classification as Repr. 1B (H360D). In the most recent PNDT study in rats, no developmental effects were seen. However, RAC considered that the new data is not convincing enough to reduce the concern for the malformations seen in the original rat study of An. (1980). The lack of connection between the maternal toxicity and severe malformations in the An. (1980) leads RAC to conclude that mancozeb meets the criteria for classification as Repr. 1B (H360D).

Industry also understood that the study with a single dose of ETU producing malformations contributed to the Repr. 1B classification. A single dose of 30 mg/kg bw/d ETU on GD 15 induced severe dilation of brain ventricles due to necrosis of brain tissue (Khera and Tryphonas, 1977). Although the study has been performed before GLP, RAC noted that the study has been well-conducted and it does not reduce the concern about developmental effects of mancozeb. Finally, industry enquired of the RAC chairman whether the discussion could be re-opened at a later stage.

The Chairman clarified that RAC used a weight of evidence approach in classifying substances and considered all information available in the CLH dossier and provided during the public consultation. He reminded that RAC adopts its scientific opinion based on the available scientific information under the criteria set out in the CLP Regulation but is not bound by either the dossier submitter's proposal, views expressed during public consultation or by previous opinions of other scientific bodies under the legislation preceding CLP. The Chairman also emphasised that the CLP classification criteria are not the same as under the DSD regulation. Results of the older studies were considered by RAC as sufficient for classification as Repr. 1B and the evidence from

the newer PNDT studies was equivocal, i.e in the weight of evidence, the new studies did not overrule the results obtained from the older studies. He informed that RAC had concluded its discussion on this endpoint at RAC 47 and that there was no evident reason to reopen it.

RAC adopted the opinion by consensus. The Chairman thanked the Rapporteur for the presentation of the arguments and the Committee Members for their comments.

13.benzyl salicylate

Benzyl salicylate is used as an ultraviolet absorbing substance in air care products, as a biocides (e.g. disinfectants, pest control products), in perfumes and fragrances, polishes and waxes, and washing and cleaning products.

The substance has no existing entry in Annex VI to the CLP Regulation.

The legal deadline for the adoption of an opinion is 28 December 2019.

RAC agreed via the fast-track procedure, i.e. with scrutiny but without plenary debate to the proposal by Germany to classify benzyl salicylate as a substance that may cause an allergic skin reaction (Skin. Sens. 1B; H317). RAC adopted the opinion by consensus.

14.trinickel disulfide; nickel subsulfide [1]; heazlewoodite [2]

The Chairman welcomed the industry dossier submitter attending the meeting and reported that trinickel disulphide is used in articles, in formulation or re-packing, at industrial sites and in manufacturing. It has an existing entry in Annex VI to the CLP Regulation as Carc. 1A; H350i, Muta. 2; H341, STOT RE 1; H372**, Skin Sens. 1; H317, Aquatic Acute 1; H400 and Aquatic Chronic 1; H410. This proposal was limited to acute toxicity via inhalation exposure. The legal deadline for adoption of the opinion is 1 December 2019.

The DS (IND) proposed classification as Acute Tox. 4; H332 (an ATE-value was not included in the original proposal; an ATE of 1.1 mg/L was proposed in the response to comments table) based on the combined mean (male and female) LC50 of 1.14 mg/L in an acute toxicity rat study. The RAC Rapporteur noted that the LC50 values were borderline between Category 3 and 4, with the female LC50 (0.92 mg/L) being below the cut-off for Category 3 and the male LC50 (1.35 mg/L) above the cut-off. The Rapporteur proposed using a weight of evidence approach, also considering the higher sensitivity in mice in short term repeated dose studies as supportive evidence, which would lead to an LC50 below the cut-off for Category 3 in mice. Based on this the Rapporteur proposed classifying the substance as Acute Tox. 3; H331, with an ATE value based on the female rat LC50 of 0.92 mg/L.

One RAC member commented that the higher sensitivity in mice is not clear as also control animals died in two of the short term studies. The same RAC member noted that other nickel compounds, e.g. nickel sulfate, which has been shown to have a higher toxicity for other endpoints, is classified as Acute Tox. 4. The DS, commented that there was no statistical difference between the LC50 for females and males and therefore the average LC50 value for rats should be used. The majority of RAC members, however, supported classification in Category 3. They argued that the reliable acute toxicity study in rats should be regarded as key information in this case, and as the LC50 value for females was below the cut-off value, classification as Acute toxicity Category 3 is warranted. Several members also noted that this would be in line with previous RAC opinions. There was also support for adding an ATE-value based on the female LC50 value. Therefore, RAC concluded on the classification for trinickel disulphide as Acute toxicity via the inhalation route in Category 3 (Acute Tox. 3; H331) with an ATE-value of 0,92 mg/L (dust/mist).

RAC adopted the opinion by consensus. The Chairman thanked the Rapporteurs for the presentation of the arguments and the Committee Members for their comments.

15.pydiflumetofen (HH hazards)

The Chairman welcomed the expert accompanying the ECPA stakeholder attending the meeting. The Chairman reported the substance is an active substance in plant protection products used as a fungicide. It has no existing entry in Annex VI to the CLP Regulation. The DS (FR) proposes to classify as Aquatic Acute 1; H400 (M=1) and Aquatic Chronic 1; H410 (M=1). The dossier was tabled for a second discussion at a RAC plenary meeting of the human health hazards. Legal deadline is 29 August 2019.

The Chairman reminded the Committee that environmental hazards and some human health hazards were agreed via fast-track procedure at RAC-47 plenary. At this plenary RAC agreed via the fast-track procedure, i.e. with scrutiny but without plenary debate, on no classification for skin irritation which was concluded on at the previous plenary.

The rat thyroid adenomas occurred in females at the highest dose at the upper bound limit of the historical control data range. The adequacy of the dose selection in this study was questioned, noting that higher doses could have been tested. There was no supporting evidence from males and no thyroid tumours were observed in mice. RAC concluded that there is no firm evidence for a neoplastic response in the rat thyroid as a consequence of exposure to pydiflumetofen.

RAC discussed the findings from the male human hepatocytes *in vitro* study. A CAR mode of action was discussed by RAC as an explanation for the increase in liver adenomas and carcinomas in the male mouse. RAC agreed that there were uncertainties with regard to the *in vitro* human liver hepatocytes test (only one donor) and the consequent species specificity.

RAC agreed on classification as Category 2 as human relevance cannot be excluded considering using a WoE approach and based on liver tumours.

RAC discussed the effects on fertility seen in both sexes (delay in vaginal opening, preputial separation), outside the historical control range (for males) which could not be explained by bodyweight changes alone, concluding that the effects are treatment related. As the effects seen may potentially impact on fertility or reproductive function, Category 2 for fertility was agreed by RAC.

With regard to the developmental toxicity, no adverse findings in rat study was observed and no significant dose or treatment-related pattern was apparent in a rabbit study.

RAC adopted the opinion by consensus. The Chairman thanked the Rapporteurs for the presentation of the arguments and the Committee Members for their comments.

9. Restrictions

9.1 Restriction Annex XV dossiers

a) General issues

1) Report from Restrictions Task Force meeting

The Secretariat presented to the Committee the report from the last Restrictions Task Force (RTF) meeting as well as the issues planned to be tackled in the near future. The Committee

welcomed the work of the RTF. It was agreed that the Secretariat will share the Action points of the last RTF meeting with RAC and SEAC via S-CIRCABC.

2) Update of the opinion development procedure

The Secretariat presented to RAC an update to the opinion development procedure for restrictions RAC/48/2019/03), the aim of which is to streamline the process and make it more flexible. The Committee agreed to use it starting from the three dossiers that were submitted in January 2019.

b) Conformity check and key issues discussion

1) Formaldehyde

The Chairman welcomed the Dossier Submitter representatives from ECHA and the RAC Rapporteurs. He informed the participants that the restriction dossier had been submitted by ECHA on 11 January 2019.

The representative of the Dossier Submitter provided an introductory presentation on the dossier. The proposal aims to restrict the placing on the market or the use of all articles releasing formaldehyde at concentrations greater than or equal to 0.124 mg/m^3 in the air of a test chamber used under the conditions prescribed in EN 717-1[6]. Formaldehyde is predominantly used as a chemical intermediate in the production of formaldehyde-based resins and other chemicals including several important resins which form the largest group of formaldehyde releasers under foreseeable conditions of use. Formaldehyde-based resins are widely used as adhesives and binders in the woodworking, pulp and paper, as well as the synthetic vitreous fibre industries, in the production of plastics and coatings, and in textile finishing.

The RAC members and representatives of the stakeholder organisations commented on the rapporteurs' recommendation to justify the DNEL value used in the restriction proposal (taken from WHO Guideline for Indoor Air Quality for formaldehyde) by comparing such a limit with DNELs derived from different endpoints using the ECHA guidance. The Chairman pointed out that use of such International values was foreseen by REACH and the WHO values could be used independently. ECHA noted that as DS it was not in a position to calculate separate DNELs should the rapporteurs request this. Comments were also made on the fact that, though the restriction covers all articles, the assessment of the risk and the impact was limited to certain categories of articles. It was pointed out that this approach is not uncommon and it has potential similarities with the restriction proposal on ammonium salts; furthermore exposures had been modelled.

The Rapporteurs presented the outcome of the conformity check and the recommendations to the Dossier Submitter, and proposed to the Committee that they consider the dossier to be in conformity. The Committee agreed that the dossier conforms to the requirements of Annex XV of the REACH Regulation. In addition, the Rapporteurs presented their key issues of the restriction proposal. The Chairman informed the Committee that the public consultation on this restriction proposal will be launched on 20 March 2019.

2) D4/D5/D6

The Chairman welcomed the Dossier Submitter's representatives from ECHA and an industry

[6] - Articles subject to the CMRs in textiles restriction as well as the use of formaldehyde and formaldehyde releasers as biocide are exempted from the proposed restriction because they are already covered by other legislation.
- Use of formaldehyde in mixtures (> 0.1 %) has already been restricted in 2018 by the Commission with the amendment to Entry 28 to Annex XVII of REACH.

expert, accompanying the regular CEFIC stakeholder observer. He informed the participants that the restriction dossier had been submitted in January 2019.

The Dossier Submitter's representative explained that the dossier proposes to restrict the placing on the market of D4, D5 and D6 as substances, as constituents of other substances, or in mixtures in a concentration equal to or greater than 0.1% w/w of each substance. These substances are mainly used as monomers (i.e. intermediates) for the production of silicone polymers (a use which is exempt from restriction) but are also used as substances on their own or in the formulation of various mixtures that are subsequently used by consumers and professionals. D4, D5 and D6 were identified by ECHA's Member State Committee as SVHC substances with PBT/vPvB properties. The proposed restriction is a follow-up of the UK Annex XV restriction proposal on D4 and D5 that was evaluated by RAC and SEAC in 2016 and will result in a total emission reduction of D4, D5 and D6 (all sources and compartments) of approximately 90%.

The Rapporteurs presented the outcome of the conformity check and the recommendations to the Dossier Submitter. They noted that they found the proposal in general very clear, with sufficiently well explained hazards, exposure and risk and they thus consider the dossier to be in conformity. The Rapporteurs recommended to the Dossier Submitter to further clarify the meaning of the terms 'wash off' and 'rinse off' in the report, what exactly is covered by the derogation for industrial sites, as well as the justifications for the lengths of the transition periods proposed for leave-on cosmetic products and for dry cleaning. The Commission observer shared the view of the Rapporteurs that the scope of the proposed restriction should be clarified. With regard to the lengths of the transitional periods for leave-on cosmetic products and for dry cleaning, one member emphasised that RAC can only look at the exposure assessment and that it will be up to SEAC to assess the justification for the proposed length of the transitional periods.

The Committee agreed that the dossier conforms to the Annex XV requirements. In addition, the Rapporteurs presented their key issues of the restriction proposal. The Chairman informed the Committee that the public consultation on this restriction proposal will be launched on 20 March 2019 (provided that also SEAC considers it in conformity).

3) Microplastics

The Chairman welcomed the RAC rapporteurs, the Dossier Submitter representatives from ECHA, supported by experts from Sweden via webex, the occasional stakeholder (A.I.S.E) and the industry expert (MIT) accompanying Cefic regular stakeholder observer. He informed the participants that the restriction dossier had been submitted in January 2019. In addition, Sweden (KemI) collaborated with ECHA in the preparation of the dossier.

The representative of the Dossier Submitter gave an introductory presentation on the dossier. He explained that the proposal aims to restrict the intentionally added microplastics in products from which they will inevitably be released to the environment. The term 'microplastic' is not consistently defined, but is typically considered to refer to small, usually microscopic, solid particles made of a synthetic polymer. The concern associated with microplastic particles stems from the following:

- the potential environmental and human health risks posed by the presence of solid particles of synthetic polymer-based materials in the environment that are small (typically microscopic) making them readily available for ingestion and potentially liable to transfer within food chains;
- they are very resistant to environmental (bio)degradation, which will lead to them being present in the environment for a long time after their initial release;
- they degrade via fragmentation into smaller and smaller particles, theoretically via

'nanoplastic' particles;
- they are practically impossible to remove from the environment after release.

