MSC/M/54/2017

(Adopted in written procedure
on 30 August 2017)

Minutes
of the 54th Meeting of the Member State Committee (MSC-54)
12-16 June 2017

I. Summary Record of the Proceedings

Item 1 - Welcome and Apologies

The Chairman of the Committee, Mr Watze de Wolf, opened the meeting and welcomed the participants to the 54th meeting of the Member State Committee (MSC) (for the full list of attendees and further details see Section II of the minutes).

Item 2 - Adoption of the Agenda

The Agenda was adopted as provided for the meeting by the MSC Secretariat without further changes (final Agenda is attached to these minutes as Section III).

Item 3 - Declarations of conflicts of interest to the items on the Agenda

The Dutch member indicated that he is project leader for the Dutch authorities related to questions about uses and emissions of, amongst others, the substance SEV-IT-024/2015 from an industrial site and the consequences thereof, which the Chairman considered was not a conflict of interest. No other potential conflicts of interest were declared by any members, experts or advisers with any item on the agenda of MSC-54.

Item 4 - Administrative issues

- Outlook for MSC-55 to MSC-57

The Chairman presented an outlook on the potential length of the next meeting which is expected to require approximately 3 plenary days. The Chairman also presented an early stage estimation for the length of the MSC-56 meeting in October. In addition, the Committee was informed of the planning of the December meeting and the importance of using the available planning tools. Members were invited to highlight this to their colleagues in charge, and to suggest avoiding booking many complex SVHC identification and SEv cases for the MSC-57 in order to keep the workload manageable. The member from Germany informed MSC on the recent SVHC intention for Bisphenol A to the Registry of Intentions based on its equivalent level of concern having probable serious effects to the environment (Article 57 f). Several members expressed their concern about the high number of dossier evaluation cases planned for the summer period and requested from ECHA's side improved planning for any CA consultations. The Chairman informed MSC of the intention to organise a round of phone discussions with members during summer to collect feedback and suggestions for improvements during the MSC agreement seeking on evaluation draft decisions.

Item 5 –Minutes of the MSC-53 meeting

The minutes of MSC-53 were adopted as modified at the meeting.

Item 6 – Substance evaluation - Decision making process

a. Written procedure report on seeking agreement on a draft decision on substance evaluation

SECR introduced the report on the outcome of the written procedure (WP) for agreement seeking on one substance evaluation case (see Section V for more detailed identification of the case). WP was launched on 18 May 2017 and closed on 29 May 2017. By the closing date, unanimous agreement was reached on the draft decision (DD).

b. Introduction to and preliminary discussion on a draft decision on substance evaluation after MS-CA's/ECHA reactions *(Session 1, open session)*:

c. Seeking agreement on a draft decision when amendments were proposed by MS-CA's/ECHA *(Session 2, closed)*

SEV-BE-003/2015 1,2,4-triazole (EC No. 206-022-9)
Session 1 (open)

Two representatives of the Registrants participated in the initial discussion. In absence of specific confidentiality concerns in relation to the draft decision (DD), an open session was held.

The evaluating Member State Competent Authority (eMSCA) from Belgium (BE-CA) presented the outcome of substance evaluation (SEv) of the above-mentioned substance which was performed on the basis of the initial grounds for concern relating to human health endpoints (reproductive toxicity, neurotoxicity, carcinogenicity and endocrine disruption), wide dispersive use, high (aggregated) tonnage and exposure to environment and consumers.

The DD consulted with the Member State Competent Authorities (MSCAs) and ECHA had two requests for information: *1) H295R Steroidogenesis Assay in vitro (OECD TG 456)*, and 2) an *extended one-generation reproductive toxicity study (EOGRTS; OECD TG 443) in rats, oral route with extension of cohort 2A and 2B (DNT cohorts), without extension of cohort 1B to mate the F1 animals to produce the F2 generation and without cohort 3 (DIT)*. Sixteen Proposals for Amendments (PfAs) were received in total on both requests.

MSC was guided by the expert from the eMSCA through the information on the substance (including PfAs, Registrant(s) comments, and the eMSCAs responses to them).

With regards to the request for the steroidogenesis assay (OECD TG 456) in one PfA it was proposed to remove the request because in view of the PfA the test is unnecessary and further information will not improve risk management measures (RMM) of this substance. As a second part of the PfA, if the request for the *in vitro* assay would be upheld, it was proposed to be specified in the decision that for negative results no further testing should be carried out and if positive the Registrant should consider carefully the next steps.

With regards to the request for EOGRTS (OECD TG 443), it was proposed to remove the request for the following reasons: *1)* A recently conducted 2-generation study is available providing sufficient information to ensure any risks are appropriately managed, and further reproductive toxicity information will not improve risk management. It was noted in the PfA that the substance is currently classified as toxic for reproduction (Repr. 2), however existing data allow to classify it as Repr. 1B, and the PfA considered that the existing data could be used to make a case for more stringent classification and identification as Substance of Very High Concern (SVHC) according to Article 57 (c). 2) Regarding developmental neurotoxicity another PfA noted that the brain weight decrease represent minimal decreases and no histopathological modifications were reported from the microscopical examination of the brain. Hence, according to the PfA these do not warrant sufficient concern to justify a new *in vivo* study including the DNT cohort nor a standalone DNT study. Another PfA requested to consider sequential testing: first the steroidogenesis assay (OECD TG 456), and in case of positive results to request EOGRTS (OECD TG 443) with the DNT cohort, and in the case of negative result to request a developmental neurotoxicity study (OECD TG 426). Another PfA supported the EOGRTS request (OECD TG 443), but suggested to delete inclusion of the DNT cohort because requesting an OECD TG 426 seemed to be more appropriate to address the neurodevelopmental concerns. The request for a developmental neurotoxicity study (OECD TG 426) would have the advantage that more parameters are investigated, but, on the other hand, using the EOGRTS DNT cohort will have the advantage that the exposure period is longer. In other PfAs it was proposed to include Morris Water Maze testing in the DNT cohort to cover cognitive effects (i.e. learning and memory). Additionally, in a PfA supporting the request for EOGRTS with DNT cohort, it was suggested to request the production of the F2 generation by mating the cohort 1B animals. This was considered justified due to because of the significant exposure of consumers or professionals through wide-dispersive uses of the substance and due to effects observed in the available *in vivo* studies, which can be associated to endocrine modes of action. Editorial PfAs regarding information on Mode of Action (MoA) obtained from EOGRTS and steroidogenesis assay were also submitted. In one PfA it was requested to remind the Registrant to update their dossier with the missing data of combined sub-chronic toxicity/neurotoxicity screening study in rats and 90-day toxicity study in mice. In another PfA it was requested to respond to Registrant comments that the arguments provided to consider that they should not be addressees of the decision are not justified

and do not constitute valid reasons to exclude them from the addressees of the decision. The eMSCA further explained that during decision making one Registrant changed the scope of his registration to merely transported isolated intermediate under strictly controlled conditions (TII under SCC).

The eMSCA based on the PfAs indicated their preference to keep the request for the steroidogenesis study, but they suggested to replace the EOGRTS with DNT cohort by a full developmental neurotoxicity study (OECD 426). The eMSCA also indicated its intention to prepare a dossier for harmonized classification and labelling of 1,2,4-triazole as Repr. 1B based on existing data as suggested in some of the PfAs.

One of the Registrants' representatives reiterated in his intervention at the meeting their written comments justifying that both requests from DD should be removed because they will not bring any additional information to be used for risk assessment. With regard to EOGRTS request, he detailed that the data provided in the registration dossier are in line with OECD guidelines and they were sufficient and adequate for regulatory requirements from other European bodies, none of them asking for additional studies. Moreover, the representative argued that requests for a DNT study as a separate request or using the EOGRTS DNT cohorts are not appropriate and not justified because additional examinations performed in standard tests provided data proving the low neurotoxic potential of triazole. Additionally, he disagreed with the proposal to classify triazole as Repr. 1B because the comparison against the CLP criteria was not clearly demonstrated as the whole data package available in all species as well as the parental toxicity should be deeply considered.

The other Registrant representative detailed his legal arguments for exclusion from the list of addressees of the decision indicating that he solely uses this substance as a transported isolated intermediate (TII) only under strictly controlled conditions (SCC). The representative indicated they changed timely (in March 2017) their registration status by deactivating ('putting to zero') the 'full' registration in a range of 1-10 tons/year, keeping only an intermediate registration under Article 18(3) REACH.

Some MSC members supported the eMSCA who agreed to prepare a dossier for harmonised classification and labelling of the substance as Repr. 1B based on existing data as suggested in some of the PfAs and the proposal to request a full developmental neurotoxicity study (OECD 426) instead of the EOGRTS with DNT cohort was discussed. In case the Risk Assessment Committee (RAC) does not follow this classification proposal in its opinion, in a subsequent follow up SEV decision the eMSCA may request an EOGRTS study. Some MSC members raised concerns about requesting the full developmental neurotoxicity study at this stage and proposed to await the outcome of the C&L discussion. If RAC would consider that not enough data are available to classify the substance as Repr. 1B, an EOGRTS might indeed still be needed to clarify the concern and it would be more proportionate for animal welfare reasons to investigate the neurotoxicity concern through the DNT cohort in the EOGRTS. In addition, one MSC member did not agree that further neurotoxicity investigations would lead to improved risk management measures for 1,2,4-triazole. MSC extensively discussed the results of developmental toxicity studies (e.g. data from histopathological investigation from DNT tests performed in 2007, brain necrosis as possible cause of infertility at different dose levels, maternal toxicity *vs.* foetus toxicity, influence of neurotoxicity on learning and memory, LOAEL values) and the need for requesting developmental neurotoxicity information. Furthermore, several members supported the request for a steroidogenesis test.

An MSC stakeholder observer highlighted that the substance is used in agriculture, outlined the importance that new tests must lead to improved RMM and appreciated the MSC and ECHA discussions for finding the most significant way for addressing the concerns for human health and for the environment.

A MSC member requested clarifications from the Registrant's representative for their justification for changing the registration status during the process of substance evaluation. The representative motivated the update of the dossier by the fact that it was a small business, which uses the substance only for synthesis in small quantities and in SCC, while the time consuming marketing activity for other uses (requiring a full

registration) in this situation is not justified. He also stressed his legal arguments for their exclusion from the list of addressees of the decision.

This MSC member also asked the Registrant's representative whether he could support a classification as Repr. 1B. The Registrant's representative indicated that he couldn't support the classification of the substance as Repr. 1B based on the available data.

SECR explained that on site isolated intermediates are automatically excluded from substance evaluation according to the REACH legal text. They further explained that the REACH legal text does not automatically exclude TII under SCC, but Registrants of TII under SCC are normally not addressed in the SEV process unless there are specific reason why the registration contributes to the concern.

Session 2 (closed)

During the closed session, MSC requested the eMSCA to clarify their preferred approach on the information requirements. The eMSCA indicated that based on the discussions it is preferred to currently only request the steroidogenesis assay to clarify the potential ED MoA and to follow the classification and labelling route first for the concern on reproductive toxicity. In case RAC is of the opinion that there is insufficient data to classify this substance as Repr. 1B, then to possibly request an EOGRTS with DNT cohorts (OECD TG 443) in a second SEV decision. . However, in case that 1,2,4-triazole is classified as Repr. 1B, a full DNT study (OECD 426) could still be requested in a second SEV decision in order to clarify the remaining concern for developmental neurotoxicity if considered appropriate. All MSC members agreed that this was the most appropriate way forward.

The eMSCA and MSC exchanged views on the legal basis for the inclusion/exclusion of a Registrant of a TII used under SCC. Some members indicated that the legal text only exempts on-site isolated intermediates (OSII) used under SCC from the REACH title on Evaluation (Article 49). SECR presented that ECHA's practice to include TII under SCC only when a justified concern is present had been announced previously in a news alert[1], and had also been applied in one specific SEv cases for which the decision was rectified by the Executive Director of ECHA s. Several MSC members considered that this publication on the ECHA website created expectations for this Registrant to be excluded from the list of addressees. Therefore, for this specific case, under the current circumstances, MSC agreed to remove the TII Registrant from the list of addressees. Several MSC members however, expressed their concern regarding ECHA's approach since normally during the substance evaluation process all uses of the substance are considered together and not the individual uses of each Registrant. Moreover, the burden of proof to justify specific grounds of concern regarding the intermediate use lies with the eMSCAs. The MSC members were also concerned that this new general approach by ECHA was neither discussed, nor agreed in MSC before. SECR agreed to carefully consider its current practice and decide on the appropriate next steps.

In conclusion, MSC agreed to amend the draft decision by keeping the requests for H295R steroidogenesis assay in vitro (OECD TG 456), and to delete the request for extended one-generation reproductive toxicity study (OECD TG 443) with DNT cohort in rats. Furthermore, MSC agreed to remove the reminder for the Registrants to update the registration dossier with the relevant studies of combined sub-chronic toxicity/neurotoxicity screening study in rats and 90-day toxicity study in mice. Due to the changes in the decision, MSC also agreed to shorten the time to provide the requested information and to update the registration dossier from 27 months to 6 months from the data of the decision. MSC agreed to remove one Registrant from the list of addressees in this particular substance evaluation decision due to a recent change in the registration status to TII under SCC only.

The MSC unanimously agreed on the draft decision as amended in the meeting. A member abstained from voting and submitted a statement to the minutes, which is attached in Section VII.

[1] https://echa.europa.eu/-/registrants-should-get-ready-to-comment-on-2015-substance-evaluation-draft-decisions

SEV-IT-024/2015 Hexafluoropropene (HFP) (EC No. 204-127-4)
Session 1 (open)

Two representatives of the Registrants participated in the initial discussion. In absence of specific confidentiality concerns in DD, an open session was held.

The eMSCA from Italy (IT-CA) presented the SEv outcome of the above-mentioned substance performed on the basis of the initial grounds for concern relating to Human health/Suspected C and R; High (aggregated) tonnage. The eMSCA considered that further information was required to clarify the concern for mutagenicity.

The draft decision (DD) consulted with the Member State Competent Authorities (MSCAs) and ECHA had one request for information for an *in vitro* mammalian cell micronucleus (MN) test (EU TM B.49/OECD TG 487).

MSC was guided by the expert from the eMSCA through the information on the substance (including PfAs, the Registrants' comments and the eMSCAs responses to them). All three PfA submitters agreed that there was a concern for chromosomal aberrations. Two proposed to immediately conduct an *in vivo* comet assay (OECD TG 489) instead of the *in vitro* MN (OECD TG 487). One proposed to perform the comet assay (OECD TG 489) by inhalation in rat or mice in the liver, glandular stomach, duodenum and bone marrow, giving the option to the Registrants to perform the comet assay also in gonadal cells. The other proposed the same information request but replacing glandular stomach and duodenum with lung tissue, and adding kidneys to the list of tissues to be tested. The latter due to the observed nephrotoxicity in the available repeated dose inhalation studies, and the Registrant's proposed read-across to tetrafluoroethene, known to induce kidney tumour formation.

The third PfA submitter proposed to remove the in vitro MN test (OECD TG 487) and to request for a combined *in vivo* comet assay in liver, kidney and bone marrow (BM) and MN test in rat via inhalation route. The rat was considered as the more relevant species due to its sensitivity to renal tumours with other haloethylenic compounds. If the in vitro MN test was kept then when positive results are obtained then the combined *in vivo* comet/MN test should be requested.

Additionally, this third PfA submitter proposed to request for detailed characterisation of metabolites of hexafluoropropene (HFP) that may be relevant for kidney carcinogenicity through an appropriate battery of *in vivo* and in vitro toxicokinetic (TK) studies that also include human tissues. If the concern was confirmed through this first step or if the existing information already sufficiently supported the concern, a carcinogenicity study needed to be performed. Even though the Registrants proposed to self-classify the substance as Carc. 2 this PfA submitter noted that a more stringent classification could apply if the carcinogenic potential of HFP is confirmed.

The eMSCA indicated they could accept the PfA to ask for a combined *in vivo* comet assay in liver, kidney and bone marrow (BM) and MN test but choose mouse as the test species instead of the proposed rat. The eMSCA also could accept the PfA to follow the carcinogenicity concern and to request in the DD for a carcinogenicity study.

The Registrants' representatives reiterated at the meeting their disagreement with the genotoxicity concern. According to the Registrants there was insufficient scientific merit to conduct further genotoxic mode of action studies on HFP based on their weight of evidence analysis submitted with their written comments. They disagreed with the PfA for a combined *in vivo* comet/MN test due to the fact that two *in vivo* MN tests already exist and cytotoxicity could disturb interpretation of any new *in vivo* test as significant cytotoxicity was found in the bone marrow, the target cell system for the MN test. The Registrants were also opposing the TK studies proposed. They were of the view that if such studies were to be conducted it should be only if a concern for a genotoxic mode of action was substantiated and there was interest in understanding underlying mechanisms. They considered the most appropriate test design to be a comet assay with kidney as tissue of evaluation in rats.

Regarding the carcinogenicity concern the Registrants' representatives expressed the view that this is not proportionate since they already self-classified the substance as Carc. 2 and have appropriate risk management measures in place. Furthermore, according to the Registrants' representatives, exposure limits are already very low to protect against kidney effects. They asked MSC when looking at the available 90-day results, not to confuse regeneration seen in the kidney (common in mice) to neoplasm.

The Registrants' representatives made a procedural comment on the compliance check (CCH) decision that was issued in December 2016 which requested for a prenatal developmental toxicity (PNDT) testing in two species and an extended one-generation reproductive toxicity (EOGRTS) test in the rat. They considered that these tests would fulfil the regulatory requirement but not have added value when compared to the risk management measures already in place. According to the Registrants the requests in the CCH decision needed to be postponed until the genotoxic mode of action testing was completed since its outcome could lead them to not performing the tests requested in the CCH decision.

Following a request for further information on the status of the studies requested in the CCH decision the Registrants' representatives explained that the PNDT study in rat was ongoing during the time of the MSC-54 meeting, and the other studies were planned and had a testing slot with a contract lab. If CCH decision is suspended they preferred to continue to perform the test that has already started and postpone the other tests and absorb the associated costs if needed.

The MSC discussed the available *in vitro* and *in vivo* data set for genotoxicity in detail. The *in vivo* data set consisted of two *in vivo* micronucleus studies - one with results reported as positive only in the high dose group in the male mice and concluded by the Registrant as negative (considered by eMSCA as potentially positive) and one with negative results; an UDS study with negative results; a dominant lethal mutation in rats with negative results. For both *in vitro* and *in vivo* tests, cytotoxicity could have contributed to the positive results and the eMSCA was of the view that this needed to be investigated, also to rule out a possible aneugenic (or clastogenic) mode of action. If *in vitro* study result come out negative for the aneugenic and clastogenic modes of action, a new *in vivo* study could be avoided. If *in vitro* result are positive eMSCA considered that an appropriated *in vivo* follow-up is needed on the basis of the MoA of the substance or, in alternative a self-classification Muta. 1B could be accepted to avoid an additional *in vivo* test.

Two stakeholder observers representing different animal welfare NGOs supported the testing strategy suggested by eMSCA and expressed their disagreement with the carcinogenicity study since according to the information on the dissemination website, there seems to be no exposure to consumers.

Session 2 (closed)

For the testing strategy MSC considered two options: 1. If mutagenicity was a concern to follow-up on, to either request only the *in vitro* test or else remove the *in vitro* request and ask for a combined comet assay with MN test, or 2. if mutagenicity was not of further concern, request for a carcinogenicity study due to structural alert for carcinogenicity with a non-genotoxic mode of action (e.g. structural similarity with substances classified as Carc. 1B). There was the general understanding that the genotoxicity concern and the carcinogenicity concern can be discussed separately without one effecting the other. However whilst deciding upon the right test to request to cover the identified concern under SEV, MSC was also considering how such test would best fit in the overall testing strategy that includes as well the PNDT and EOGRTS already requested under the CCH decision.