The Dossier Submitter has estimated that approximately 36 000 tonnes of intentionally added microplastics are currently released to the environment per year. These are most likely to accumulate in terrestrial environments.

Data on the toxicological and ecotoxicological effects of microplastics are limited, particularly for the terrestrial environment, which makes conventional risk assessment challenging. The Dossier Submitter has considered the risk assessment of microplastics using the threshold, non-threshold and 'case-by-case' approaches outlined in Annex I of REACH and considers that microplastics should be treated as a group of non-threshold substances for the purposes of risk assessment, similar to PBT/vPvB substances. Overall, the Dossier Submitter concludes that the intentional use of microplastics in products result in releases to the environment that are not adequately controlled. The proposal would prevent the placing on the market of intentionally added microplastics in products from which they will inevitably be released to the environment and introduces new requirements for labelling, reporting and conditions of use for products where their release to the environment can be minimised. The scope covers a wide range of uses in consumer and professional products, including cosmetic products, detergents and maintenance products, paints and coatings, construction materials and medical products, as well as various products used in agriculture and horticulture. The proposed restriction is estimated to result in a cumulative emission reduction of approximately 400 thousand tonnes of microplastics over the 20 year period following its entry into force. This represents a reduction of 85-95% of the quantified emissions that would otherwise have occurred in the absence of the restriction taking effect.

The (co-)rapporteurs then presented the outcome of the conformity check and the recommendations to the Dossier Submitter, and they consider the dossier to be in conformity. Following the presentation, a RAC member asked some clarifications with regard to alternatives and whether these could lead to a more problematic situation. The representative of the Dossier Submitter explained that different uses have different alternatives, and it falls within SEAC's mandate to assess them, unless there is a clear risk. Another member pointed out a challenge for analytical methods for nanoparticles (0.01 % w/w). One stakeholder observer expert pointed out that in her view, there is lack of clarity in justification for a proposed derogation for (bio)degradable substances.

The Committee agreed that the dossier conforms to the Annex XV requirements. The Chairman informed the Committee that the public consultation on this restriction proposal will be launched on 20 March 2019.

c) Opinion development

1) *N,N*-dimethylformamide – first draft opinion

The Chairman welcomed the Dossier Submitter's representatives from Italy (via WebEx), the occasional stakeholder observer from CIRFS, as well as the expert accompanying the occasional stakeholder, and the RAC Rapporteurs. He informed the participants that the restriction dossier had been submitted by Italy on 5 October 2018. The proposal aims to restrict the uses of the substance on its own or in mixtures in a concentration equal or greater than 0.3 %, unless exposure conditions described as DNEL values for inhalation (3.2 mg/m^3) and dermal (0.79 mg/kg bw/day) exposure of workers are met. DMF is manufactured in the EU, and used in the production of fine chemicals, pharmaceuticals, polymers, textiles, non-metallic products,

and perfumes/fragrances. It is also used in the petrochemical industry and as a laboratory reagent. There is no consumer use of DMF.

RAC discussed the first draft opinion and the approach taken by the Rapporteurs for the hazard evaluation. Some members pointed out that the DNEL value could potentially be derived based on the biomonitoring data, as there will always be combined exposure. In addition, several RAC members noted that there is no established method for the monitoring of dermal exposure at the workplace. The expert accompanying the CIRFS stakeholder observer also supported use of biomonitoring data for DNEL derivation. He indicated that, in workplaces using DMF, biomonitoring is nowadays 'state of the art' compared to airborne monitoring, he also informed that the additional information, in particular, on biomonitoring data, and correlation information between biomonitoring and airborne contamination could be submitted by the relevant industrial sectors through the public consultation. A representative of the European Commission also advised the Committee to consider a SCOEL opinion (2006) on DMF, in which biological exposure limit for workers was also proposed (even if not taken forward in the legislation).

Based on the currently available data in the dossier, RAC agreed on the identified hazards and on the DNELs proposed by the rapporteurs on a preliminary basis. The Committee agreed to derive the dermal DNEL from dermal developmental toxicity studies giving a value of 1.1 mg/kg/day. In addition, the Committee agreed to consider biomonitoring, should further information come in through public consultation before the next RAC meeting. RAC considered a systemic long term DNEL of 6 mg/m^3 for the inhalation route based on a combination of human data and rabbit data, taking into account liver toxicity and developmental toxicity, respectively.

The exposure and risk related elements were also presented and uncertainties related to the PROCs used and the available exposure information – limited measured data to support modelling results – were discussed. The rapporteurs pointed out that some additional measured data has already become available through the public consultation. It was agreed to discuss the exposure and risk again, when it would be possible to take into consideration new data submitted by the industry.

The Rapporteurs were requested to take the discussion of RAC-48 and the results of the RAC consultation into account in the second draft RAC opinion. The Chairman concluded that the Committee will continue discussions on exposure and risk part of the draft RAC opinion at the next Committee's meeting RAC-49 in June 2019. He also encouraged industry to contribute actively to the ongoing public consultation by submitting available exposure and biomonitoring data with the accompanying contextual information ahead of the next RAC plenary meeting in June.

2) Cobalt salts – first draft opinion

The Chairman welcomed the Dossier Submitter's representatives from ECHA, and industry experts accompanying the regular CEFIC and Eurometaux stakeholder observers. He informed the participants that the restriction dossier had been submitted in October 2018 and proposes to restrict the placing on the market, manufacture and use of the cobalt salts as substances on their own or in mixtures in a concentration equal to or above 0.01% by weight in industrial and professional applications. The five cobalt salts (cobalt sulphate, cobalt dichloride, cobalt dinitrate, cobalt carbonate and cobalt di(acetate)) are manufactured and used in a variety of sectors within the European Economic Area, including the manufacture of chemicals, catalysts, battery production, surface treatment, fermentation processes, health applications, feed grade materials, biogas, etc. They are classified as Carc. 1B (inhalation), Muta. 2, Repr. 1B and skin and respiratory sensitisers. In 2016, RAC had agreed that these salts should be considered as genotoxic carcinogens with a non-threshold mode of action and had agreed a dose-response

relationship for these substances.

The Rapporteurs reminded the Committee that, as concluded by RAC in 2016, the current mode of action considerations support that water-soluble cobalt substances may be threshold carcinogens but because of the difficulties to identify the threshold and uncertainties regarding all the mechanisms involved, RAC proposed a non-threshold approach in that document. However, the Rapporteur suggested that this could be revisited by RAC.

Several members expressed the view that currently there is not enough data for RAC to deviate from its previous opinion. The industry representatives mentioned that they are planning to submit additional information on the mode of action within the ongoing public consultation in the next few weeks. RAC agreed that the Dossier Submitter's approach to base hazard characterisation on RAC 2016 opinion (applied to the inhalable fraction) on cancer dose-response of cobalt salts is a default position, but other options will be explored, also taking into account possible new information submitted in the public consultation by stakeholders.

A new large epidemiological study by Marsh et al (2017) from hard metal production does not show increased cancer risk associated to cobalt exposure in humans. However, detecting or excluding with confidence the increased cancer risks in the study population is challenging (it would roughly correspond to a relative risk in the exposed population of 1.2-1.3).

With regard to exposure assessment, the Committee agreed that the Rapporteurs should consider both 50% and 100% respirable fraction in the next version of the opinion. The industry representatives promised to provide information on the particle size distribution within the ongoing public consultation. Stakeholders were encouraged to provide this information, as well as the information on the mode of action latest by 8 April 2019, in order for the Rapporteurs and the Committee to consider it.

The Chairman informed the participants that the Secretariat will launch a written consultation on the first draft opinion after RAC-48. The Rapporteurs were requested to take the RAC-48 discussion and the RAC written consultation into account in the second version of the draft opinion. Furthermore, the Rapporteurs and the Secretariat were requested to consider the need for organising an ad-hoc working group back-to-back the second Rapporteurs' dialogue or next RAC plenary meeting.

10. Authorisation

10.1 General authorisations issues

a) Update on incoming/future applications

The Secretariat informed the Committee that twelve new applications for authorisation were received during the February 2018 submission window. Three of them are on uses of chromium (VI) substances for surface treatment of steel for high performance transformers, as an anticorrosion agent in a cooling system, and as suppressant of the parasite reactions in electrolytic production of sodium chlorite. Another three are applications for authorisation for the uses of coal tar pitch, high temperature (CTPHT) in formulation of mixtures and production of nozzle throats for civilian and military aerospace launchers. The other six applications for authorisation are for the uses of octylphenol ethoxylates (five applications) and nonylphenol ethoxylates (one application) in the life sciences sector, including production of pharmaceutical active ingredient, formulation of reagents further incorporated in in vitro devices, their production and their use by professionals, such as laboratories, hospitals etc. Key issues in the new applications for authorisation will be discussed at RAC-49 plenary meeting in June 2019.

The Secretariat also informed about high numbers of applications for authorisation expected to be received during May 2019 submission window and in the end of 2019 and the beginning of 2020 amounting to possibly ca. 120 applications for authorisation on more than 200 uses of chromium (VI) substances, octyl- and nonylphenol ethoxylates, coal tar pitch, high temperature, and trichloroethylene and chromium (VI) substances.

b) Working group on application for authorisation

The Secretariat asked the Committee to agree with the proposed mandate for the Working Group on Applications for Authorisation for RAC. An initial draft mandate for the Working Group on applications for authorisation was presented at RAC-47 and is now revised into a further developed proposal to prepare Applications for Authorisations fully in a working group.

The Committee agreed with the revised draft mandate for the Working Group on applications for authorisation (RAC/48/2019/04). The Secretariat will organise the first Working Group on Applications for Authorisation in April 2019.

The Secretariat to publish the mandate of the Working Group on applications for authorisation on ECHA's website.

c) Update on the approach of evaluation of the upcoming applications for authorisation for environmental endocrine disruptors (octyl- and nonylphenol ethoxylates)

The Secretariat reminded the Committee about the document "Risk-related considerations in applications for authorisation for endocrine disrupting substances for the environment, specifically OPnEO and NPnEO" agreed by the Committee at the RAC-43 plenary meeting. The document provides general advice to companies intending to apply for authorisation of uses of OPnEO and NPnEO with regard to environmental risk assessment. However, it does not define any 'preferred approach', nor does it give reference values.

During the discussion the RAC members noted the approach and discussed several of the common issues that are foreseen to arise during the evaluation of these applications for authorisation.

10.2 Authorisation applications

a) Discussion on key issues

1. Five applications for authorisation from the November 2018 submission window (chromium trioxide)

The Secretariat in cooperation with the RAC Rapporteurs provided general information regarding the new applications for authorisation listed below.

CT_Thyssen

This is an application with a relatively broad scope regarding the following two uses of chromium trioxide.

Use 1: Use of chromium trioxide for Passivation of tinplated steel (ETP)

Use 2: Use of chromium trioxide for Electrolytic Chromium Coating of Steel (ECCS)

The substance is used on one site in Germany. 95 tonnes of chromic acid (24.7 tonnes Cr(VI)) are used for use 1, and 7-year long review period is requested starting from expected decision in 2020 by the applicant. 200 tonnes of chromic acid (52 tonnes Cr(VI)) are used for use 2, and a review period until end 2028 is requested by the applicant.

The Rapporteur indicated that A-listing might be an option since the data provided are of good quality. The Rapporteur will propose A-listing to RAC if the applicant´s answers to RAC questions clarify the remaining issues.

CT_Aloys

This is an application with a narrow, well-defined scope regarding the following single use of chromium trioxide.

Use: Functional chrome plating with decorative character for sanitary applications

The substance is used on one site in Germany. 1-10 tonnes of chromium trioxide are used for the use 1, and 12-year long review period is requested by the applicant.

The Rapporteur indicated that A-listing might be an option since the data provided are of good quality. The Rapporteur will propose A-listing to RAC if the applicant´s answers to RAC questions clarify the remaining issues.

CT_Ideal

This is an application with a narrow, well-defined scope regarding the following two uses of chromium trioxide.

Use 1: Electroplating of different types of substrates using chromium trioxide to achieve functional surfaces with high durability and a bright or matt silvery appearance for sanitary applications

Use 2: Etching of plastics with chromium trioxide as pre-treatment step for electroplating processes

The substance is used on one site in Germany, one site in Portugal and two sites in Bulgaria. 10-100 tonnes of chromium trioxide are used for use 1, and 12-year long review period is requested by the applicant. However, 1-10 tonnes of chromium trioxide are used for use 2, and 12-year long review period is requested.

The Rapporteur indicated that A-listing might be an option since the data provided are of good quality. The Rapporteur will propose A-listing to RAC if the applicant´s answers to RAC questions clarify the remaining issues.

CT_Keuco

This is an application with a narrow, well-defined scope regarding the following two uses of chromium trioxide.

Use 1: Electroplating of different types of substrates using chromium trioxide to achieve functional surfaces with high durability and a bright or matt silvery appearance for sanitary applications

Use 2: Etching of plastics with chromium trioxide as pre-treatment step for electroplating processes

The substance is used on one site in Germany. 1-10 tonnes of chromium trioxide are used for uses 1 and 2, and 12-year long review period is requested by the applicant.