Overall MSC agreed that the genotoxicity data set, specifically related to chromosome aberrations, was considered inconclusive and further experimental data were needed to clarify the concern for genotoxicity which could also inform on the potential MoA. MSC therefore agreed to keep the request for *in vitro* mammalian cell micronucleus test + FISH (fluorescence *in situ* hybridisation) and add the option for immunochemical labelling of kinetochores CREST (EU TM B.49/OECD TG 487) with the aim to discriminate between

clastogenic and aneugenic effects. If the *in vitro* MN give negative results, the *in vivo* effect observed can be attributed to cytotoxicity and further follow-up not needed. However, in case of positive results, and depending on the mode of action, further germ cell mutagenicity testing or a carcinogenicity study seems to be needed and can be requested in a next decision.

During the discussion on carcinogenicity MSC considered the exposure potential of the substance. MSC unanimously agreed not to request the carcinogenicity study at this stage and to encourage the Registrants in the DD to provide all available information related to exposure since this can be used in the follow-up to assess the residual carcinogenicity concern together with read-across information for structurally similar substances.

Finally, MSC unanimously agreed on the draft decision as amended in the meeting.

SEV-IT-026/2015 Di-tert-pentyl peroxide (DTPP) (EC No. 234-042-8)
Session 1 (open)

One representative of the Registrants participated in the initial discussion. In absence of specific confidentiality concerns in DD, an open session was held.

The eMSCA from Italy (IT-CA) presented the SEv outcome of the above-mentioned substance performed on the basis of the initial grounds for concern relating to suspected C, suspected M, wide dispersive use, exposure of workers. The eMSCA considered that further information was required to clarify the concern for mutagenicity.

The DD consulted with the Member State Competent Authorities (MSCAs) and ECHA had one request for information for an *in vitro* mammalian cell micronucleus (MN) test + FISH (fluorescence *in situ* hybridisation) (EU TM B.49/OECD TG 487).

MSC was guided by the expert from the eMSCA through the information on the substance (including PfAs, the Registrants' comments and the eMSCAs responses to them). One PfA submitter was of the view that this test will not address the concern for germ cell mutagenicity, and they proposed to delete the request for the *in vitro* MN test and request instead an appropriate *in vivo* germ cell study, such as an *in vivo* transgenic rodent somatic and germ cell mutation assay (TGR; OECD TG 488) or a mammalian spermatogonial chromosome aberration test (spermatogonial CA; OECD TG 483). Otherwise, if the *in vitro* MN test was to be kept in the draft decision (DD), then a clear sequential testing starting with *in vitro* followed by specific *in vivo* tests (dependent on the outcome of the *in vitro* tests) were to be requested in one decision.

A second PfA submitter also proposed to remove the request for the *in vitro* MN test. In their view, the read across data from di-tert-butyl-peroxide (DTBP) brought forward by the Registrants was fully relevant for the registered substance, di-tert-pentyl peroxide (DTPP). Hence they considered the negative spermatogonial CA test available for the read across substance, DTBP as relevant for DTPP (pending confirmation the test that has no significant deficiencies). Furthermore, this PfA submitter supported Muta. 2 self-classification based on the positive intraperitoneal (IP) MN study on somatic cells with DTPP. Hence they proposed to address the carcinogenic potential of DTPP. However, since DTBP is under evaluation by a different eMSCA also for mutagenic and carcinogenic concerns, the PfA submitter was of the view that both SEV requests needed to be coordinated.

The Registrants' representative agreed to perform the requested *in vitro* genotoxicity assay. According to the Registrants, and contrary to the eMSCA's assessment of their read across between DTPP and DTBP, there is no significant difference in the eye irritation potential between DTPP and DTBP. Regarding the skin irritation the factors that could have influenced dermal irritation (higher volatility of DTBP and the higher lipophilic potential of DTPP) have no influence on a germ cells assay performed by the i.p. route. The Registrants' representative explained the expression of genotoxic action at high dose by oral or i.p. routes due to an overload of the detoxification metabolism which was not seen by inhalation exposure.

The Registrants disagreed with the PfA requesting to perform *in vivo* germ cell study due to existing OECD TG 483 study on DTBP and absence of any sign of testicular toxicity in the repeated dose toxicity study with DTPP and DTBP (the read across substance). They also disagreed with the carcinogenicity concern mentioned based on current data from DTPP and DTBP and the closely related substances tert-amyl hydroperoxide (TAHP) and tert-butyl hydroperoxide (TBHP).

The Registrants' representative asked for clarification on the further information that was needed for full acceptance of their read across argumentation.

During the discussion the eMSCA clarified that they consider the read across as scientifically plausible and that all that is needed from the side of the Registrant was a better justification. They agreed to provide further guidance on the deficiencies to the Registrant in the DD. This conclusion was also supported by a stakeholder observer representing an animal welfare NGO.

Since the read across was considered plausible the main open question was the possibility of an aneugenic mode of action of the substance on somatic cells.

Session 2 (closed)

In the open session the eMSCA had made reference to data gaps on the prenatal developmental and repeat-dose toxicity studies, and subsequently proposed in closed session to first conduct a 90-day study instead of going directly to a carcinogenicity study. However, the Chairman reminded that since there were no PfAs in this regards, the Registrants' rights to be heard would be breached and hence that this suggestion cannot be followed by MSC.

With regard to the mode of action of the substance it was argued that because peroxides are used as positive controls in comet assay, the most likely mode of action is clastogenic and not aneugenic. However, in order to address any uncertainty it was agreed to still request the FISH staining. In addition, another option for detecting the mode of action was also included in the request - immunochemical labelling of kinetochores CREST. MSC agreed that to proceed with an appropriate *in vivo* follow-up it is necessary to understand the mechanistic basis *in vitro.*

For the carcinogenicity endpoint one PfA had included a suggestion to improve coordination between this and an ongoing substance evaluation case on another peroxide. This led to the inclusion in the DD of a request for a more detailed justification for the read across since the read across justification document is not accepted in its current form due to the lack of an appropriate reasoning why and how a prediction can be made, neither for genotoxic properties nor for the other high tier human health properties. The failure of showing the appropriateness of the read across could trigger a request for further *in vivo* testing.

In conclusion MSC agreed to keep the request for *in vitro* mammalian cell micronucleus test + FISH (fluorescence *in situ* hybridisation) and add the option for immunochemical labelling of kinetochores CREST (OECD 487/B.49 EU).

MSC unanimously agreed on the draft decision as amended in the meeting.

SEV-NL-029/2015 Tetrapropylenebenzene (benzene, mono-C11-C13-branched alkyl derivatives) (EC No. 810-801-4)
Session 1 (open)

Two representatives of the Registrants participated in the initial discussion. In absence of specific confidentiality concerns in DD, an open session was held.

The eMSCA from The Netherlands (NL-CA) presented the SEv outcome of the above-mentioned substance performed on the basis of the initial grounds for concern relating to Environment/Suspected PBT, Human health/Suspected CMR, Exposure/Aggregated tonnage. The evaluating MSCA considered that further information was required to clarify these concerns.

The DD consulted with the MSCAs and ECHA had eight requests for information – one request related to reproductive toxicity and seven requests covering the environmental concerns.

Benzene, mono-C11-C13-branched alkyl derivatives (tetrapropylenebenzene) (BAB) is a UVCB with several hundreds of components all together representing a wide range of physicochemical properties, which are of environmental relevance. Whilst the request for extended one generation study (EOGRTS) was to be carried out on the whole substance, the environmental requests are to be carried out on two fractions of the substance. The two fractions proposed were the C9 constituent fraction and the C12 constituent fraction. The C12 fraction is representative for the main bulk of components in the registered substances because >65% of the components in the registered substance have a C12 constituent. The C9 fraction represents only about 2% of the components, but it represents the lower weight components that are more mobile and more bioavailable than the C12 fraction resulting in different environmental exposure, toxicity, degradation and bioaccumulation.

MSC was guided by the expert from the eMSCA through the information on the substance (including PfAs, the Registrants' comments and the eMSCAs responses to them). The PfAs received on the human health related request for an extended one-generation reproductive toxicity study were accepted by the eMSCA, so these were not discussed at MSC meeting. The MSC meeting discussion focused on the PfAs related to the environmental concerns which are presented below.

All the environmental tests for P, B and T were requested to be done in parallel.

With regard to simulation degradation testing in a water-sediment system (OECD TG 308) at 12ºC, using fractions of radiolabelled BAB representative for C9 and C12, three PfAs were received: 1) to request the most soluble fraction (C9 substituted components) to be tested in a simulation degradation test in surface water (OECD TG 309) instead of a water-sediment system (OECD TG 308) if this is technically feasible, while the C12 substituted component testing in a water-sediment system (OECD TG 308) should be maintained; 2) for the Registrant to justify his choice of extraction procedure/solvent for minimizing non-extractable residues (NER); 3) to add the substance directly to the sediment to reduce dissipation of test substance due to its high volatility related to the high Henry's Law constant and adsorption to test vessel.

With regard to bioaccumulation in fish, aquatic exposure (OECD TG 305-I) five PfAs were submitted: 1) One MSCA disagreed with requesting the P, B and T testing in parallel, and proposed to perform the P and non-vertebrate eco-toxicity studies before the B test. In their view, exposure concerns can be first addressed by requesting further information on the environmental emissions rather than requesting a vertebrate test. 2) Another MSCA proposed to justify better why it is judged possible to document that the aqueous concentration of the test substance can be kept sufficiently constant in a concentration below the water solubility of the test substance during the 28 days exposure period and 3) to give the option to the Registrant to conduct a dietary study if he can convincingly document that the conduct of an aquatic study is technically unfeasible. 4) It was also proposed that the bioaccumulation test should be conditional to the results of the simulation test on the two fractions C9 and C12, i.e. test either C9 or C12 depending on which results to be P, or else test nothing at all if none results to be P. 5) A fifth PfA asked for the concern for secondary poisoning (substance is found in molluscs) to be further substantiated in the DD.

With regard to aquatic toxicity testing with molluscs (ASTM E724), three PfAs were received proposing to: 1) ask for a long term test with mussels instead of the acute test, since this would provide a definitive result for T; 2) replace the request for testing in marine molluscs with a freshwater mollusc using OECD TG 242 or OECD TG 243, or else to include a justification why a marine species is requested; 3) remove all eco-toxicity testing (i.e. tests 1.4-1.8) from Section 1 of the DD since there is no need to test the toxicity of the substance for the purposes of PBT assessment, as the substance already fulfils the T criteria on the basis of the self-classification as category 2 for reproductive toxicity.

Otherwise it was proposed to provide more justification in the DD explaining why the ecotoxicity tests on the C9 and C12 fractions are needed.

With regard to fish, early-life stage toxicity test (FELS; OECD TG 210), three PfAs were submitted proposing to 1) request this test sequentially, so that the persistence test (1.2), non-vertebrate ecotoxicity tests (1.4, 1.5, 1.6), then bioaccumulation test (1.3) are performed prior to the FELS test; 2) give the Registrants the option to read across the result of one fraction to the other in the interest of animal welfare; 3) adjust the deadline accordingly.

With regard to Sediment-Water Chironomid Life-Cycle Toxicity Test Using Spiked Sediment (OECD TG 233), two PfAs were received proposing 1) to replace the requested test with an OECD TG 218 since this test method has been accepted as providing a NOEC/EC10 for risk assessment. Otherwise give the choice to the Registrants between the two methods and 2) make this test conditional on the PBT outcome, since if substance is confirmed as PBT or vPvB there would be no need for the sediment toxicity test.

The representatives of the Registrants explained at the meeting that they agree with clarifying the concern on the substance. They explained that to perform the tests in parallel it requires much effort since the fractions are UVCB substances themselves and synthesis of radiolabelled fractions is very difficult. The solubility of each fraction is very low. The alternative proposal of the labs was to select two representative molecules, one for C9 and one for C12. According to the labs if they select these two molecules and take into account the PfAs, the best approach to get interpretable results was by doing the test with pure substances. The representatives of the Registrants suggested testing using single structural compounds (not fractions) as examplars (C9 and C12 chains). The labs recommended a tiered testing strategy instead of parallel testing. In their view, this supports the PfAs that suggested not to do the P, B and T testing in parallel, and the PfA in regard aquatic toxicity testing to be done sequentially to the results of the P and B testing.

The Registrant representatives explained the testing strategy which they had already submitted in response to comments. This consisted of defining the appropriate molecules, the synthetic route and the radiolabelled substance to do the test with P and B. If testing with this representative molecule for C9 results in P, the B is conducted. If it results to be B then the substance is PBT so Registrants can apply the proper risk management measures (RMM). If C9 is not P, then they would test C12. If C12 is P then they would test B also with C12. If C12 is B then the total substance will be P and B. To solve the T issue, the representatives of the Registrants stated that they know that the registered substance is toxic because it has been tested in other media. Hence performing *Daphnia* and alga studies in the non-radiolabelled molecule could answer the environmental toxicity concern.

During the discussion the Chairman asked the eMSCA expert if the comments of the Registrant representatives on the testing strategy can be considered as comments on the PfAs or on the DD itself. The eMSCA expert replied saying that based on the comments from the Registrants on the first DD, the DD was not amended and PfAs were not submitted on this. So they considered that intervention at the meeting as a comment on the DD. The eMSCA expert explained that they ask the Registrants to test for C9 and C12 even though they are UVCB themselves and if difficult to perform to choose a molecule representative of each fraction.

Furthermore, the representatives of the Registrants were asked to explain the term ‘PBT labelling’ used in their written comments to the PfAs. They explained that when they were preparing the registration dossier following many QSARs and solubility testing they found big difficulties in analysing the substance when trying to test on the substance itself. They therefore proposed to handle the substance as a PBT and informed the users of the substance to use it under strictly controlled conditions.

A stakeholder observer representing an animal welfare NGO expressed his disagreement with performing an EOGRTS due to the lack of consumer exposure. The Chairman explained that since there was no PfA asking to remove the request for EOGRTS it implies that there are no diverging views from the MSCAs and ECHA on requesting such study, hence the study request remains in the DD.

Session 2 (closed)

The main discussion centred around whether to perform the environmental tests sequentially (as per PBT testing strategy in the ECHA guidance) or in parallel (for CSR-related reasons) and with two fractions (C9 or C12, or representative components there-off).

The reason for parallel testing for P and B was based by the eMSCA on a concern for secondary poisoning to predators in the environment that was indicatively calculated by the eMSCA. The calculation resulted in preliminary risk quotients that ranged from 0.4 up to 66 and 27 up to 4800 for two emission scenarios described in the CSR. According to the eMSCA estimations on the risk for human consumption of fishery products would lead to even higher risk quotients than the calculations of risk quotients for predators because for human exposure the risk for the individual is concerned while the risk for predators covers the whole population.

Additional to these calculations, two publications show that the substance or constituents thereof are found in the environment (Booth et al., 2007, Eganhouse and Pontolillo, 2008), indicating that the substance may be released to the environment. The MSC spent some time discussing the relevance of the content of these two papers with regard to this SEV, like if they are an indication of recent emissions or else emissions from decades ago, and the source. It was agreed that these papers confirm the presence of this substance in the environment through recent emissions, since the sediment study measured the substance in different sediment layers and the mussel studies also confirm such recent emissions. There was also a discussion to give the explicit possibility for the Registrants to further refine the environmental exposure assessment instead a refinement of the hazard assessment through toxicity testing, however, it was noted after review of the CSR that Registrants had already a refined the environmental exposure assessment in the CSR.

MSC discussed three options for this case-specific draft decision. Option 1 was the original proposal of performing the P (degradation study), T (aquatic toxicity study on mollusc, algae, daphnid and FELS) and B (bioaccumulation study) testing in parallel and, conditional to the results of the aquatic toxicity studies, perform a sediment toxicity study as a second step. This would take 2.25 years (27 months).

Option 2 was to perform the P, T (invertebrate only aquatic toxicity study – mollusc, algae and daphnid) and B testing in parallel and, as a second step or in a follow up decision, perform the 1) FELS toxicity study based on the outcome of the P, B and $T_{invertebrate}$ and /or refined risk assessment conditional to the P, B and $T_{invertebrate}$ and/or refined risk and 2) sediment toxicity study conditional to the results of the aquatic toxicity studies. This would take 2.75 years (33 months).

Option 3 was to perform P and $T_{invertebrate}$ testing as a first step. Then perform B as a second step conditional to P and $T_{invertebrate}$ or refined risk. In a third step or a follow up decision the 1) FELS toxicity study based on the outcome of the P, B and $T_{invertebrate}$ testing and/or refined risk assessment conditional to P, B and $T_{invertebrate}$ and 2) sediment toxicity study conditional to the results of the aquatic toxicity study. This would take 3.5 years (42 months).

MSC established that for this specific case the environmental risk concerns provided arguments to make an exception from the general sequential testing approach when following-up on a PBT or vPvB concern, and they agreed to perform parallel testing for Persistence, Bioaccumulation and aquatic Toxicity for environmental invertebrates (Option 2). The testing on fish is conditional to the PBT-assessment and risk characterisation following the newly generated information, and only has to be performed on either the C9 or C12 fraction (or representative component) of this UVCB, whichever is most toxic in the invertebrate tests. MSC also unanimously agreed for this case on the spiking of sediment for P-testing, and that the sediment organism toxicity testing is conditional to the outcome of an initial risk assessment for sediment organisms based on results derived in the aquatic toxicity tests using equilibrium partitioning (EPM). Furthermore, MSCA unanimously agreed to introduce an additional deadline for submission of the requested

information- a deadline of 27 months if the FELS test is not performed and a deadline of 33 months if the FELS test is performed.

The MSC agreed unanimously on the DD as amended at the meeting. The UK MSC member abstained from voting for the reasons explained in Section VII.

Item 7 – Dossier evaluation

a. Written procedure report on seeking agreement on draft decisions on dossier evaluation

SECR introduced the report on the outcome of the written procedure (WP) for agreement seeking on twelve dossier evaluation cases (see Section VI for more detailed identification of the cases). WP was launched on 18 May 2016. By the closing date 29 May 2016, MSC reached unanimous agreement on twelve DDs. One member abstained from voting on four cases. SECR further informed MSC that in line with some comments made by a MSC member SECR had made an editorial change for internal alignment of the DD text on one case.

b. Introduction to and preliminary discussion on draft decisions on compliance checks and testing proposals when amendments were proposed by MS-CA's (Session 1, open session)

c. Seeking agreement on draft decisions on compliance checks and testing proposal examinations when amendments were proposed by MS-CA's *(Session 2, closed)*

CCH-020/2017 Butyl glycollate (EC No. 230-991-7)

Session 1 (open)

Two representatives of the Registrant participated in the initial discussion. In absence of specific confidentiality concerns in the DD, an open session was held.

SECR explained that five proposals for amendment (PfA) to ECHA's DD had been submitted. The first general PfA concluded, for pre-natal developmental toxicity (PNDT) and reproductive toxicity, that insufficient scientific justification to support the negligible systemic exposure of butyl glycollate and some of its metabolites has been provided. Then it noted that toxicodynamic (species) differences between rabbit and rat were not addressed for PNDT. Further, it requested reproductive toxicity information not only on fertility, which was referred to in the DD, but also on pre-, peri- and postnatal development. Finally, it suggested including developmental neurotoxicity (DNT) and immunotoxicity (DIT) cohorts in extended one-generation reproductive toxicity study (EOGRTS; OECD testing guidelines (TG) 443).

The second PfA on PNDT in a second species suggested not to consider the proposed read across plausible, because of concerns on pH dependence of hydrolysis; predictability of metabolism based on water solubility, Log Kow and accumulation, and because esterases involved in metabolism were not specified. It further argued that the formation and impact of glyoxylic acid butyl ester and oxalic acid mono butyl ester, which the Registrant regarded to be insignificant intermediate side metabolites, had not been sufficiently addressed. It concluded that based on these shortcomings there was insufficient evidence to support the rapid hydrolysis rate, which would result in low systemic exposure of the parent compound (butyl glycollate) and to support the claim of negligible impact of the intermediate side metabolites.