The Rapporteur indicated that A-listing might be an option since the data provided are of good quality. The Rapporteur will propose A-listing to RAC if the applicant´s answers to RAC questions clarify the remaining issues.CT_Schell

This is an application with a narrow, well-defined scope regarding the following single use of chromium trioxide.

Use: Functional chrome plating with decorative character for sanitary applications

The substance is used on one site in Germany. 1-10 tonnes of chromium trioxide are used for the use 1, and 12-year long review period is requested by the applicant.

The Rapporteur indicated that A-listing might be an option since the data provided are of good quality. The Rapporteur will propose A-listing to RAC if the applicant´s answers to RAC questions clarify the remaining issues.

The Secretariat in cooperation with the RAC Rapporteur provided general information regarding these new applications. In the presentation of the case, the Secretariat outlined the key issues identified by the Rapporteurs and asked the Committee for comments and further suggestions.

The Committee discussed these key issues. Where needed, RAC will request further clarifications from the Applicants on the issues identified and discussed by the Committee.

10.3 Review reports

a) Adoption of draft opinions

1. RR1_TCE_Spolana (1 use)

This is a review report and the original application for authorisation for the use of TCE by Spolana was evaluated by the Committees in 2014-2015. The Commission granted the authorisation on 8 February 2017. The date of expiry of the review period is 21 April 2020. This application covers only Spolana's use of trichloroethylene (TCE) as an extraction solvent in caprolactam production. The review period requested is 12 years. The tonnage has been reduced from 150 t/y in the original application to 100 t/y. Up to 100 workers are directly exposed. The highest combined excess risk for workers is 3.82×10^{-5} and for man via the environment 3.41×10^{-7}.

Following the Rapporteur's presentation and her request concerning the analysis of the risk of the proposed alternatives, RAC advised to state that it is doubtful whether TCE can be suitably replaced by toluene, which is flammable and has a Repro 2 classification, nor by benzene. Then RAC discussed the level of the annual losses of TCE from the installation which is equal to 50 % of the total volume of TCE in the system. The Rapporteur replied that, compared to the initial application, the applicant holder has reduced the use of TCE by 50 tonnes per year and is expecting to further reduce the use of TCE to 85 tonnes. In addition, it is estimated that the level of fugitive emissions have decreased by 17 tonnes in 2018 due to the improvements in the RMMs and OCs introduced. The Rapporteur clarified that in the case of the review report submitted by Spolana, the application holder has provided a statistical analysis of the monitoring data on worker exposure.

The Committee agreed on the draft opinion as proposed by the Rapporteur. RAC acknowledged the efforts made by the application holder regarding the implementation of RMMs to reduce exposure for workers and for humans via the environment and is of the opinion that the RMMs now described are appropriate and effective in limiting the risk to workers. However, the authorisation holder should continue to improve their RMMs and OCs to further reduce TCE emissions, based on measurement results of releases to air and wastewater and regular air and biomonitoring campaigns. RAC agreed to recommend monitoring arrangements for the review report. RAC also agreed to give no advice to SEAC on the length of the review period.

11. AOB

1. RAC consultation on ECHA Guidance Appendix to R.8-17 'Guidance for proposing Occupational Exposure Limits'

The Secretariat informed the Committee on the status and the general outline of the ECHA Guidance Appendix to R.8-17, and the main comments received during the PEG consultation on the REACH-OSH interface of the draft guidance.

The RAC consultation on the ECHA Guidance Appendix to R.8 -17 is foreseen in March 2019.

2. Court cases involving RAC opinions

The Secretariat (Legal Affairs Unit) gave an overview of Court cases involving RAC opinions and an update with further details concerning recent cases. A first overview was given at the ENV rapporteurs' workshop back-to-back RAC-47.

The perspective on Committee interaction and presentation of Court cases was found very useful by the participating Members.

3. Report from the Workshop on progressing the Rapid Removal concept for metals classification held on 8 February 2019

The Secretariat gave a brief report to RAC from the *Workshop on progressing the Rapid Removal concept for metals classification* held on 8 February 2019. The workshop aimed in particular at having an information exchange among scientists, industry, Member State representatives and some RAC members with the focus on following aspects:

- recent scientific and technical developments of research by industry;
- exchange of views on the applicability of the Rapid Removal concept for hazard classification purposes;
- identification of the critical elements for further discussion.

Areas for further work were identified; namely relevance of particles (further clarification needed concerning standard conditions), inorganics *versus* organics, speciation of metals in the partitioned phase and outstanding issues related to the test conditions in the extended T/Dp.

The Secretariat further informed RAC about a second workshop envisaged back-to-back with RAC 49 in June. The outcome of the discussions would then be brought to the attention of the CARACAL for their agreement on the next steps.

4.Training session on INTERACT project

The Secretariat provided training (based on software demo) on the Interact Portal and the collaboration tool, which release in the production environment is scheduled in April 2019.

15 March 2019

Part II. Conclusions and action points

MAIN CONCLUSIONS & ACTION POINTS

RAC 48 **6-8 March 2019**
12-15 March 2019
(Adopted at the meeting)

Agenda point	
Conclusions / agreements / adoptions	**Action requested after the meeting (by whom/by when)**
2. Adoption of the Agenda	
The Agenda (**RAC/A/48/2019**) was adopted.	**SECR** to upload the adopted Agenda to the RAC CIRCABC and to the ECHA website as part of the RAC-48 minutes.
4. Appointment of (co-)rapporteurs	
a) Appointment of (co-)rapporteurs for CLH dossiers, restriction dossiers, authorisation applications, DNEL/dose-response relationships, Article 95(3) requests and Article 77(3)(c) requests	
5. Report from other ECHA bodies and activities	
a) Report on RAC 47 action points, written procedures and other ECHA bodies **SECR** presented document **RAC/48/2019/01.**	**SECR** to upload the document to the CIRCABC non-confidential website.
b) RAC work plan for all processes	
c) Revision of Rules of Procedure RAC agreed on the revised Rules of Procedure of the Committee for Risk Assessment (document RAC/48/2019/02).	**SECR** to inform the Management Board on the agreement of RAC on the proposed revised Rules of Procedures.
6. Requests under Article 77 (3)(c)	
Copper compounds (M-factor) RAC adopted by consensus the opinion with a proposal for chronic M-factors for the copper	**Rapporteurs** to revise the opinion in accordance with the discussion and provide it to the Secretariat.

substances listed in Commission Regulation (EU) 2016/1179[7] (Table 2). RAC agreed to add a note (addendum) to the opinion on the potential impact of the updated copper ecotoxicity database on the acute ERVs (following re-calculation) and in particular on the acute M-factors.	**SECR** to launch a short RAC consultation on the final opinion. **SECR** to make an editorial check of the opinion in consultation with the Rapporteurs. **SECR** to forward the adopted opinion and its annexes to COM and publish it on the ECHA website.
7. Requests under Article 95 (3)	
-	
8. Harmonised classification and labelling (CLH)	
8.1 General CLH issues	
Please see the short summary of the workshop in Annex VI.	
8.2 CLH dossiers	

A. Substances with hazard classes for agreement by A-listing following the usual scrutiny but without plenary debate

Please mention any ATE values for acute toxicity, together with the applicable route of exposure, where these were agreed by RAC through fast-tracking.

- Prothioconazole (ISO): physical hazards (as open for the public consultation), acute toxicity, skin corrosion / irritation, serious eye damage / eye irritation, skin sensitisation, germ cell mutagenicity, carcinogenicity, STOT SE, STOT RE, environmental hazards
- Thiophanate-methyl (ISO): physical hazards (as open in the public consultation), acute toxicity, skin corrosion / irritation, serious eye damage / eye irritation
- Tolpyralate: physical hazards (as open in the public consultation), acute toxicity, skin corrosion / irritation, serious eye damage / eye irritation, respiratory / skin sensitisation, STOT SE, environmental hazards
- p-cymene: physical hazard (flammable liquids), acute toxicity, skin corrosion / irritation, germ cell mutagenicity, STOT SE, STOT RE, aspiration hazard
- d-limonene: physical hazard (flammable liquids), aspiration hazard
- alpha-terpinene: physical hazard (flammable liquids), acute oral toxicity, germ cell mutagenicity, aspiration hazard
- 1,2,4-triazole: acute oral toxicity
- sedaxane: physical hazards, acute toxicity, skin corrosion/ irritation, serious eye damage / eye irritation, respiratory / skin sensitisation, germ cell mutagenicity, STOT SE, STOT RE, aspiration hazard
- tolclofos-methyl (ISO): physical hazards (as open in the public consultation), acute toxicity, skin corrosion / irritation, serious eye damage / eye irritation, skin

[7] Commission Regulation (EU) 2018/669 of 16 April 2018 amending, for the purposes of its adaptation to technical and scientific progress, Regulation (EC) No 1272/2008 of the European Parliament and of the Council on classification, labelling and packaging of substances and mixturesText with EEA relevance.

sensitisation, germ cell mutagenicity, carcinogenicity, toxicity to reproduction, STOT SE, environmental hazards

- mancozeb (ISO): germ cell mutagenicity
- benzyl salicylate: skin sensitisation
- pydiflumetofen: skin irritation

B. Substances with hazard classes for agreement in plenary session

Please mention any ATE values for acute toxicity, together with the applicable route of exposure, where these were agreed by RAC, including those agreed through fast-tracking.

- 1,4-dioxane
- flumioxazin (ISO)
- prothioconazole (ISO)
- thiophanate-methyl (ISO)
- tolpyralate
- p-cymene
- d-limonene
- alpha-terpinene
- 1,2,4-triazole
- sedaxane
- tolclofos-methyl (ISO)
- mancozeb (ISO)
- trinickel disulfide; nickel subsulfide [1]; heazlewoodite [2]
- pydiflumetofen *(HH hazards)*

1. 1,4-dioxane

RAC adopted <u>by consensus</u> the opinion with a proposal for the harmonised classification and labelling as indicated in Table 1 below. [Carc. 1B; H350]	**Rapporteurs** to revise the opinion in accordance with the discussion in RAC and to provide it to SECR. **SECR** to make an editorial check of the opinion documents in consultation with the Rapporteurs. **SECR** to forward the adopted opinion and its annexes to COM and publish it on the ECHA website.

2. flumioxazin (ISO)

RAC adopted <u>by consensus</u> the opinion with a proposal for the harmonised classification and labelling as indicated in Table 1 below. [Repr. 2; H361d]	**Rapporteur** to revise the opinion in accordance with the discussion in RAC and to provide it to SECR. **SECR** to make an editorial check of the opinion documents in consultation with the Rapporteur.

	SECR to forward the adopted opinion and its annexes to COM and publish it on the ECHA website.
3. prothioconazole (ISO)	
RAC adopted <u>by consensus</u> the opinion with a proposal for the harmonised classification and labelling as indicated in Table 1 below. [Aquatic Acute 1; H400, M = 10, Aquatic Chronic 1; H410, M = 1)]	**Rapporteurs** to revise the opinion in accordance with the discussion in RAC and to provide it to SECR. **SECR** to make an editorial check of the opinion documents in consultation with the Rapporteurs. **SECR** to forward the adopted opinion and its annexes to COM and publish it on the ECHA website.
4. thiophanate-methyl (ISO)	
RAC adopted <u>by consensus</u> the opinion with a proposal for the harmonised classification and labelling as indicated in Table 1 below. [Acute Tox. 4; H332 (ATE = 1.7 mg/L), Skin Sens. 1; H317, Muta. 2; H341, Carc. 2; H351, Aquatic Acute 1; H400 (M=10), Aquatic Chronic 1: H410 (M=10)]	**Rapporteurs** to revise the opinion in accordance with the discussion in RAC and to provide it to SECR. **SECR** to make an editorial check of the opinion documents in consultation with the Rapporteurs send them for the final consultation with RAC. **SECR** to forward the adopted opinion and its annexes to COM and publish it on the ECHA website.
5. tolpyralate	
RAC adopted <u>by consensus</u> the opinion with a proposal for the harmonised classification and labelling as indicated in Table 1 below. [Carc. 2; H351, Repr. 2; H361fd, STOT RE 2; H373 (eye), Aquatic Acute 1; H400, M=10, Aquatic Chronic 1; H410, M=100]	**Rapporteurs** to revise the opinion in accordance with the discussion in RAC and to provide it to SECR. **SECR** to make an editorial check of the opinion documents in consultation with the Rapporteurs. **SECR** to forward the adopted opinion and its annexes to COM and publish it on the ECHA website.
6. *p*-cymene	
RAC adopted <u>by consensus</u> the opinion with a proposal for the harmonised classification and labelling as indicated in Table 1 below. [Flam. Liq. 3; H226, Acute Tox. 3; H331 (inhalation ATE = 3 mg/L (vapour)), Asp. Tox. 1; H304, Aquatic Chronic 2; H411]	**Rapporteurs** to revise the opinion in accordance with the discussion in RAC and to provide it to SECR. **SECR** to make an editorial check of the opinion documents in consultation with the Rapporteurs. **SECR** to forward the adopted opinion and its annexes to COM and publish it on the ECHA website.
7. *d*-limonene	