The third, fourth and fifth PfA were on EOGRTS. The third PfA suggested keeping the request for EOGRTS with similar reasoning as in the second PfA not to consider the proposed read across plausible. The fourth PfA requested extension to DNT cohorts 2A and 2B, because of particular concern based on studies performed with ethylene glycol, a

structurally analogous substance, resulting in delayed neurotoxic effects and acute effects showing a mechanism of action. Also, ethylene glycol raised a concern on interference with sex hormonal system, because of observed effects with fish estrogen receptors as well as interference with estrogen and androgen receptors in *in vitro* studies. The fifth PfA requested extension to DIT cohort 3, due to particular concern for the analogue ethylene glycol showing a particular concern for developmental immunotoxicity.

SECR had not modified the DD in advance of the meeting based on the PfAs.

The Registrant had provided written comments on the DD (not reflected here) and on the PfAs. The representatives of the Registrant reiterated their disagreement with all PfAs and noted that the substance was already classified for developmental toxicity. They recognised the challenges in preparing their proposal for read across, which they had significantly improved through their commenting on the initial DD and the PfAs. The read across was complex and introduced different substances, which could lead to similar metabolites through multiple metabolic routes. The representatives of the Registrant did not consider requests for further studies proportionate. Also, they argued that butanol (a metabolite) had adverse effects on reproductive toxicity only at high dose levels but none on developmental toxicity.

A MSC member reasoned that the read across had been improved, but did not consider it sufficient yet and would deem it plausible only with a request to generate further supporting data, for example, through hydrolysis and/or screening studies. An expert to a MSC member argued that the Registrant assumed rapid hydrolysis but there was no evidence to support this, and other metabolic pathways could play a role. Therefore, the (relative) pathways and rates of butyl glycollate metabolite formation were difficult to quantify. An expert to another MSC member considered the read across plausible, but recognised a need for further quantitative information on reproductive toxicity assessment.

A stakeholder representative was of the view that the read across was acceptable enough and could be updated if needed. Another stakeholder representative welcomed improvements in the read across and invited proposals for modifying it to become acceptable.

SECR clarified the proposed read across with a scheme of substances, metabolic pathways and metabolites, and presented a table on available information on related substances (all based on information provided by the Registrants) to better understand and identify missing information. It noted that additional toxicokinetic studies could improve the assessment; however, SECR considered that similar toxicological profiles (same target organ(s) with similar doses) of the registered and source substances were sufficient to support the read-across. SECR would consider dossier updates, which the Registrant had not yet done, in the follow up and, if found sufficient, would consider the requests fulfilled.

Session 2 (closed)

A MSC member emphasized that it could not be excluded that side metabolites could be formed to a significant level and that fertility and perinatal effects would occur. Several MSC members and experts supported the conclusion that the information requests would need to be kept. However, the text in the DD could be revised to identify shortcomings in read across based on discussions in the open session. SECR supported to clarify remaining deficiencies in the read across but reminded that the responsibility to address them was upon the Registrant.

MSC concluded, mainly due to the complexity of this proposal for read across, to further revise the DD to indicate the deficiencies and the pieces of supporting information, which would be further needed to consider the read-across approach plausible but which were currently lacking.

MSC agreed unanimously to the DD as amended at the meeting.

CCH-021/2017 Acrylic acid, monoester with propane-1,2-diol (EC No. 247-118-0)

Session 1 (open)

No representative of the Registrant participated in the initial discussion. In absence of specific confidentiality concerns in the DD, an open session was held.

SECR explained that five PfAs were received in total to the ECHA's DD and were discussed in the meeting. One PfA requested clarification in the description of the chromosomal aberration. Three PfAs were related to the request for an *in vivo* mammalian alkaline comet assay (OECD TG 489) or transgenic rodent (TGR) somatic and germ cell gene mutation assays (OECD TG 488). For TGR it was proposed to request both glandular stomach and duodenum to align the tissues with those requested in the comet assay. One PfA requested a modified comet assay to detect cross-linking. The investigation for cross-linking should be done by collecting two sets of slides, one subject to normal experimental conditions and another to modified experimental conditions that enable detection of DNA-DNA and DNA-protein cross-links.

The fifth PfA on EOGRTS (OECD TG 443) suggested conducting first the comet/TGR study and using results, with other relevant information, to decide on the EOGRTS design.

SECR had modified the DD in advance of the meeting based on the PfAs on cross-linking and on clarifying the DD text (PfAs 1, 3 and 4).

The Registrant had provided written comments prior to the meeting on the DD (not reflected here) and on the PfAs. He agreed with the first and third PfAs on text clarifications for the *in vivo* genotoxicity request. He disagreed with the cross-linking issue, making reference to a new Ames study with five strains (not included yet in a dossier update) that was negative. He also disagreed with the fifth PfA on EOGRTS (OECD TG 443) and intends to provide additional toxicokinetics information supporting rapid metabolisation of the registered substance.

The MSC member from the MSCA that made the fifth PfA on EOGRTS (OECD TG 443) asked to clarify how no exposure to professionals and consumers was assessed. SECR responded that the registered substance was reported to be used only in an industrial settings, with mostly polymer uses and no release of the monomer from the polymer. There were no widespread professional or consumer uses reported in the dossier. Therefore, the results of the *in vivo* genetic toxicity study would not influence the EOGRTS design.

Regarding the fourth PfAs on *in vivo* genotoxicity, a MSC member inquired whether the Registrant in his comments had addressed the potential cross-linking. SECR summarised that there was some level of uncertainty on detecting cross-linking mutagens due to differences in the results in two available Ames studies, which used various bacteria strains.

The MSC member continued to discuss the second PfA, on tissue selection in TGR, to address potential site of contact mutagens. He reminded the MSC that for the comet assay, MSC had agreed in earlier MSC meetings to sample glandular stomach and duodenum to address remaining scientific uncertainties in the sensitivities of these tissues. He now recommended aligning the requests made for the two tests and thus proposed to sample duodenum also for TGR.

Another MSC member suggested that in TGR, the second tissue, i.e. duodenum, could be sampled and kept frozen for later analysis. Such option would not be possible for the comet assay, where tissues must be analysed immediately after sampling. Duodenum would be analysed in TGR only if the result of the analysis of the other tissues (liver and glandular stomach) would be negative. SECR informed that additional sampling would not increase the total study cost (it is the analysis that is costly), and this approach would save costs in case the second tissue would not need to be analysed.

Session 2 (closed)

The MSC member from the MSCA that made the fifth PfA on EOGRTS (OECD TG 443) was satisfied with the response that the exposure from the registered substance would not

justify the implementation of second generation in EOGRTS. The member also suggested that ECHA Forum of MSCAs is informed on this decision that a test was excluded since there was no information in the dossier on professional uses and that the competent authority could check on this on site.

Regarding the fourth PfA on *in vivo* genotoxicity regarding cross-linking, a MSC member further noted that for the Ames study included in the registration dossier there were no data on the purity of the tested substance. This was also the reason why the Registrant in their comments on the proposals for amendment considered this study to be unreliable. However, MSC considered that the positive study result could not be disregarded and uncertainty of the possible differences in sensitivities in the different strains remained. MSC concluded that there would be no need for an *in vivo* genetic toxicity study regarding gene mutation mutagenic mode of action, if there was a negative result from a reliable and adequate Ames study, using strains recommended to detect crosslinking mutagens, which would remove the uncertainty of the positive Ames study included in the registration dossier.

Regarding the second PfA on analysing duodenum in TGR, an MSC member raised the concern when two tissues (liver and glandular stomach) were negative. It would then be likely that duodenum would be negative as well, thus not warranting its analysis. If one of the first two tissues were positive, then analysis of the third tissue would not be needed. An MSC member clarified that there was a potential for the first site of contact tissue (glandular stomach) to produce false positive results. The MSC member further concluded that if corrosivity was shown in the testing, then the sampling of duodenum should be included in order to minimise the possibility of a false positive result (due to corrosivity) in the glandular stomach. Another MSC member emphasized that as TGR is an expensive study and storage and analysis of additional sampled tissues increases the cost significantly, and that any additional regulatory requirements would need to be pragmatic. Thus, duodenum should be analysed only when necessary and when other tissues were negative. MSC concluded that sampling and freezing was a justified request, which they considered would result in little or no additional costs for the step, based on information from some CROs. It was agreed that for TGR duodenum would need to be harvested and stored for up to 5 years, and analysed only if results from two other tissues (liver, glandular stomach) were negative. A MSC member concluded that there has been an agreement why to request duodenum to be sampled and analysed in comet assay and there should be no deviation in TGR; for pragmatic reasons the duodenum tissue in TGR would be frozen and, only if needed, analysed at a later stage. MSC further noted that the approach may be reapplied in decisions which request a TGR.

MSC agreed unanimously to the DD as amended at the meeting.

CCH-034/2017 Terpineol (EC No. 232-268-1)

Session 1 (open)

No representative of the Registrant participated in the initial discussion. In absence of specific confidentiality concerns in DD, an open session was held.

SECR introduced the case and the two PfAs submitted to ECHA's DD. The first PfA on PNDT in a second species (i.e. rabbits) oral route suggested the Registrants to perform a dose-range finding test first to ensure that the study in rabbits can be conducted at a sufficient high dose (considering its antimicrobial activity), to specifically name an alternative non-rodent test species (as mammalian non-rodent laboratory species: dogs, cats, ferrets, mini-pigs, and non-human primates) while removing the option for a second rodent species unless a further justification can be provided why a second rodent species could be used as alternative for rabbits. The second PfA on the appropriate route of exposure specify that administration by gavage may not be appropriate for this substance and the most relevant route of human exposure, inhalation or diet, should be considered.

The Registrant provided written comments prior to the meeting and agreed to conduct a dose-range finding study, and to conduct an additional preliminary study with non-pregnant females. Considering the proposed protocol the Registrant requested for the extension of deadline to submit the study results from 12 months to 18 months. The Registrant disagreed with the suggested use of other non-rodent species considering the potential low litter sizes and lack of historical control data for those species.