RAC adopted by consensus the opinion with a proposal for the harmonised classification and labelling as indicated in Table 1 below. [Flam. Liq. 3; H226, Asp. Tox. 1; H304, Skin Sens. 1B; H317, Aquatic Acute 1; H400 (M=1), Aquatic Chronic 3; H412]	**Rapporteurs** to revise the opinion in accordance with the discussion in RAC and to provide it to SECR. **SECR** to make an editorial check of the opinion documents in consultation with the Rapporteurs. **SECR** to forward the adopted opinion and its annexes to COM and publish it on the ECHA website.
8. alpha-terpinene	
RAC adopted by consensus the opinion with a proposal for the harmonised classification and labelling as indicated in Table 1 below. [Flam. Liq. 3; H226, Acute Tox. 4; H302 (ATE=1 680 mg/kg), Asp. Tox. 1; H304, Skin Sens. 1; H317, Aquatic Chronic 2; H411]	**Rapporteurs** to revise the opinion in accordance with the discussion in RAC and to provide it to SECR. **SECR** to make an editorial check of the opinion documents in consultation with the Rapporteurs. **SECR** to forward the adopted opinion and its annexes to COM and publish it on the ECHA website.
9. 1,2,4-triazole	
RAC adopted by consensus the opinion with a proposal for the harmonised classification and labelling as indicated in Table 1 below. [Acute Tox. 4; H302, ATE(oral)=1320 mg/kg bw, Repr. 1B; H360FD]	**Rapporteur** to revise the opinion in accordance with the discussion in RAC and to provide it to SECR. **SECR** to make an editorial check of the opinion documents in consultation with the Rapporteur. **SECR** to forward the adopted opinion and its annexes to COM and publish it on the ECHA website.
10.sedaxane	
RAC adopted by consensus the opinion with a proposal for the harmonised classification and labelling as indicated in Table 1 below. [Carc. 2; H351, Aquatic Acute 1; H400 (M=1), Aquatic Chronic 2; H411]	**Rapporteurs** to revise the opinion in accordance with the discussion in RAC and to provide it to SECR. **SECR** to make an editorial check of the opinion documents in consultation with the Rapporteurs. **SECR** to forward the adopted opinion and its annexes to COM and publish it on the ECHA website.
11. tolclofos-methyl (ISO)	
RAC adopted by consensus the opinion with a proposal for the harmonised classification and labelling as indicated in Table 1 below. [Skin Sens. 1B; H317, Aquatic Acute 1; H400 (M=1), Aquatic Chronic 1; H410 (M=1)]	**Rapporteurs** to revise the opinion in accordance with the discussion in RAC and to provide it to SECR. **SECR** to make an editorial check of the opinion documents in consultation with the Rapporteurs.

	SECR to forward the adopted opinion and its annexes to COM and publish it on the ECHA website.
12. mancozeb (ISO)	
RAC adopted by consensus the opinion with a proposal for the harmonised classification and labelling as indicated in Table 1 below. Carc. 2; H351, Repr. 1B; H360D, Skin Sens. 1; H317, STOT RE 2; H373 (thyroid, nervous system), Aquatic Acute 1; H400 M=10 and Aquatic Chronic 1; H410 M=10.	**Rapporteurs** to revise the opinion in accordance with the discussion in RAC and to provide it to SECR. **SECR** to make an editorial check of the opinion documents in consultation with the Rapporteurs. **SECR** to forward the adopted opinion and its annexes to COM and publish it on the ECHA website.
13. benzyl salicylate	
RAC adopted by consensus the opinion with a proposal for the harmonised classification and labelling as indicated in Table 1 below. [Skin Sens. 1B; H317]	**SECR** to make an editorial check of the opinion documents in consultation with the Rapporteur. **SECR** to forward the adopted opinion and its annexes to COM and publish it on the ECHA website.
14. trinickel disulfide; nickel subsulfide [1]; heazlewoodite [2]	
RAC adopted by consensus the opinion with a proposal for the harmonised classification and labelling as indicated in Table 1 below. [Acute Tox. 3; H331, ATE inhalation= 0,92 mg/L]	**Rapporteurs** to revise the opinion in accordance with the discussion in RAC and to provide it to SECR. **SECR** to make an editorial check of the opinion documents in consultation with the Rapporteurs. **SECR** to forward the adopted opinion and its annexes to COM and publish it on the ECHA website.
15. pydiflumetofen (HH hazards)	
RAC adopted by consensus the opinion with a proposal for the harmonised classification and labelling as indicated in Table 1 below. [Carc. 2; H351, Repr. 2; H361f] [Aquatic Acute 1; H400 (M=1), Aquatic Chronic 1; H410 (M=1)]	**Rapporteurs** to revise the opinion in accordance with the discussion in RAC and to provide it to SECR. **SECR** to make an editorial check of the opinion documents in consultation with the Rapporteurs. **SECR** to forward the adopted opinion and its annexes to COM and publish it on the ECHA website.
9. Restrictions	
9.1 General restriction issues	
RAC took note of the report from the Restrictions Task Force meeting. RAC also took note of the update to the opinion development procedure for restrictions (in line with	**SECR** to share the Action points of the last RTF meeting with the Committee. **SECR** to publish the new procedure in S-CIRCABC as well as on the ECHA website.

the meeting document RAC/48/2019/03 and agreed to use it starting from the three January restriction dossiers.	
9.2 Restriction Annex XV dossiers	
a) Conformity check and key issues discussion	
1. Formaldehyde and formaldehyde releasers	
RAC agreed that the dossier conforms to the Annex XV requirements. RAC took note of the recommendations to the dossier submitter.	**SECR** to compile the RAC and SEAC final outcomes of the conformity check and upload this to S-CIRCABC IG.
2. D4/D5/D6	
RAC agreed that the dossier conforms to the Annex XV requirements. RAC took note of the recommendations to the dossier submitter.	**SECR** to compile the RAC and SEAC final outcomes of the conformity check and upload this to S-CIRCABC IG.
3. Microplastics	
RAC agreed that the dossier conforms to the Annex XV requirements. RAC took note of the recommendations to the dossier submitter.	**SECR** to compile the RAC and SEAC final outcomes of the conformity check and upload this to S-CIRCABC IG.
b) Opinion development	
1. N,N-dimethylformamide	
Rapporteurs presented and RAC discussed the first draft opinion. RAC agreed on identified hazard: RAC agreed to base dermal DNEL on dermal developmental toxicity. RAC preliminary agreed on dermal DNEL of 1.1 mg/kg/day based on a dermal study. RAC preliminary agreed on a systemic long term DNEL of 6 mg/m^3 for the inhalation route based on a combination of human data and rabbit toxicity data. RAC agreed to consider biomonitoring, should further information come in through public consultation.	**SECR** to launch written consultation on the first version of the draft opinion. **Rapporteurs** to prepare the second draft opinion, taking into account RAC-48 discussions and RAC consultation, by early May 2019.
2. Cobalt salts	

Rapporteurs presented and RAC discussed the first draft opinion. RAC agreed that the DS approach to base hazard characterisation on RAC 2016 opinion on cancer dose-response of cobalt salts is a default position, but other options will be explored, also taking into account possible new information submitted in the public consultation by stakeholders. RAC agreed that the Rapporteurs should consider both 50% and 100% respirable fraction in the exposure assessment in the next version of the opinion. STOs are expected to provide information on mode of action and particle size distribution latest by 8 April, in order for the Rapporteurs to consider it.	**SECR** to launch written consultation on the first draft opinion after RAC-48. **SECR** and **Rapporteurs** to consider the need for organising an ad-hoc working group back-to-back the 2nd dialogue. **Rapporteurs** to prepare the second draft opinion, taking into account RAC-48 discussions and RAC consultation, by early May 2019.
10. Authorisation	
10.1 General authorisation issues	
a) Update on incoming/future applications	
RAC noted the information presented by the Secretariat.	
b) Working group on application for authorisation	
RAC agreed with the mandate for a working group of the Committee for Risk Assessment to handle Applications for Authorisation (document RAC/48/2019/04)	Secretariat to organise the first Working Group on Applications for Authorisation in April 2019.
c) Update on the approach of evaluation of the upcoming applications for authorisation for environmental endocrine disruptors (octyl- and nonylphenol ethoxylates)	
RAC noted and discussed the information presented by the Secretariat.	
10.2 Authorisation applications	
a) Discussion on key issues	
1. Five applications for authorisation from the November 2018 submission window (chromium trioxide) RAC discussed the key issues in the five applications for authorisation.	**SECR** to inform SEAC about the outcome of the discussion.

10.3 Review Reports	
a) Agreement of draft opinions	
1. RR1_TCE_Spolana (1 use) RAC agreed on the draft opinion as proposed by the Rapporteur. RAC concluded that there appear to be no alternatives that would further reduce the overall risks. RAC is of the opinion that the RMMs and OCs described in the application are appropriate and effective in limiting the risk to workers and the humans via the environment. For the review, RAC concludes that certain information is required. The suggested monitoring arrangements and adjustment of RMMs for the review report are expected to address RAC's low concerns. RAC agreed to give no advice to SEAC on the length of the review period.	**Rapporteur** together with **SECR** to do the final editing of the draft opinion. **SECR** to send the draft opinion to the applicants for commenting.
11. AOB	
a. RAC consultation on ECHA Guidance Appendix to R.8-17 'Guidance for proposing Occupational Exposure Limits'	
b. Court cases involving RAC opinions	
c. Report from the Workshop on progressing the Rapid Removal concept for metals classification held on 8 February 2019	
d. Training session on INTERACT project	
12. Action points and main conclusions of RAC-48	
SECR to upload the adopted action points to CIRCA BC.	

Table 1: CLH opinions which were adopted at RAC-48

1. Mancozeb (ISO)
2. Pydiflumetofen
3. 1,4-dioxane
4. Flumioxazin (ISO)
5. Prothioconazole
6. Thiophanate-methyl (ISO)
7. 1,2,4-triazole
8. Sedaxane
9. Benzyl salicylate
10. Trinickel disulphide
11. Tolclofos-methyl (ISO)
12. p-cymene
13. d-limonene
14. alpha-terpinene
15. Tolpyralate

1. Mancozeb

Classification and labelling in accordance with the CLP Regulation (Regulation (EC) 1272/2008)

	Index No	International Chemical Identification	EC No	CAS No	Classification		Labelling			Specific Conc. Limits, M-factors and ATE	Notes
					Hazard Class and Category Code(s)	Hazard statement Code(s)	Pictogram, Signal Word Code(s)	Hazard statement Code(s)	Suppl. Hazard statement Code(s)		
Current Annex VI entry	006-076-00-1	mancozeb (ISO); manganese ethylenebis(dithiocarbamate) (polymeric) complex with zinc salt	-	8018-01-7	Repr. 2 Skin Sens. 1 Aquatic Acute 1	H361d *** H317 H400	GHS08 GHS07 GHS09 Wng	H361d *** H317 H400		M=10	
Dossier submitters proposal	006-076-00-1	mancozeb (ISO); manganese ethylenebis(dithiocarbamate) (polymeric) complex with zinc salt	-	8018-01-7	**Retain** Skin Sens. 1 Aquatic Acute 1 **Add** STOT RE 2 Aquatic Chronic 1 **Remove** Repr. 2	**Retain** H317 H400 **Add** H373 (thyroid, nervous system)(oral) H410 **Remove** H361d ***	**Retain** GHS08 GHS07 GHS09 Wng	**Retain** H317 **Add** H373 (thyroid, nervous system)(oral) H410 **Remove** H361d *** H400		**Retain** M=10 **Add** M=10	
RAC opinion	006-076-00-1	mancozeb (ISO); manganese ethylenebis(dithiocarbamate) (polymeric) complex with zinc salt	-	8018-01-7	**Modify** Repr. 1B **Retain** Skin Sens. 1 Aquatic Acute 1 **Add** STOT RE 2 Aquatic Chronic 1 Carc. 2	**Modify** H360D **Retain** H317 H400 **Add** H373 (thyroid, nervous system) H410 H351	**Retain** GHS08 GHS07 GHS09 **Modify** Dgr	**Modify** H360D **Retain** H317 **Add** H373 (thyroid, nervous system) H410 H351 **Remove** H400		**Retain** M=10 **Add** M=10	
Resulting entry in Annex VI if adopted by RAC and agreed by Commission	006-076-00-1	mancozeb (ISO); manganese ethylenebis(dithiocarbamate) (polymeric) complex with zinc salt			Carc. 2 Repr. 1B STOT RE 2 Skin Sens. 1 Aquatic Acute 1 Aquatic Chronic 1	H351 H360D H373 (thyroid, nervous system) H317 H400 H410	GHS08 GHS07 GHS09 Dgr	H351 H360D H373 (thyroid, nervous system) H317 H410		M=10 M=10	

2. Pydiflumetofen

Classification and labelling in accordance with the CLP Regulation (Regulation (EC) 1272/2008)