The MSC adviser from the MSCA submitting the first PfA informed the MSC that his institute is currently engaged in an ongoing project to compare PNDT testing results for rats and rabbits. He explained that terpineol likely has antibiotic properties and destroys intestinal microflora, provided information on the proven gastro – intestinal sensitivity of rabbits to antibiotics, and proposed mice as the more appropriate second species, or to give to laboratory the chance to choose the most appropriate species.

Another MSC member considered that the choice of the second species in PNDT tests should be aligned, properly justified and decided in MSC meeting, and not to be left on the responsibility of the Registrant nor of the testing laboratory.

An adviser to a MSC member recognised the added value of requesting the dose-finding study this study because of different sensitivity and results of e.g. non-pregnant *vs* pregnant females for the rabbit species used in the study.

Session 2 (closed)

During the closed session, MSC members agreed mice as a second species might be appropriate and as informative as any non-rodent species (e.g. rabbit, guinea pig) because it is not as sensitive to antimicrobials thus avoiding a potential significant animal welfare challenge. An adviser to a MSC member reminded the meeting participants that the data presented in the dossier prove the antimicrobial effects of terpineol (on e.g. *Staphylococcus aureus, Salmonella*).

SECR informed meeting participants ECHA has an on-going project which could also be a source for future discussions on the appropriateness of rabbit as non-rodent species for substances leading to gastrointestinal toxicity, that it plans to share final results of the project with MSC as starting point for a discussion at appropriate level on revision of the testing policy as/if appropriate.

In conclusion MSC acknowledged that based on the comments provided by the Registrant, rabbit may not be an appropriate species for testing the registered substance, therefore any mention to rabbit as the preferred species to be tested was removed from the DD. MSC agreed for this case to request the Registrant to perform the PNDT study in a species he should select and duly justify.

MSC agreed unanimously the DD as amended during the meeting.

Item 8 – SVHC identification - Seeking agreement on Annex XV proposals

a. Seeking agreement on Annex XV proposals for identification of SVHC

4,4'-isopropylidenediphenol (bisphenol A, BPA) (EC No. 201-245-8)

The dossier submitter (DS) representative from the French CA presented to MSC the Annex XV proposal for identification of Bisphenol A (BPA) as an SVHC under Article 57 (f) of REACH due to its endocrine disrupting properties for which there is evidence of probable serious adverse effects to human health giving rise to equivalent level of concern (ELoC) to CMR substances under Article 57 (a)-(e). The DS explained the rationale for preparing the dossier. Further, the DS pointed out that the assessment was based on the WHO/IPCS definition of endocrine disrupters further elaborated by the European Commission's Endocrine Disruptors Expert Advisory Group, and also on the factors relevant for the assessment of an Equivalent Level of Concern (ELoC) as specified in ECHA's generic approach paper on SVHC identification according to Article 57 (f) with sensitisers mentioned as an example. The dossier focused primarily on the alteration by BPA of reproductive function, mammary gland development, cognitive function and metabolism,

with the disruption of estrogens and estrogenic pathways being essential in the mediation of each of these effects.

The DS outlined the main comments received in the public consultation on the proposal and the DS's responses to them. The DS concluded that several comments were outside the scope of the SVHC identification process, e.g. those concerning economic impact, the difficulty to substitute BPA and whether SVHC identification is the best regulatory risk management measure. With regard to the comments received on the four types of adverse effects described in the dossier, all MSC members agreed that the evidence for the alteration of reproductive function was sufficient to establish an equivalent level of concern for BPA due to its endocrine disrupting properties.

As for mammary gland development, some comments indicated that there may be uncertainties regarding the reliability and reproducibility of the evidence, meaning there may be insufficient evidence that BPA increases the risk of breast/prostate cancer in humans. The DS replied that the effect has not been investigated in multi-generational studies as there is no such test guideline available and that there is no relevant epidemiology study available either. However, the DS did find evidence in the literature (reviews conducted between 1980 and 2015) that concludes that the mammary gland changes described may predispose individuals to cancer development.

Comments on the cognitive function and metabolism aspects noted conflicting evidence (e.g. negative guideline studies) in the dossier. The DS responded that there are several reasons (e.g. differences in window of exposure, doses, routes of exposure, sex, species and strains) that may explain apparent discrepancies and highlighted that sex-specific effects should not be seen as inconsistencies. Overall, while the DS acknowledged that there may be uncertainties in dose-response for risk assessment, these do not impact hazard assessment (and mode of action considerations) to the same extent. The DS took note of the comments regarding e.g. low dose effects and made the appropriate deletions in the support document.

In the subsequent discussion, some members sought further clarification with regard to the potential uncertainties regarding both the relevance of the effects to human health and the connection between the observed effects and the proposed possible serious effects on human health (i.e. related to breast cancer, neuro-behavioral disorders and diabetes). The DS responded that in their view, the current evidence is considered sufficient to conclude that these effects have probable serious effects on human health which give rise to an equivalent level of concern to those of other substances listed in paragraphs (a) to (e) of Article 57.

An adviser to an MSC ASO observer re-iterated their comments (provided during the public consultation) that in their view, there are inconsistencies between the dossier presented to MSC compared to the work of EFSA on BPA (for example, the weight given to various studies in EFSA's Scientific Opinion *vs*. the weight given by the DS in the current dossier). He also mentioned that the Clarity-BPA research project is ongoing which results, in his view, should be awaited. The DS disagreed with the industry's comments and replied that the two assessments (that of the DS and of EFSA) are not comparable. The main difference between the current BPA dossier and the work done by EFSA is the level of information available at the time the two assessments were conducted. The DS also stated that they already have sufficient information available to conclude on the endocrine disrupting properties of BPA, and forthcoming information from the Clarity-BPA project would not override available and reliable findings.

EFSA's CEF Panel assessment of BPA, published in 2015, was based primarily on literature collected up to 2012. However, a significant number of scientific studies have been published since then which contribute new information to the assessment. Furthermore, in August 2016, BPA was formally classified as a reproductive toxicant (Repr. 1B) under the Classification, Labelling and Packaging (CLP) legislation[2] and disruption of oestrogenic signalling was considered to be the main mode of action by RAC.

[2] http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32016R1179&from=EN

In the MSC's current assessment prepared by the DS, a weight of evidence approach is used, meaning that a combination of information from several independent sources is used to provide sufficient evidence to fulfil an information requirement. Each study is considered for its strengths (e.g. investigation of structural changes in addition to corresponding functional endpoints or detailed investigation of a specific effect) and limitations (e.g. design limited to one sex or limited number of doses). The overall weight given to the available evidence depends on factors such as the quality of the data, consistency of results and relevance of the information for the effect under consideration.

MSC went through the proposal for BPA identification for human health and the text of the Support Document with amendments introduced at the meeting. MSC unanimously supported the text and conclusion on identification of BPA as SVHC due to its endocrine disrupting properties under Article 57 (f) and also unanimously acknowledged that there is scientific evidence on the endocrine disrupting activity of BPA and on the link between this activity and the adverse effects to human health.

When the MSC agreement document and support document were brought to a vote, the members unanimously agreed to identification of BPA as SVHC due to its endocrine disrupting properties under 57(f), i.e. the available information for BPA was sufficient to conclude that there is scientific evidence of probable serious effects giving rise to an equivalent level of concern in relation to human health (i.e. to substances listed in points (a) to (e) in Article 57 of the REACH Regulation).

Two members abstained from the vote and requested to add a joint statement to the minutes (see Section VIII).

The Chair thanked the dossier submitter for the proposal submitted to the SVHC identification process, and MSC for its deliberations on it. Also the dossier submitter expressed appreciation for the support and further input provided, as well as for the unanimous agreement reached.

Perfluorohexane-1-sulphonic acid and its salts (PFHxS)

The DS's representative from the Swedish CA presented to MSC the proposal for identifying Perfluorohexane-1-sulphonic acid and its salts (PFHxS) as substances of very high concern due to their very persistent and very bioaccumulative (vPvB) properties (REACH Article 57 (e)). The comments of the public consultation and the modifications in the draft support document based on these comments were also briefly introduced.

Concerning the persistency of PFHxS, based on the evidence provided in the support documents, the members supported the conclusion of the dossier submitter that this substance can be considered as very persistent (vP) and this was therefore not further discussed.

The property of PFHxS as very bioaccumulative (vB) was supported by many commenting parties in the public and MSCAs' consultation, however, some comments made this the main discussion point for MSC. The DS explained that, due to their properties, the numerical bioaccumulation (B)/(vB) criteria defined for aquatic species in the REACH Annex XIII (sections 1.1.2 and 1.2.2) are not suitable to assess the bioaccumulation potential of PFHxS. Instead, a weight-of-evidence approach (WoE) needs to be followed to conclude that PFHxS can be considered as very bioaccumulative substances. Data on bioaccumulation potential in terrestrial species as well as in endangered species was used, together with results from human elimination studies. The latter derived very long elimination half-lives that are considered a very important element of the proposed WoE argumentation.

In response to a comment questioning the reported human elimination half-lives, the DS introduced supplementary literature data on blood concentration levels in workers to put the reported elimination half-lives in perspective. Following a short discussion, MSC supported the DS' interpretation of the relevance and reliability of the elimination half-lives.

In the plenary discussions, several MSC members supported the nomination of PFHxS as SVHC based on its vPvB properties, noting that the substance is of great regulatory interest to their countries. Also an NGO observer expressed her support to the well-written SVHC proposal and its conclusions. She highlighted the very high elimination half-lives and the presence of these substances in the arctic environment as evidence for their vPvB-properties. She expressed support to the proposal also to avoid any regrettable substitution.

An expert to a member of MSC acknowledged the comprehensive response of the dossier submitter to the public consultation comments, pointing out that this is an unusual case because of the data available to support bioaccumulation, and the absence of toxicity data meant that vB rather than B was key for SVHC identification. It was noted that in their view the case depended on the use of half-lives for discrimination between B and vB but numerical criteria are currently not available. The only guiding precedent to date was the decision identifying PFOA as B. For PFHxS, the very long half-lives for both non-rodent mammals and humans together did indicate vB, and there was benefit in the comparison made in the dossier with the data with PFOS. It was also noted that in using half-lives, body burden needed to be considered. As there were remaining uncertainties in the field data, these should be seen as supporting data.