	Index No	International Chemical Identification	EC No	CAS No	Classification		Labelling			Specific Conc. Limits, M-factors and ATE	Notes
					Hazard Class and Category Code(s)	Hazard statement Code(s)	Pictogram, Signal Word Code(s)	Hazard statement Code(s)	Suppl. Hazard statement Code(s)		
Current Annex VI entry	No current Annex VI entry										
Dossier submitters proposal	616-RST-VW-Y	*N*-methoxy-*N*-[1-methyl-2-(2,4,6-trichlorophenyl)-ethyl]-3-(difluoromethyl)-1-methylpyrazole-4-carboxamide; pydiflumetofen	-	1228284-64-7	Aquatic Acute 1 Aquatic Chronic 1	H400 H410	GHS09 Wng	H410		M=1 M=1	
RAC opinion	616-RST-VW-Y	*N*-methoxy-*N*-[1-methyl-2-(2,4,6-trichlorophenyl)-ethyl]-3-(difluoromethyl)-1-methylpyrazole-4-carboxamide; pydiflumetofen	-	1228284-64-7	Carc. 2 Repr. 2 Aquatic Acute 1 Aquatic Chronic 1	H351 H361f H400 H410	GHS08 GHS09 Wng	H351 H361f H410		M=1 M=1	
Resulting Annex VI entry if agreed by COM	616-RST-VW-Y	*N*-methoxy-*N*-[1-methyl-2-(2,4,6-trichlorophenyl)-ethyl]-3-(difluoromethyl)-1-methylpyrazole-4-carboxamide; pydiflumetofen	-	1228284-64-7	Carc. 2 Repr. 2 Aquatic Acute 1 Aquatic Chronic 1	H351 H361f H400 H410	GHS08 GHS09 Wng	H351 H361f H410		M=1 M=1	

3. 1,4-dioxane

Classification and labelling in accordance with the CLP Regulation (Regulation (EC) 1272/2008)

	Index No	International Chemical Identification	EC No	CAS No	Classification		Labelling			Specific Conc. Limits, M-factors and ATE	Notes
					Hazard Class and Category Code(s)	Hazard statement Code(s)	Pictogram, Signal Word Code(s)	Hazard statement Code(s)	Suppl. Hazard statement Code(s)		
Current Annex VI entry	603-024-00-5	1,4-dioxane	204-661-8	123-91-1	Flam. Liq. 2 Carc. 2 STOT SE 3 Eye Irrit. 2	H225 H351 H335 H319	GHS02 GHS08 GHS07 Dgr	H225 H351 H335 H319	EUH019 EUH066		Note D
Dossier submitters proposal	603-024-00-5	1,4-dioxane	204-661-8	123-91-1	**Retain** Flam. Liq. 2 STOT SE 3 Eye Irrit. 2 **Add** Muta. 2 **Modify** Carc. 1B	**Retain** H225 H335 H319 **Add** H341 **Modify** H350	**Retain** GHS02 GHS08 GHS07 Dgr	**Retain** H225 H335 H319 **Add** H341 **Modify** H350	**Retain** EUH019 EUH066		**Retain** Note D
RAC opinion	603-024-00-5	1,4-dioxane	204-661-8	123-91-1	**Retain** Flam. Liq. 2 STOT SE 3 Eye Irrit. 2 **Modify** Carc. 1B	**Retain** H225 H335 H319 **Modify** H350	**Retain** GHS02 GHS08 GHS07 Dgr	**Retain** H225 H335 H319 **Modify** H350	**Retain** EUH019 EUH066		**Retain** Note D
Resulting Annex VI entry if agreed by COM	603-024-00-5	1,4-dioxane	204-661-8	123-91-1	Flam. Liq. 2 Carc. 1B STOT SE 3 Eye Irrit. 2	H225 H350 H335 H319	GHS02 GHS08 GHS07 Dgr	H225 H350 H335 H319	EUH019 EUH066		Note D

4. Flumioxazin (ISO)

Classification and labelling in accordance with the CLP Regulation (Regulation (EC) 1272/2008)

	Index No	International Chemical Identification	EC No	CAS No	Classification		Labelling			Specific Conc. Limits, M-factors and ATE	Notes
					Hazard Class and Category Code(s)	Hazard statement Code(s)	Pictogram, Signal Word Code(s)	Hazard statement Code(s)	Suppl. Hazard statement Code(s)		
Current Annex VI entry	613-166-00-X	flumioxazin (ISO); *N*-(7-fluoro-3,4-dihydro-3-oxo-4-prop-2-ynyl-2*H*-1,4-benzoxazin-6-yl)cyclohex-1-ene-1,2-dicarboximide	-	103361-09-7	Repr. 1B Aquatic Acute 1 Aquatic Chronic 1	H360D H400 H410	GHS08 GHS09 Dgr	H360D H410		M=1000 M=1000	
Dossier submitters proposal	613-166-00-X	flumioxazin (ISO); *N*-(7-fluoro-3,4-dihydro-3-oxo-4-prop-2-ynyl-2*H*-1,4-benzoxazin-6-yl)cyclohex-1-ene-1,2-dicarboximide	-	103361-09-7	**Retain** Aquatic Acute 1 Aquatic Chronic 1 **Modify** Repr. 2	**Retain** H400 H410 **Modify** H361d	**Retain** GHS08 GHS09 **Modify** Wng	**Retain** H410 **Modify** H361d		**Retain** M=1000 M=1000	
RAC opinion	613-166-00-X	flumioxazin (ISO); *N*-(7-fluoro-3,4-dihydro-3-oxo-4-prop-2-ynyl-2*H*-1,4-benzoxazin-6-yl)cyclohex-1-ene-1,2-dicarboximide	-	103361-09-7	**Retain** Aquatic Acute 1 Aquatic Chronic 1 **Modify** Repr. 2	**Retain** H400 H410 **Modify** H361d	**Retain** GHS08 GHS09 **Modify** Wng	**Retain** H410 **Modify** H361d		**Retain** M=1000 M=1000	
Resulting Annex VI entry if agreed by COM	613-166-00-X	flumioxazin (ISO); *N*-(7-fluoro-3,4-dihydro-3-oxo-4-prop-2-ynyl-2*H*-1,4-benzoxazin-6-yl)cyclohex-1-ene-1,2-dicarboximide	-	103361-09-7	Repr. 2 Aquatic Acute 1 Aquatic Chronic 1	H361d H400 H410	GHS08 GHS09 Wng	H361d H410		M=1000 M=1000	

5. Prothioconazole (ISO)

Classification and labelling in accordance with the CLP Regulation (Regulation (EC) 1272/2008)

	Index No	International Chemical Identification	EC No	CAS No	Classification		Labelling			Specific Conc. Limits, M-factors and ATE	Notes
					Hazard Class and Category Code(s)	Hazard statement Code(s)	Pictogram, Signal Word Code(s)	Hazard statement Code(s)	Suppl. Hazard statement Code(s)		
Current Annex VI entry	No current Annex VI entry										
Dossier submitters proposal	TBD	prothioconazole (ISO); 2-[2-(1-chlorocyclopropyl)-3-(2-chlorophenyl)-2-hydroxypropyl]-2,4-dihydro-3H-1,2,4-triazole-3-thione	-	178928-70-6	Aquatic Acute 1 Aquatic Chronic 1	H400 H410	GHS09 Wng	H410		M=10 M=1	
RAC opinion	TBD	prothioconazole (ISO); 2-[2-(1-chlorocyclopropyl)-3-(2-chlorophenyl)-2-hydroxypropyl]-2,4-dihydro-3H-1,2,4-triazole-3-thione	-	178928-70-6	Aquatic Acute 1 Aquatic Chronic 1	H400 H410	GHS09 Wng	H410		M=10 M=1	
Resulting Annex VI entry if agreed by COM	TBD	prothioconazole (ISO); 2-[2-(1-chlorocyclopropyl)-3-(2-chlorophenyl)-2-hydroxypropyl]-2,4-dihydro-3H-1,2,4-triazole-3-thione	-	178928-70-6	Aquatic Acute 1 Aquatic Chronic 1	H400 H410	GHS09 Wng	H410		M=10 M=1	

6. Thiophanate-methyl (ISO)

Classification and labelling in accordance with the CLP Regulation (Regulation (EC) 1272/2008)

	Index No	International Chemical Identification	EC No	CAS No	Classification		Labelling			Specific Conc. Limits, M-factors and ATE	Notes
					Hazard Class and Category Code(s)	Hazard statement Code(s)	Pictogram, Signal Word Code(s)	Hazard statement Code(s)	Suppl. Hazard statement Code(s)		
Current Annex VI entry	006-069-00-3	thiophanate-methyl (ISO); dimethyl (1,2-phenylenedicarbamothioyl)biscarbamate; dimethyl 4,4′-(o-phenylene)bis(3-thioallophanate)	245-740-7	23564-05-8	Muta. 2 Acute Tox. 4* Skin Sens. 1 Aquatic Acute 1 Aquatic Chronic 1	H341 H332 H317 H400 H410	GHS08 GHS07 GHS09 Wng	H341 H332 H317 H410			
Dossier submitters proposal	006-069-00-3	thiophanate-methyl (ISO); dimethyl (1,2-phenylenedicarbamothioyl)biscarbamate; dimethyl 4,4′-(o-phenylene)bis(3-thioallophanate)	245-740-7	23564-05-8	**Add** STOT RE 2 Carc. 2 **Modify** Muta. 1B Acute Tox. 4 **Retain** Skin Sens. 1 Aquatic Acute 1 Aquatic Chronic 1	**Add** H373 H351 **Modify** H340 **Retain** H332 H317 H400 H410	**Retain** GHS08 GHS07 GHS09 **Modify** Dgr	**Add** H373 H351 **Modify** H340 **Retain** H332 H317 H410		**Add** M=10 M=10	
RAC opinion	006-069-00-3	thiophanate-methyl (ISO); dimethyl (1,2-phenylenedicarbamothioyl)biscarbamate; dimethyl 4,4′-(o-phenylene)bis(3-thioallophanate)	245-740-7	23564-05-8	**Retain** Muta. 2 Skin Sens. 1 Aquatic Acute 1 Aquatic Chronic 1 **Add** Carc. 2 **Modify** Acute Tox. 4	**Retain** H341 H332 H317 H400 H410 **Add** H351 **Modify**	**Retain** GHS08 GHS07 GHS09 **Modify** Dgr	**Retain** H341 H332 H317 H410 **Add** H351 **Modify**		**Add** inhalation: ATE = 1.7 mg/L (dusts and mists) M=10 M=10	
Resulting Annex VI entry if agreed by COM	006-069-00-3	thiophanate-methyl (ISO); dimethyl (1,2-phenylenedicarbamothioyl)biscarbamate;	245-740-7	23564-05-8	Carc. 2 Muta. 2 Acute Tox. 4 Skin Sens. 1 Aquatic Acute 1	H351 H341 H332 H317 H400	GHS08 GHS07 GHS09 Dgr	H351 H341 H332 H317 H410		inhalation: ATE = 1.7 mg/L (dusts and mists)	

		dimethyl 4,4′-(o-phenylene)bis(3-thioallophanate)			Aquatic Chronic 1	H410				M=10 M=10	

7. 1,2,4-triazole

Classification and labelling in accordance with the CLP Regulation (Regulation (EC) 1272/2008)

	Index No	International Chemical Identification	EC No	CAS No	Classification		Labelling			Specific Conc. Limits, M-factors and ATE	Notes
					Hazard Class and Category Code(s)	Hazard statement Code(s)	Pictogram, Signal Word Code(s)	Hazard statement Code(s)	Suppl. Hazard statement Code(s)		
Current Annex VI entry	613-111-00-X	1,2,4-triazole	206-022-9	288-88-0	Acute Tox. 4* Eye Irrit. 2 Repr. 2	H302 H319 H361d***	GHS08 GHS07 Wng	H302 H319 H361d***			
Dossier submitters proposal	613-111-00-X	1,2,4-triazole	206-022-9	288-88-0	**Modify** Acute Tox. 4 Repr. 1B	**Retain** H302 **Modify** H360FD	**Retain** GHS08 GHS07 **Modify** Dgr	**Retain** H302 **Modify** H360FD			
RAC opinion	613-111-00-X	1,2,4-triazole	206-022-9	288-88-0	**Modify** Acute Tox. 4 Repr. 1B	**Retain** H302 **Modify** H360FD	**Retain** GHS08 GHS07 **Modify** Dgr	**Retain** H302 **Modify** H360FD		**Add** oral: ATE = 1320 mg/kg bw	
Resulting Annex VI entry if agreed by COM	613-111-00-X	1,2,4-triazole	206-022-9	288-88-0	Repr. 1B Acute Tox. 4 Eye Irrit. 2	H360FD H302 H319	GHS08 GHS07 Dgr	H360FD H302 H319		oral: ATE = 1320 mg/kg bw	

8. Sedaxane

Classification and labelling in accordance with the CLP Regulation (Regulation (EC) 1272/2008)