The support document was revised according to these discussions and it was concluded that the comments received had sufficiently been addressed.

Following the discussion, the support document and the respective agreement document for PFHxS were updated to highlight also in the summary part that the half-lives for PFHxS are the longest observed for any polyfluoroalkyl substances (PFAS) for some mammals so as to further substantiate the bioaccumulation potential.

In conclusion, MSC unanimously agreed to identify PFHxS and its salts as SVHC in accordance with Article 57 (e) of Regulation (EC) 1907/2006 (REACH) due to their vPvB properties. MSC unanimously agreed on the support document and agreement as amended during the meeting.

The Chairman thanked the dossier submitter for presenting the proposal, everybody for the discussion and MSC for the decision taken. Also the Swedish member expressed his appreciation for the support and further input provided, as well as for the unanimous agreement reached.

Following the agreement, the member from Norway informed MSC that her country has nominated this substance to the Stockholm Convention and that the POPs review is expected in October 2017.

b) Proposal for an update of MSC Working procedures for SVHC identification

SECR presented a proposal for an update to MSC's working procedures concerning identification of substances proposed as SVHCs under Article 57. One of the main changes suggested was to stop providing comments received during the public and MSCA consultations (RCOMs) to MSC via S-CIRCABC during and right after the closure of commenting period, since SECR has established a new practise of publishing these on ECHA website. Few other clarifications and technical adjustments were also proposed. MSC adopted the update to its working procedures without further discussion.

Item 9 – Any other business

- Update on appeals and court cases (*partly closed session*)

SECR gave an overview of the status of recent appeals on evaluation submitted to the Board of Appeal of ECHA and pending cases submitted to the European Court of Justice relating to the authorisation process. MSC took note of the information received.

- Brief report from an *ad-hoc* scoping group meeting on UVCBs

The Chair of the UVCB *ad hoc* scoping group informed MSC of the topics discussed in the meeting that took place on 26th of April and introduced the agreed next steps. The following actions will be contacting the industries to discuss their ongoing activities and possible scientific workshop, and compile an overview of current available guidances.

Secretariat will circulate the minutes of the meeting to MSC once agreed by the scoping group.

- Suggestions from members

An UK expert pointed out that for mutagenicity testing aneugens can be risk assessed via the threshold approach and if the micronucleus test is aneugen positive then additional information is needed as follow-up to establish dose response relationship. It was suggested to consider what additional information could be requested in dossier or substance evaluation decisions. This was supported by some MSC members who requested ECHA to give this further consideration.

The Chairman stated he will request a view from ECHA mutagenicity experts on possible follow-up steps in REACH when exclusively an aneugenic mechanism has been established and report back to MSC for further discussion.

Item 10– Adoption of conclusions and action points

The conclusions and action points of the meeting were adopted at the meeting (see Section IV).

II. List of attendees

Members/Alternate members
ALMEIDA, Inês (PT)
ANDRIJEWSKI, Michal (PL)
ATTIAS, Leonello (IT)
COCKSHOTT, Amanda (UK)
CONWAY, Louise (IE)
DIMCHEVA, Tsvetanka (BG)
DUNAUSKIENE, Lina (LT)
FINDENEGG, Helene (DE)
HERMES, Joe (LU)
HORSKA, Alexandra (SK)
HUMAR-JURIC, Tatjana (SI)
JANTONE, Anta (LV)
KREKOVIĆ, Dubravka (HR)
KULHANKOVA, Pavlína(CZ)
LONDESBOROUGH, Susan (FI)
LUNDBERGH, Ivar (SE)
MARTÍN, Esther (ES)
MIHALCEA UDREA, Mariana (RO)
NYITRAI, Viktor (HU)
PALEOMILITOU, Maria (CY)
REIERSON, Linda (NO)
STESSEL, Helmut (AT)
TYLE, Henrik (DE)
VANDERSTEEN, Kelly (BE)
VESKIMÄE, Enda (EE)
WIJMENGA, Jan (NL)
WODLI, Jordane (FR)
Representatives of the Commission
SCHUTTE, Katrin (DG ENV)
Observers
ANNYS, Erwin (Cefic)
BERNARD, Alice (ClientEarth)
CINGOTTI, Natacha (HEAL)
DROHMANN, Dieter (ORO)
HYNES, Jarlath (HIS)
HÖK, Frida (ChemSec)
KERÄNEN; Hannu (CONCAWE)
LOONEN, Helene (EEB)
MUSU, Tony (ETUC)
STODDART, Gilly (PISC)
WAETERSCHOOT, Hugo (Eurometaux)

ECHA staff
AJAO, Charmaine
ANASTASI, Audrey Anne
BERCARU, Ofelia
BICHLMAIER, Ingo
BROERE, William
CARLON, Claudio
CLENAGHAN, Conor
DE WOLF, Watze
DELOFF-BIAŁEK, Anna
DREVE, Simina
FALCK, Ghita
FEDTKE, Norbert
HAUTAMÄKI, Anne
HERBATSCHEK, Nicolas
HUUSKONEN, Hannele
JAAGUS, Triin
JOHANSSON, Matti
KARHU, Elina
KOJO, Anneli
KORJUS, Pia
KUITTINEN, Marko
LE CURIEUX, Frank
NAUR, Liina
O'FARRELL, Norah
PELLIZATO, Francesca
PELTOLA-THIESS, Johanna
PREVEDOUROS, Konstantinos
RÖNTY, Kaisu
SPUTH, Linda
TAI, Kaihsu
TRNKA; Jan Peter
VAHTERISTO, Liisa
VASILEVA, Katya
VÁZQUEZ RODRÍGUEZ, Jesus
WALKER, Lee

Proxies
- MARTÍN, Esther (ES) also acting as proxy of KOUTSODIMOU, Aglaia (EL).
- STESSEL, Helmut (AT) also acting as proxy of ANDRIJEWSKI, Michal (PL) on 16 June.
- ALMEIDA, Inês (PT) also acting as proxy of HUMAR-JURIC, Tatjana (SI) on 12 June at 12:00-13:00.
- HUMAR-JURIC, Tatjana (SI) also acting as proxy of ALMEIDA, Inês (PT) on 16 June from 11:00 onwards.
- TYLE, Henrik (DK) also acting as proxy of DUNAUSKIENE, Lina (LT) for short periods during the meeting.

Experts and advisers to MSC members
ALIVERNINI, Silvia (IT) (expert to ATTIAS, Leonello)

COPOIU, Oana (RO) (expert to MIHALCEA UDREA, Mariana)
DANIHELOVA, Martina (SK) (expert to HORSKA, Alexandra)
DE KNECHT, Joop (NL) (expert to WIJMENGA, Jan)
DOBRAK-VAN BERLO, Agnieszka (BE) (expert to VANDERSTEEN, Kelly)
DOYLE, Ian (UK) (expert to COCKSHOTT, Amanda)
GRACZYK, Anna (PL) (expert to ANDRIJEWSKI, Michal)
GRINCEVICIUTE, Otilija (LT) (expert to DUNAUSKIENE, Lina)
HØJRIIS, Sara (DK) (expert to TYLE, Henrik)
INDANS, Ian (UK) (adviser to COCKSHOTT, Amanda)
KOZMIKOVA, Jana (CZ) (expert to KULHANKOVA, Pavlina)
LE, Elisa (FR) (adviser to WODLI, Jordane)
MALKIEWICZ, Katarzyna (SE) (expert to LUNDBERGH, Ivar)
MENDONÇA, Elsa (PT) (expert to ALMEIDA, Inês)
MICHEL, Cécile (FR) (expert to WODLI, Jordane)
RISSANEN, Eeva (FI) (adviser to LONDESBOROUGH, Susan)
SAKSA, Jana (EE) (expert to VESKIMÄE, Enda)
SCHULTZ, Thomas (DE) (adviser to FINDENEGG, Helene)
UNKELBACH, Christian (DE) (expert to FINDENEGG, Helene)
VAN HERWIJNEN (NL) (adviser to WIJMENGA, Jan)
ZELJEZIC, Davor (HR) (expert to KREKOVIĆ, Dubravka)

MSCA experts for SEv cases:
BOUWMAN, Tialda (NL)
CATONE, Tiziana (IT)
GORREBEECK, Carine (BE)

MSCA experts for SVHC cases:
HENRIKSSON, Jörgen (SE)
PASQUIER, Elodie (FR)

Advisers to the regular observers:
BEYER, Dieter (Bayer AG) (adviser to ANNYS, Ewin)
MARTIN, Olwenn (Brunel University London) (adviser to BERNARD, Alice)

By WEBEX/phone connection:
During the agenda item 8 on BPA: Claire BEAUSOLEIL (FR), Christine BJØRGE (NO),Anna Federica CASTOLDI (EFSA), Michel FRANZ (FR), Margareta HALIN LEJONKLOU (SE), Georges KASS (EFSA), Birgitte LINDEMAN (NO), Claudio PUTZU (EFSA) and Christophe ROUSSELLE (FR)
During the agenda item 6 on SEV-BE-003/2015: Laura McCABE (UK) and Catherine MEYS (BE)
During the agenda item 6 on SEV-IT-024/2015 and SEV-IT-026/2015: Gabriele AQUILINA (IT) and Maria Teresa RUSSO (IT)
During the whole meeting from DG GROW: Valentina BERTATO, Ana Maria BLASS RICO, Anna BORRAS HERRERO, Enrique GARCÍA JOHN and Georg STRECK

Case owners:
Representatives of the Registrants were attending under the agenda item 6b for SEV-BE-003/2015, SEV-NL-029/2015, SEV-IT-024/2015 and SEV-IT-026/2015; under the agenda item 7b for CCH-020/2017.