	Index No	International Chemical Identification	EC No	CAS No	Classification		Labelling			Specific Conc. Limits, M-factors and ATE	Notes
					Hazard Class and Category Code(s)	Hazard statement Code(s)	Pictogram, Signal Word Code(s)	Hazard statement Code(s)	Suppl. Hazard statement Code(s)		
Current Annex VI entry	No current Annex VI entry										
Dossier submitters proposal	TBD	*N*-{2-[[1,1'-bi(cyclopropyl)]-2-yl]phenyl}-3-(difluoromethyl)-1-methyl-1*H*-pyrazole-4-carboxamide; sedaxane		874967-67-6	Carc. 2 Aquatic Acute 1 Aquatic Chronic 2	H351 H400 H411	GHS08 GHS09 Wng	H351 H410		M=1	
RAC opinion	TBD	*N*-{2-[[1,1'-bi(cyclopropyl)]-2-yl]phenyl}-3-(difluoromethyl)-1-methyl-1*H*-pyrazole-4-carboxamide; sedaxane		874967-67-6	Carc. 2 Aquatic Acute 1 Aquatic Chronic 2	H351 H400 H411	GHS08 GHS09 Wng	H351 H410		M=1	
Resulting Annex VI entry if agreed by COM	TBD	*N*-{2-[[1,1'-bi(cyclopropyl)]-2-yl]phenyl}-3-(difluoromethyl)-1-methyl-1*H*-pyrazole-4-carboxamide; sedaxane		874967-67-6	Carc. 2 Aquatic Acute 1 Aquatic Chronic 2	H351 H400 H411	GHS08 GHS09 Wng	H351 H410		M=1	

9. Benzyl salicylate

Classification and labelling in accordance with the CLP Regulation (Regulation (EC) 1272/2008)

	Index No	International Chemical Identification	EC No	CAS No	Classification		Labelling			Specific Conc. Limits, M-factors and ATE	Notes
					Hazard Class and Category Code(s)	Hazard statement Code(s)	Pictogram, Signal Word Code(s)	Hazard statement Code(s)	Suppl. Hazard statement Code(s)		
Current Annex VI entry	No current Annex VI entry										
Dossier submitters proposal	TBD	Benzyl salicylate	204-262-9	118-58-1	Skin Sens. 1B	H317	GHS07 Wng	H317			
RAC opinion	TBD	Benzyl salicylate	204-262-9	118-58-1	Skin Sens. 1B	H317	GHS07 Wng	H317			
Resulting Annex VI entry if agreed by COM	TBD	Benzyl salicylate	204-262-9	118-58-1	Skin Sens. 1B	H317	GHS07 Wng	H317			

10. Trinickel disulphide

Classification and labelling in accordance with the CLP Regulation (Regulation (EC) 1272/2008)

	Index No	International Chemical Identification	EC No	CAS No	Classification		Labelling			Specific Conc. Limits, M-factors and ATE	Notes
					Hazard Class and Category Code(s)	Hazard statement Code(s)	Pictogram, Signal Word Code(s)	Hazard statement Code(s)	Suppl. Hazard statement Code(s)		
Current Annex VI entry	028-007-00-4	trinickel disulfide; nickel subsulfide; [1] heazlewoodite [2]	234-829-6 [1] – [2]	12035-72-2 [1] 12035-71-1 [2]	Carc. 1A Muta. 2 STOT RE 1 Skin Sens. 1 Aquatic Acute 1 Aquatic Chronic 1	H350i H341 H372** H317 H400 H410	GHS08 GHS07 GHS09 Dgr	H350i H341 H372** H317 H410			
Dossier submitter's proposal	028-007-00-4	trinickel disulfide; nickel subsulfide; [1] heazlewoodite [2]	234-829-6 [1] – [2]	12035-72-2 [1] 12035-71-1 [2]	**Add** Acute Tox. 4	**Add** H332		**Add** H332			
RAC opinion	028-007-00-4	trinickel disulfide; nickel subsulfide; [1] heazlewoodite [2]	234-829-6 [1] – [2]	12035-72-2 [1] 12035-71-1 [2]	**Add** Acute Tox. 3	**Add** H331	**Add** GHS06 **Remove** GHS07	**Add** H331		**Add** inhalation: ATE = 0.92 mg/L (dusts and mists)	
Resulting Annex VI entry if agreed by COM	028-007-00-4	trinickel disulfide; nickel subsulfide; [1] heazlewoodite [2]	234-829-6 [1] – [2]	12035-72-2 [1] 12035-71-1 [2]	Carc. 1A Muta. 2 Acute Tox. 3 STOT RE 1 Skin Sens. 1 Aquatic Acute 1 Aquatic Chronic 1	H350i H341 H331 H372** H317 H400 H410	GHS08 GHS06 GHS09 Dgr	H350i H341 H331 H372** H317 H410		inhalation: ATE = 0.92 mg/L (dusts and mists)	

11. Tolclofos-methyl (ISO)

Classification and labelling in accordance with the CLP Regulation (Regulation (EC) 1272/2008)

	Index No	International Chemical Identification	EC No	CAS No	Classification		Labelling			Specific Conc. Limits, M-factors and ATE	Notes
					Hazard Class and Category Code(s)	Hazard statement Code(s)	Pictogram, Signal Word Code(s)	Hazard statement Code(s)	Suppl. Hazard statement Code(s)		
Current Annex VI entry	015-113-00-0	tolclofos-methyl (ISO); O-(2,6-dichloro-p-tolyl) O,O-dimethyl thiophosphate	260-515-3	57018-04-9	Skin Sens. 1 Aquatic Acute 1 Aquatic Chronic 1	H317 H400 H410	GHS07 GHS09 Wng	H317 H410			
Dossier submitters proposal	015-113-00-0	tolclofos-methyl (ISO); O-(2,6-dichloro-p-tolyl) O,O-dimethyl thiophosphate	260-515-3	57018-04-9	**Modify** Skin Sens. 1B **Retain** Aquatic Acute 1 Aquatic Chronic 1	**Retain** H317 H400 H410	**Retain** GHS07 GHS09 Wng	**Retain** H317 H410		**Add** M=1 M=1	
RAC opinion	015-113-00-0	tolclofos-methyl (ISO); O-(2,6-dichloro-p-tolyl) O,O-dimethyl thiophosphate	260-515-3	57018-04-9	**Modify** Skin Sens. 1B **Retain** Aquatic Acute 1 Aquatic Chronic 1	**Retain** H317 H400 H410	**Retain** GHS07 GHS09 Wng	**Retain** H317 H410		**Add** M=1 M=1	
Resulting Annex VI entry if agreed by COM	015-113-00-0	tolclofos-methyl (ISO); O-(2,6-dichloro-p-tolyl) O,O-dimethyl thiophosphate	260-515-3	57018-04-9	Skin Sens. 1B Aquatic Acute 1 Aquatic Chronic 1	H317 H400 H410	GHS07 GHS09 Wng	H317 H410		M=1 M=1	

12. p-cymene

Classification and labelling in accordance with the CLP Regulation (Regulation (EC) 1272/2008)

	Index No	International Chemical Identification	EC No	CAS No	Classification		Labelling			Specific Conc. Limits, M-factors and ATE	Notes
					Hazard Class and Category Code(s)	Hazard statement Code(s)	Pictogram, Signal Word Code(s)	Hazard statement Code(s)	Suppl. Hazard statement Code(s)		
Current Annex VI entry	No current Annex VI entry										
Dossier submitters proposal	TBD	1-isopropyl-4-methylbenzene; p-cymene	202-796-7	99-87-6	Flam. Liq. 3 Acute Tox. 3 Asp. Tox. 1 Aquatic Acute 1 Aquatic Chronic 3	H226 H331 H304 H400 H412	GHS02 GHS06 GHS08 GHS09 Dgr	H226 H331 H304 H410		M=1	
RAC opinion	TBD	1-isopropyl-4-methylbenzene; p-cymene	202-796-7	99-87-6	Flam. Liq. 3 Acute Tox. 3 Asp. Tox. 1 Aquatic Chronic 2	H226 H331 H304 H411	GHS02 GHS06 GHS08 GHS09 Dgr	H226 H331 H304 H411		inhalation: ATE = 3 mg/L (vapours)	
Resulting Annex VI entry if agreed by COM	TBD	1-isopropyl-4-methylbenzene; p-cymene	202-796-7	99-87-6	Flam. Liq. 3 Acute Tox. 3 Asp. Tox. 1 Aquatic Chronic 2	H226 H331 H304 H411	GHS02 GHS06 GHS08 GHS09 Dgr	H226 H331 H304 H411		inhalation: ATE = 3 mg/L (vapours)	

13. d-limonene

Classification and labelling in accordance with the CLP Regulation (Regulation (EC) 1272/2008)

	Index No	International Chemical Identification	EC No	CAS No	Classification		Labelling			Specific Conc. Limits, M-factors and ATE	Notes
					Hazard Class and Category Code(s)	Hazard statement Code(s)	Pictogram, Signal Word Code(s)	Hazard statement Code(s)	Suppl. Hazard statement Code(s)		
Current Annex VI entry	Existing (as part of a group entry 601-029-00-7)	(*R*)-p-mentha-1,8-diene; d-limonene	227-813-5	5989-27-5	Flam. Liq. 3 Skin Irrit. 2 Skin Sens. 1 Aquatic Acute 1 Aquatic Chronic 1	H226 H315 H317 H400 H410	GHS02 GHS07 GHS09 Wng	H226 H315 H317 H410			Note C
Dossier submitters proposal	TBD	(*R*)-p-mentha-1,8-diene; d-limonene	227-813-5	5989-27-5	**Retain** Aquatic Acute 1 **Add** Asp. Tox. 1 **Modify** Skin Sens. 1B Aquatic Chronic 3	**Retain** H317 H400 **Add** H304 **Modify** H412	Retain GHS02 GHS07 GHS09 **Add** GHS08 **Modify** Dgr	**Retain** H317 H410 **Add** H304		**Add** M=1	
RAC opinion	TBD	(*R*)-p-mentha-1,8-diene; d-limonene	227-813-5	5989-27-5	**Retain** Aquatic Acute 1 **Add** Asp. Tox. 1 **Modify** Skin Sens. 1B Aquatic Chronic 3	**Retain** H317 H400 **Add** H304 **Modify** H412	**Retain** GHS02 GHS07 GHS09 **Add** GHS08 **Modify** Dgr	**Retain** H317 H410 **Add** H304		**Add** M=1	
Resulting Annex VI entry if agreed by COM	TBD	(*R*)-p-mentha-1,8-diene; d-limonene	227-813-5	5989-27-5	Flam. Liq. 3 Skin Irrit. 2 Skin Sens. 1B Asp. Tox. 1 Aquatic Acute 1 Aquatic Chronic 3	H226 H315 H317 H304 H400 H412	GHS02 GHS07 GHS08 GHS09 Dgr	H226 H315 H317 H304 H410		M=1	

14. alpha-terpinene

Classification and labelling in accordance with the CLP Regulation (Regulation (EC) 1272/2008)

	Index No	International Chemical Identification	EC No	CAS No	Classification		Labelling			Specific Conc. Limits, M-factors and ATE	Notes
					Hazard Class and Category Code(s)	Hazard statement Code(s)	Pictogram, Signal Word Code(s)	Hazard statement Code(s)	Suppl. Hazard statement Code(s)		
Current Annex VI entry	No current Annex VI entry										
Dossier submitters proposal	TBD	p-mentha-1,3-diene; 1-isopropyl-4-methylcyclohexa-1,3-diene; alpha-terpinene	202-795-1	99-86-5	Flam. Liq. 3 Repr. 2 Skin Sens. 1A Asp. Tox. 1 Aquatic Acute 1 Aquatic Chronic 3	H226 H361 H317 H304 H400 H412	GHS02 GHS07 GHS08 GHS09 Dgr	H226 H361 H317 H304 H410		M=1	
RAC opinion	TBD	p-mentha-1,3-diene; 1-isopropyl-4-methylcyclohexa-1,3-diene; alpha-terpinene	202-795-1	99-86-5	Flam. Liq. 3 Acute Tox. 4 Skin Sens. 1 Asp. Tox. 1 Aquatic Chronic 2	H226 H302 H317 H304 H411	GHS02 GHS07 GHS08 GHS09 Dgr	H226 H302 H317 H304 H411		oral: ATE = 1680 mg/kg bw	
Resulting Annex VI entry if agreed by COM	TBD	p-mentha-1,3-diene; 1-isopropyl-4-methylcyclohexa-1,3-diene; alpha-terpinene	202-795-1	99-86-5	Flam. Liq. 3 Acute Tox. 4 Skin Sens. 1 Asp. Tox. 1 Aquatic Chronic 2	H226 H302 H317 H304 H411	GHS02 GHS07 GHS08 GHS09 Dgr	H226 H302 H317 H304 H411		oral: ATE = 1680 mg/kg bw	

15. Tolpyralate

Classification and labelling in accordance with the CLP Regulation (Regulation (EC) 1272/2008)

	Index No	International Chemical Identification	EC No	CAS No	Classification		Labelling			Specific Conc. Limits, M-factors and ATE	Notes
					Hazard Class and Category Code(s)	Hazard statement Code(s)	Pictogram, Signal Word Code(s)	Hazard statement Code(s)	Suppl. Hazard statement Code(s)		
Current Annex VI entry	No current Annex VI entry										
Dossier submitters proposal	TBD	(*RS*)-1-{1-ethyl-4-[4-mesyl-3-(2-methoxyethoxy)-*o*-toluoyl]pyrazol-5-yloxy}ethyl methyl carbonate; tolpyralate	n/a	1101132-67-5	Carc. 2 STOT RE 2 Aquatic Acute 1 Aquatic Chronic 1	H351 H373 (eyes, kidney) H400 H410	GHS08 GHS09 Wng	H351 H373 (eyes, kidney) H410		M=10 M=100	
RAC opinion	TBD	(*RS*)-1-{1-ethyl-4-[4-mesyl-3-(2-methoxyethoxy)-*o*-toluoyl]pyrazol-5-yloxy}ethyl methyl carbonate; tolpyralate	n/a	1101132-67-5	Carc. 2 Repr. 2 STOT RE 2 Aquatic Acute 1 Aquatic Chronic 1	H351 H361d H373 (eye) H400 H410	GHS08 GHS09 Wng	H351 H361fd H373 (eye) H410		M=10 M=100	
Resulting Annex VI entry if agreed by COM	TBD	(*RS*)-1-{1-ethyl-4-[4-mesyl-3-(2-methoxyethoxy)-*o*-toluoyl]pyrazol-5-yloxy}ethyl methyl carbonate; tolpyralate	n/a	1101132-67-5	Carc. 2 Repr. 2 STOT RE 2 Aquatic Acute 1 Aquatic Chronic 1	H351 H361fd H373 (eye) H400 H410	GHS08 GHS09 Wng	H351 H361fd H373 (eye) H410		M=10 M=100	

Table 2 Art. 77.3.c request – chronic M-factors for copper compounds as listed in Commission Regulation (EU) 2016/1179[8]:

RAC opinion: RAC considers that the following chronic M-factors are appropriate:

Copper (II) oxide	10	[lower than previous opinion]
Copper (I) oxide	10	[lower than previous opinion]
Copper (II) hydroxide, copper dihydroxide	10	[no change]
Copper (II) carbonate - copper (II) hydroxide (1:1)	10	[no change]
Dicopper chloride trihydroxide	10	[no change]
Copper thiocyanate	10	[no change]
Copper sulphate pentahydrate	1	[lower than previous opinion]
Tetracopper hexahydroxide sulphate [& hydrate]	10	[no change]
Bordeaux mixture	1	[lower than previous opinion]
Copper flakes (coated with aliphatic acid)	10	[no change]

[8] Commission Regulation (EU) 2018/669 of 16 April 2018 amending, for the purposes of its adaptation to technical and scientific progress, Regulation (EC) No 1272/2008 of the European Parliament and of the Council on classification, labelling and packaging of substances and mixtures Text with EEA relevance.

Part III. List of Attendees of the RAC-48 meeting

RAC Members
Aquilina Gabriele
Andreou Kostas
Barański Bogusław
Biró Anna
Bjørge Christine
Borg Daniel
Branisteanu Radu (co-opted member)
Carvalho João
Chankova-Petrova Stephka
Chiurtu Elena (co-opted member)
Czerczak Sławomir
de la Flor Tejero Ignacio
Dobrev Ivan
Dunauskienė Lina
Dungey Stephen
Geoffroy Laure
Hakkert Betty
Heederik Dick (co-opted member)
Husa Stine
Ilie Mihaela
Kadiķis Normunds
Kapelari Sonja
Karadjova Irina
Leinonen Riitta
Losert Annemarie
Lund Bert-Ove
Martínek Michal
Menard Srpčič Anja
Moeller Ruth
Moldov Raili
Mullooly Yvonne
Murray Brendan
Neumann Michael
Paris Pietro
Polakovičová Helena
Pribu Mihaela
Pronk Marja
Rucki Marian
Santonen Tiina
Schlüter Urs
Schulte Agnes
Séba Julie
Smith Andrew
Sørensen Hammer Peter
Sogorb Miguel A.
Spetseris Nikolaos
Stahlmann Ralf
Tobiassen Lea Stine
Užomeckas Žilvinas
Van der Haar Rudolf (co-opted member)
Varnai Veda
Apologies, Members
Agapiou Agapios
Gruiz Katalin
Hartwig Andrea (co-opted member)
Printemps Nathalie
Tsitsimpikou Christina
Zeljezic Davor

Members' advisers
Esposito Dania (Pietro Paris)
Hyytinen Eija-Riitta (Riitta Leinonen)
Kuittinen Marko (Riitta Leinonen)
Mahiout Selma (Tiina Santonen)
Martin Theresa (Ralf Stahlmann)_CLH adviser for 1,2,4-triazole
Peczkowska Beata (Boguslaw Baranski)_CLH adviser for d-limonene, p-cymene, alpha-tepinene
Russo Maria Teresa (Gabriele Aquilina)_CLH adviser for thiophanate methyl
Commission
Kilian Karin (DG ENV)
Luvara Giuseppina (DG ENV)
Morris Alick (DG EMPL)
Rozwadowski Jacek (DG GROW)
Regular stakeholder observers
Annys Erwin (CEFIC)
Barry Frank (ETUC)
Comini Andrea (EuCheMS)
Fornabaio Lara (ClientEarth)
Romano Mozo Dolores (EEB)
Rowe Rocky (ECPA)
Verougstraete Violaine (Eurometaux)
Waeterschoot Hugo (Eurometaux)

Dossier submitters
Lang Camilla (SE)_CLH thiophanate-methyl
Taylor Mike (Johnson Matthey)_CLH trinickel disulphide
Occasional stakeholder observers
Arregui Cristina (IFRA)_CLH alpha-terpinene, d-limonene, py-cymene
Akdag Ali (CIRFS)_restriction DMF
Protzen Jens Achim (EFEO)_CLH alpha-terpinene, d-limonene, py-cymene
Scazzola Roberto (A.I.S.E)_restriction microplastics
Stakeholder experts
Barlow Sue (ECPA/Sumitomo)_flumioxazin
Gaoua-Chapelle Wassila (Cefic/Arkema)_1,2,4-triazole
Gelbke Heinz-Peter (CIRFS/BASF)_DMF
Harder Volker (ECPA/Nisso)_thiophanate-methyl
Jacobi Sylvia (Cefic/Sector group catalysts Europe)_cobalt salts
Köhl Werner (IFRA/Lead Registrant Symrise)_alpha-terpinene, p-cymene
Leibold Edgar (Cefic/Formacare)_formaldehyde
Lloyd Sara (ECPA/Syngenta)_pydiflumetofen_sedaxane
Mackie Carol (Eurometaux/Copper compounds consotium)_copper compounds
Paul Thomas (EFEO/CEHTRA)_d-limonene
Plotzke Kathy (Cefic/CES-Silicone Europe)_D4D5D6
Provan Mac (ECPA/ISK)_tolpyralate
Ruckman Steve (ECPA/Mancozeb Task Force)_mancozeb

	Stahl Christina (ECPA/Bayer)_prothioconazole
	Vallotton Nathalie (Cefic/MIT)_microplastics

Vey Matthias (IFRA/lead Registrant DRT)_d-limonene	**Dossier submitters**
Viegas Vanessa (Eurometaux/Cobalt Institute and Cobalt REACH Consortium Ltd)_Cobalt salts	**DE**
Zorrilla Leah (ECPA/Bayer CropScience)_alpha-terpinene, p-cymene	Hoffmann Frauke (formaldehyde)
	Müller Andre (1,4-dioxane)
Invited expert	**FR**
Pasquier Elodie	Angeli Karine (sedaxane, pydiflumetofen)
	IT
REMOTE PARTICIPANTS	Russo Maria Teresa (DMF)
RAC Members	**NL**
Aquilina Gabriele	Geraets Liesbeth (alpha-terpinene,d-limonene,p-cymene,1,4-dioxane)
Kapelari Sonja	Gomes Contreras Jeannette (p-cymene,d-limonene-alpha-terpinene)
Tsitsimpikou Christina	Groothuis Floris (d-limonene, alpha-terpinene, p-cymene, 1,4-dioxane)
Members' advisers	Müller Andre (1,4-dioxane)
Catone Tiziana (Gabriele Aquilina)	**SE**
Hoffmann Frauke (Ralf Stahlmann)	Cederberg Inger (microplastics)
Huhse Bettina (Agnes Schulte)	Johansson Olof (microplastics)
Martin Theresa (Ralf Stahlmann)	**UK**
Moilanen Marianne (Riitta Leinonen	Peppin Lindsay (mancozeb)
Mühlegger Simone (Annemarie Losert)	**Commission**
Müller Andre (Betty Hakkert)	Bertato Valentina
Paludan Ditte (Peter Hammer Soerensen)	Hualde-Grasa Eva-Patricia
Russo Maria Teresa (Gabriele Aquilina)	Kilian Karin
SEAC rapporteurs	Krassnig Christian
Fankhauser Simone (Cobalt salts)	**EFSA**
Fock Lars (DMF)	Chiusolo Arianna
Joyce John (CT)	Court Marques Daniele
Luedeke Andreas (cobalt salts, N,N-dimethylformamide)	De Lentdecker Chloé
	Gatto Valeria
	Istace Frederique

Mangas Iris
Parra Morte Juan Manuel

ECHA staff
Blainey Mark
Bowmer Tim, Chairman
Broeckaert Fabrice
Di Bastiano Augusto
Dvorakova Dana
Georgiadis Nikolaos
Gmeinder Michael
Hellsten Kati
Jaagus Triin
Jones Stella
Karjalainen Ari
Kivelä Kalle
Kokkola Leila
Kosk-Bienko Joanna
Lapenna Silvia
Lefevre-Brevart Sandrine
Ludborzs Arnis
Luschutzky Evita
Marques-Camacho Mercedes
Mushtaq Fesil
Nicot Thierry
Nygren Jonas
Orispää Katja
O´Rourke Regina
Ottati Maria
Peltola Jukka
Perazzolo Chiara
Pillet Monique
Prevedouros Konstantinos

Regil Pablo
Sadam Diana
Simpson Peter
Smilovici Simona
Sosnowski Piotr
Spjuth Linda
Uphill Simon
Van Haelst Anniek

Part IV. LIST OF ANNEXES

ANNEX I Final Agenda of the RAC-48 meeting

ANNEX II List of documents submitted to the Members of the Committee for Risk Assessment for the RAC-48 meeting

ANNEX III Declarations of conflicts of interest to the Agenda of the RAC-48 meeting

ANNEX IV Administrative issues and information items

ANNEX V Short summary: workshop on human relevance and Modes of Action (MoAs)

6 March 2019
RAC/A/48/2019

Final Agenda

48th meeting of the Committee for Risk Assessment

6 - 8 March 2019
and
12 - 15 March 2019

ECHA Conference Centre (Annankatu 18, Helsinki)

Wednesday 6 March starts at 09.00
Friday 8 March breaks at 13.00
Tuesday 12 March resumes at 14.00
Friday 15 March ends at 13.00

Item 1 – Welcome and Apologies

Item 2 – Adoption of the Agenda

RAC/A/48/2019
For adoption

Item 3 – Declarations of conflicts of interest to the Agenda

Item 4 – Appointment of (co-)rapporteurs

a) Appointment of (co-)rapporteurs for CLH dossiers, restriction dossiers, authorisation applications, DNEL/dose-response relationships, Article 95(3) requests and Article 77(3)(c) requests

For agreement

Item 5 – Report from other ECHA bodies and activities

a) Report on RAC 47 action points, written procedures and update on other ECHA bodies

RAC/48/2019/01
(room document)
For information

b) RAC workplan for all processes

For information

c) Revision of Rules of Procedure

RAC/48/2019/02
For agreement

Item 6 – Requests under Article 77(3)(c)

Copper compounds (M-factor)

For agreement

Item 7 – Requests under Article 95 (3)

None

Item 8 – Harmonised classification and labelling (CLH)

8.1 General CLH issues

a) Feedback from the workshop on CLH-related human health issues and information on the expert group on T25/SCLs for carcinogens

8.2 CLH dossiers

A. Hazard classes for agreement without plenary debate (fast-track)

Prothioconazole (ISO): physical hazards (as open for the public consultation), acute toxicity, skin corrosion / irritation, serious eye damage / eye irritation, skin sensitisation, germ cell mutagenicity, carcinogenicity, STOT SE, STOT RE, environmental hazards

Thiophanate-methyl (ISO): physical hazards (as open in the public consultation), acute toxicity, skin corrosion / irritation, serious eye damage / eye irritation, skin sensitisation, STOT RE

Tolpyralate: physical hazards (as open in the public consultation), acute toxicity, skin corrosion / irritation, serious eye damage / eye irritation, respiratory / skin sensitisation, STOT SE, environmental hazards

p-cymene: physical hazard (flammable liquids), acute toxicity, skin corrosion / irritation, germ cell mutagenicity, STOT SE, STOT RE, aspiration hazard

d-limonene: physical hazard (flammable liquids), aspiration hazard

alpha-terpinene: physical hazard (flammable liquids), acute oral toxicity, germ cell mutagenicity, aspiration hazard

1,2,4-triazole: acute oral toxicity

sedaxane: physical hazards, acute toxicity, skin corrosion/ irritation, serious eye damage / eye irritation, respiratory / skin sensitisation, germ cell mutagenicity, STOT SE, STOT RE, aspiration hazard

tolclofos-methyl (ISO): physical hazards (as open in the public consultation), acute toxicity, skin corrosion / irritation, serious eye damage / eye irritation, skin sensitisation, germ cell mutagenicity, carcinogenicity, toxicity to reproduction, STOT SE, environmental hazards

mancozeb (ISO): germ cell mutagenicity

benzyl salicylate: skin sensitisation

pydiflumetofen: skin sensitisation

B. Hazard classes for agreement with plenary debate

1) 1,4-dioxane
2) flumioxazin (ISO)
3) prothioconazole (ISO)
4) thiophanate-methyl (ISO)
5) tolpyralate
6) p-cymene
7) d-limonene
8) alpha-terpinene
9) 1,2,4-triazole
10) sedaxane
11) tolclofos-methyl (ISO)
12) mancozeb (ISO)
13) benzyl salicylate
14) trinickel disulfide; nickel subsulfide [1]; heazlewoodite [2]
15) pydiflumetofen *(HH hazards)*

For discussion and adoption

Item 9 – Restrictions

9.1 Restriction Annex XV dossiers

a) General items:
   1) Report from Restrictions Task Force meeting

For information

   2) Update of the opinion development procedure

RAC/48/2019/03

For information

b) Conformity check and key issues discussion
   1) Formaldehyde
   2) D4/D5/D6
   3) Microplastics

For agreement

c) Opinion development
   1) *N*,*N*-dimethylformamide – first draft opinion
   2) Cobalt salts – first draft opinion

For discussion

Item 10 – Authorisation

10.1 General authorisation issues

a) Update on incoming/future applications

For information

b) Working group on application for authorisation

c) Update on the approach of evaluation of the upcoming applications for authorisation for environmental endocrine disruptors (octyl- and nonylphenol ethoxylates)

For information/discussion

10.2. Authorisation applications

a) Discussion on key issues
   1. Five applications for authorisation from the November 2018 submission window (chromium trioxide)

For discussion

10.3. Review reports

a) Agreement of draft opinions
   1. RR1_TCE_Spolana (1 use)

For discussion and agreement

Item 11 – AOB

5. RAC consultation on ECHA Guidance Appendix to R.8-17 'Guidance for proposing Occupational Exposure Limits'
6. Court cases involving RAC opinions
7. Training session on INTERACT project

For information/discussion

Item 12 – Action points and main conclusions of RAC-48

Table with Conclusions and Action points from RAC-48

For adoption

Annex II (RAC 48)

Documents submitted to the Members of the Committee for Risk Assessment for the RAC 48 meeting.

Document number	Title
RAC/A/48/2019	Final Draft Agenda
RAC/A/48/2019 Restricted	Draft outline agenda
RAC/48/2019/01 Room document	Administrative issues and information items
RAC/48/2019/02	Revised Rules of Procedure for the Committee for Risk Assessment
RAC/48/2019/03	Draft revised working procedure for RAC and SEAC on developing opinions on Annex XV restriction dossiers
RAC/48/2019/04	Working group on application for authorisation

The following participants, including those for whom the Chairman declared the interest on their behalf, declared potential conflicts of interest with the Agenda items (according to Art 9 (2) of RAC RoPs)

AP/Dossier / DS	RAC Member	Reason for potential CoI / Working for
ALREADY DECLARED AT PREVIOUS RAC PLENARY MEETING(S)		
Applications for Authorisation		
All chromates	Urs SCHLUTER	Institutional & personal involvement; asked to refrain from voting in the event of a vote on this group of substances - other mitigation measures may be applied by the Chairman.
Harmonised classification & labelling		
Mancozeb (ISO) **UK**	Andrew SMITH	Working for the CA submitting the dossier; asked to refrain from voting in the event of a vote on this substance - no other mitigation measures applied. No personal involvement.
	Steve DUNGEY	Working for the CA submitting the dossier; asked to refrain from voting in the event of a vote on this substance - no other mitigation measures applied. Personal involvement in drafting / commenting on the environmental part of the dossiers.
Pydiflumetofen **FR**	Nathalie PRINTEMPS	Working for the CA submitting the dossier; asked to refrain from voting in the event of a vote on this substance - no other mitigation measures applied. No personal involvement.
Requests under Article 77(3) (c)		
-		
Restrictions		
-		

New dossiers

AP/Dossier / DS	RAC Member	Reason for potential CoI / Working for
NEW		
Article 77.3(c)		
-	-	-
Restrictions		
-	-	-
Applications for Authorisation		
-	-	-
Harmonised classification & labelling		
benzyl salicylate **DE**	Agnes SCHULTE	Working for the CA submitting the dossier; asked to refrain from voting in the event of a vote on this substance - no other mitigation measures applied. Personal involvement.
	Urs SCHLUTER	Working for the CA submitting the dossier; asked to refrain from voting in the event of a vote on this substance - no other mitigation measures applied. No personal involvement
	Michael NEUMANN	Working for the CA submitting the dossier; asked to refrain from voting in the event of a vote on this substance - no other mitigation measures applied. No personal involvement.
1) tolclofos-methyl (ISO) **2) thiophanate-methyl (ISO)** **SE**	Bert-Ove LUND	Working for the CA submitting the dossier; asked to refrain from voting in the event of a vote on this substance - no other mitigation measures applied. No personal involvement.
	Daniel BORG	Working for the CA submitting the dossier; asked to refrain from voting in the event of a vote on this substance - no other mitigation measures applied. No personal involvement.

AP/Dossier / DS	RAC Member	Reason for potential CoI / Working for
1) Sedaxane **2) Pydiflumetofen** **FR**	Elodie PASQUIER (invited expert)	Working for the CA submitting the dossier; asked to refrain from voting in the event of a vote on this substance - no other mitigation measures applied. No personal involvement.
1) 1,4-dioxane **2) p-cymene** **3) d-limonene** **4) alpha-terpinene** **NL**	Betty HAKKERT	Working for the CA submitting the dossier; asked to refrain from voting in the event of a vote on this substance - no other mitigation measures applied. No personal involvement.
	Marja PRONK	Working for the CA submitting the dossier; asked to refrain from voting in the event of a vote on this substance - no other mitigation measures applied. No personal involvement
1,2,4-triazole **BE**	Julie SEBA	Working for the CA submitting the dossier; asked to refrain from voting in the event of a vote on this substance - no other mitigation measures applied. No Personal involvement
Flumioxazin (ISO) **CZ**	Michal Martinek	Working for the CA submitting the dossier; asked to refrain from voting in the event of a vote on this substance - no other mitigation measures applied. No Personal involvement.
	Marian Rucki	Working for the CA submitting the dossier; asked to refrain from voting in the event of a vote on this substance - no other mitigation measures applied. No Personal involvement.
1) tolpyralate **2) prothioconazole (ISO)** **UK**	Andrew SMITH	Working for the CA submitting the dossier; asked to refrain from voting in the event of a vote on this substance - no other mitigation measures applied. Personal involvement in (1); no personal involvement in (2).
	Steve DUNGEY	Working for the CA submitting the dossier; asked to refrain from voting in the event of a vote on this substance - no other mitigation measures applied. Personal involvement in drafting /

AP/Dossier / DS	RAC Member	Reason for potential CoI / Working for
		commenting on the environmental part of the dossiers (1) and (2).

Annex IV

Helsinki, 1 March 2019

RAC/48/2019/01

ROOM DOCUMENT

48TH MEETING OF THE COMMITTEE FOR RISK ASSESSMENT

6 – 8 March 2019
and
12 – 15 March 2019

Helsinki, Finland

Concerns: **Administrative issues and information items**

Agenda Point: **5a**

Action requested: **for information**

ADMINISTRATIVE ISSUES AND INFORMATION ITEMS

1 Status report on the RAC-47 Action Points

The RAC-47 action points due for RAC-48 are completed.

2 Outcome of written procedures & other consultations

2.1 Written procedures for adoption of RAC opinions / minutes of the meeting

Opinions / minutes adopted via written procedure	Deadline	Report on the outcome
Written procedure for adoption of the CLH opinion on lysmeral	28 January 2019	closed
Written procedure for adoption of the minutes of RAC-47	15 February 2019	closed

2.2 RAC consultations (status by 1 March 2019)

Subject / document	Deadline	Status / follow-up
Harmonised classification and labelling		
1,4-dioxane	11 February 2019	closed
flumioxazin (ISO)	5 February 2019	closed
prothioconazole (ISO)	13 February 2019	closed
thiophanate-methyl (ISO)	8 February 2019	closed
(RS)-1-{1-ethyl-4-[4-mesyl-3-(2-methoxyethoxy)-o-toluoyl]pyrazol-5-yloxy}ethyl methyl carbonate; tolpyralate	11 February 2019	closed
1-isopropyl-4-methylbenzene; p-cymene	8 February 2019	closed
(R)-p-mentha-1,8-diene; d-limonene	8 February 2019	closed
p-mentha-1,3-diene; 1-isopropyl-4-methylcyclohexa-1,3-diene; alpha-terpinene	8 February 2019	closed
1,2,4-triazole	4 February 2019	closed
sedaxane	11 February 2019	closed
Mancozeb (ISO)	8 February 2019	closed
benzyl salicylate	1 February 2019	closed
trinickel disulfide; nickel subsulfide; [1] heazlewoodite [2]	12 February 2019	closed
pydiflumetofen	15 February 2019	closed
Tolclofos-methyl (ISO)	11 February 2019	closed

Subject / document	Deadline	Status / follow-up
Application for Authorisation / Review Report		
CT_Aloys CT_Ideal CT_Keuco CT_Schell CT_Thyssen Consultation on applications for authorisation	3 April 2019	ongoing
RR1_TCE_Spolana Consultation on draft opinion	21 February 2019	closed
Restrictions		
Consultation on the restriction proposal on DMF and on the restriction proposal on Cobalt	11 January 2019	closed
Consultation on the conformity of Annex XV dossiers on D4/D5/D6, Microplastics, and formaldehyde and formaldehyde releasers	25 February 2019	closed
Art. 77. 3. c request		
no consultations		
Art. 77. 3. c request on evaluations OELs		
no consultations		

2.3 Other written consultations of RAC (status by 1 March 2019)

Subject / document	Deadline	Status / follow-up
Written procedure for adoption of the minutes of RAC-47	15 February 2019	closed

2.4 Calls for expression of interest

Calls for expression of interest	Date	Outcome
Harmonised classification and labelling		
Call for expression of interest in rapporteurship for CLH dossiers	31 January - 8 February 2019	4 volunteers expressed their interest
Application for Authorisation		
Call for expression of interest in rapporteurship on applications for authorisation on SVHCs in 12 new entries in Annex XIV of the REACH Regulation. Full list of the new entries is published in		

Annex of the Commission Regulation (EU) 2017/999[9].		
Restriction Call for expression of interest in rapporteurship for the restriction dossiers to be submitted in April and July 2019	Until 20 February 2019	closed

2.5 Written procedures for the appointment of (co-)rapporteurs

Appointment of (Co-)rapporteur(s)	Substance	Deadline	Outcome
Harmonised classification and labelling - no written procedures			
Written procedure for the appointment of (co-)rapporteurs	▪ ethametsulfuron-methyl (ISO) ▪ dimethomorph (ISO) ▪ thiamethoxam (ISO) ▪ 24-Epibrassinolide ▪ 4,4'-oxydi(benzenesulphonohydrazide)	26 Feb 2019	closed No comments were received from RAC members on the recommendation of the Chairman; the RAC (co-)Rapporteurs were appointed with tacit agreement.
Applications for Authorisation– no written procedures			
Restrictions – no written procedures			

2.6 Follow-up on the opinions on applications for authorisation adopted by RAC and SEAC

Opinion(s)	Sent on
Opinions sent to the European Commission, the Member States and applicants	
CT_Hapoc_2 (1 opinion)	17 December 2018
RR1_DEHP_PP (2 opinions)	17 December 2018
CT_Doosan (1 opinion)	24 January 2019
CT_MAHLE (1 opinion)	1 March 2019

[9] Commission Regulation (EU) 2017/999 of 13 June 2017 amending Annex XIV to Regulation (EC) No 1907/2006 of the European Parliament and of the Council concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH)

ANNEX V Short summary: workshop on human relevance and Modes of Action (MoAs)

The Secretariat provided a short summary from a workshop on Modes of Action (MoAs) and human relevance in the context of classification and labelling (CLH) that took place on the 5th of March 2019 at ECHA, ahead of the RAC-48 plenary meeting. It was attended by 68 experts, including 37 RAC members, and in addition 12 WebEx participants.

The workshop was set up to bring together human health and regulatory experts dealing with the hazard assessment of (agro)chemicals, to discuss and exchange views on scientific and regulatory activities in the field of MoAs and identify and collect issues for further work, in particular for the CLP Guidance on the application of the CLP criteria. RAC is regularly confronted with CLH dossiers which contain mechanistic data of varying size and quality, generated using different approaches, which can complicate the assessment for a particular substance, unless the reviewer is very familiar with the above topics. There is therefore a need to ensure up to date scientific knowledge and consistency in decision-making by RAC.

It was re-iterated that the generation of information that enables the MoA analysis and human relevance framework to be applied is of scientific and regulatory value since it builds confidence and reduces uncertainty in the RAC decision-making process. It has been recognised that the revisions of chemical regulations regarding information requirements may trigger the need for further research on MoA. The workshop continued to promote the use of the WHO/IPCS MoA/HRF templates for hazard assessment under CLP. Industry also emphasised the difficulty of fulfilling all regulatory frameworks and new areas of concern like endocrine disruption.