Apologies:
BORG, Ingrid (MT)
DEIM, Szilvia (HU)
FRANZ, Michel (FR)
KOUTSODIMOU, Aglaia (EL)
PISTOLESE, Pietro (IT)
WAGENER, Alex (LU)

MSC/A/054/2017

Agenda

54th meeting of the Member State Committee

12-16 June 2017
ECHA Conference Centre
Annankatu 18, in Helsinki, Finland

12 June: starts at 9 am
16 June: ends at 1 pm

Item 1 – Welcome and Apologies

Item 2 – Adoption of the Agenda

MSC/A/054/2017
For adoption

Item 3 – Declarations of conflicts of interest to items on the Agenda

Item 4 – Administrative issues

- Outlook for MSC-55 to MSC-57

For information

Item 5 – Minutes of the MSC-53

- Draft minutes of MSC-53

MSC/M/53/2017
For adoption

Item 6 – Substance evaluation - Decision making process

Timing: Day 1 - Day 2 for item 6b
Closed session for 6c

a. Written procedure report on seeking agreement on a draft decision on substance evaluation

ECHA/MSC-54/2017/001
For information

b. Introduction to and preliminary discussion on a draft decision on substance evaluation after MS-CA's/ECHA reactions *(Session 1, open session)*:

ECHA/MSC-54/2017/002
For information

For discussion followed by agreement seeking under 6c:

MSC code	Substance name	EC No./Document n:o
SEV-BE-003/2015	1,2,4-triazole	206-022-9 ECHA/MSC-54/2017/005-006
SEV-IT-024/2015	Hexafluoropropene	204-127-4 ECHA/MSC-54/2017/007-008
SEV-IT-026/2015	Di-tert-pentyl peroxide	234-042-8 ECHA/MSC-54/2017/009-010
SEV-NL-029/2015	Tetrapropylenebenzene (benzene, mono-C11-C13-branched alkyl derivatives)	810-801-4 (previously 246-772-4) ECHA/MSC-54/2017/011-012

For discussion

c. Seeking agreement on a draft decision when amendments were proposed by MS-CA's/ECHA *(Session 2, closed)*

Cases as listed above under 6b

For agreement

Item 7 – Dossier evaluation
Timing: Day 3 (pm) - Day 4 for item 7b
Closed session for 7c

a. Written procedure report on seeking agreement on draft decisions on dossier evaluation

ECHA/MSC-54/2017/003
For information

b. Introduction to and preliminary discussion on draft decisions on compliance checks and testing proposals when amendments were proposed by MS-CA's *(Session 1, open session)*

ECHA/MSC-54/2017/004
For information

For discussion followed by agreement seeking under 7c:

Compliance checks

MSC code	Substance name	EC No./Document No.
CCH-020/2017	Butyl glycollate	230-991-7 ECHA/MSC-54/2017/013-014
CCH-021/2017	Acrylic acid, monoester with propane-1,2-diol	247-118-0 ECHA/MSC-54/2017/024-025
CCH-034/2017	Terpineol	232-268-1 ECHA/MSC-54/2017/015-016

c. Seeking agreement on draft decisions on compliance checks and testing proposal examinations when amendments were proposed by MS-CA's *(Session 2, closed)*

Cases as listed above under 7b

For agreement

Item 8 – SVHC identification - Seeking agreement on Annex XV proposals

Start of item 8 BPA is Day 1 (am) and PFHxS is Day 3 (pm)

a. Seeking agreement on Annex XV proposals for identification of SVHC

Substance name	EC No.	Document No.
4,4'-isopropylidenediphenol (bisphenol A, BPA)	201-245-8	ECHA/MSC-54/2017/017-019
Perfluorohexane-1-sulphonic acid and its salts (PFHxS)	-	ECHA/MSC-54/2017/020-022

For discussion and agreement

b. Proposal for an update of MSC Working procedures for SVHC identification

ECHA/MSC-54/2017/023

For discussion and possible adoption

Item 9 – Any other business

- Update on appeals and court cases (*partly closed session*)

For information

- Brief report from an *ad-hoc* scoping group meeting on UVCBs

For information

- Suggestions from members

For information

Item 10 – Adoption of main conclusions and action points

- Table with conclusions and action points from MSC-54

For adoption

Information documents

Information documents are not allocated a specific agenda time but the documents are available on MSC CIRCABC before the meeting. Based on the listed documents and the meeting agenda, if any MSC member considers that information documents may merit a discussion under any agenda point, they should inform MSC Secretariat

- Status report on on-going substance evaluation work (presentation slides)
- Preannouncement of substance evaluation workshop (ECHA/MSC/I/2017/014)
- Status report on on-going dossier evaluation work (presentation slides)

Main conclusions and action points
MSC-54, 12-16 June 2017
(adopted at MSC-54)

CONCLUSIONS / DECISIONS / MINORITY OPINIONS	ACTIONS REQUESTED
Item 4 – Administrative issues • Outlook for MSC-55 • Outlook for MSC-57	
MSC took note of the plans and requested for even distribution/ well-coordinated planning of evaluation and SVHC cases with MSCAs. MSC also requested from ECHA's side improved planning in particular for any CA consultations.	MSC Chairman to organise a round of phone discussions with members during summer to collect feedback.
Item 5 – Minutes of the MSC-53	
MSC adopted the draft minutes as modified at the meeting.	MSC-S to upload final version of the minutes on MSC S-CIRCABC by 19 June 2017 and on ECHA website without undue delay.
Item 6 - Substance evaluation - Decision making process a. Written procedure report on seeking agreement on a draft decision on substance evaluation	
MSC took note of the written procedure report.	MSC-S to upload on MSC S-CIRCABC the final ECHA decision agreed in written procedure.
c. Seeking agreement on draft decisions when amendments were proposed by MS-CA's/ECHA *(Session 2, closed)*	
MSC reached unanimous agreement on the following ECHA draft decisions as modified in the meeting: SEV-BE-003/2015 1,2,4-triazole (EC number 206-022-9) SEV-IT-024/2015 Hexafluoropropene (EC number 204-127-4) SEV-IT-026/2015 Di-tert-pentyl peroxide (EC number 234-042-8) SEV-NL-029/2015 Tetrapropylenebenzene (benzene, mono-C11-C13-branched alkyl derivatives) (EC number 810-801-4, previously 246-772-4)	MSC-S to upload on MSC S-CIRCABC the final ECHA decisions of the agreed cases. Those MSC members who made statements (with their SEV-BE-003/2015 and SEV-NL-029/2015 votes) and requested for their attachment to the minutes, to provide these statements in writing to the MSC-S by 19 June 2017.
Item 7 – Dossier evaluation a. Written procedure report on seeking agreement on draft decisions on dossier evaluation	
MSC took note of the report.	MSC-S to upload on MSC S-CIRCABC the final ECHA decisions agreed in written procedure.
Item 7 – Dossier evaluation b. Introduction to and preliminary discussion on draft decisions on testing proposals and compliance checks after MS-CA reactions *(Session 1, open session)* c. Seeking agreement on draft decisions on a testing proposal examination and a compliance check when amendments were proposed by MS-CA's (Session 2, closed)	
MSC reached unanimous agreement on the following ECHA draft	MSC-S to upload on MSC S-CIRCABC the

CONCLUSIONS / DECISIONS / MINORITY OPINIONS	ACTIONS REQUESTED
decisions (as modified in the meeting): <u>Compliance checks</u> CCH-020/2017 Butyl glycollate (EC number 230-991-7) CCH-021/2017 Acrylic acid, monoester with propane-1,2-diol (EC number 247-118-0) CCH-034/2017 Terpineol (EC number 232-268-1)	final ECHA decisions of the agreed cases.
Item 8 – SVHC identification - Seeking agreement on Annex XV proposals a. Seeking agreement on Annex XV proposals for identification of SVHC	
MSC reached unanimous agreement on the following Annex XV proposals (as modified in the meeting): • 4,4'-isopropylidenediphenol (bisphenol A, BPA) (EC No. 201-245-8) • Perfluorohexane-1-sulphonic acid and its salts (PFHxS)	SECR to add the newly identified SVHCs to the Candidate List. MSC-S to upload the agreements and support documents, as well as the RCOMs, on MSC S-CIRCABC and to publish them on the ECHA website. Those MSC members who made statements (with their BPA votes) and requested for their attachment to the minutes to provide these statements in writing to the MSC-S by 16 June 2017.
b. Proposal for an update of MSC Working procedures for SVHC identification	
MSC agreed with the Secretariat's proposal for an update of the MSC Working procedure for identification of substances of very high concern.	MSC-S to upload the updated MSC working procedure to MSC S-CIRCABC and ECHA website after the meeting.
Item 9 – Any other business • Brief report from an ad-hoc scoping group meeting on UVCBs • Suggestions from members – FISH/CREST staining requests in MN testing	
UVCB *ad hoc* scoping group informed MSC of the topics discussed in the meeting that took place on 26th of April and introduced the agreed next steps. FISH/CREST staining requests in MN testing.	MSC-S to circulate the minutes to MSC once agreed by the scoping group. The Chairman to request a view from ECHA mutagenicity experts on possible follow-up steps in REACH when exclusively an aneugenic mechanism has been established, and report back to MSC for further discussion.
Item 10 – Adoption of main conclusions and action points	
MSC adopted the main conclusions and action points of MSC-54 at the meeting.	MSC-S to upload the main conclusions and action points on MSC S-CIRCABC by 16 June 2017.

V. Substance evaluation cases agreed by MSC in written procedure (WP) in advance of the meeting:

MSC ID number	Substance name used in draft decision	EC/List number
SEV-NL-028/2015	[1,3(or 1,4)-phenylenebis(1-methylethylidene)]bis[tert-butyl] peroxide	246-678-3

VI. Dossier evaluation cases agreed by MSC in WP in advance of the meeting:

Compliance checks (CCH)

MSC ID number	Substance name used in draft decision	EC or List number
CCH-024/2017	Diethyl ether	200-467-2
CCH-025/2017	Disodium 4,4'-bis[(4,6-dianilino-1,3,5-triazin-2-yl)amino]stilbene-2,2'-disulphonate	205-117-2
CCH-026/2017	Perfluamine	206-420-2
CCH-027/2017	1-phenylethanol	202-707-1
CCH-031/2017	2,4,6-triisopropyl-m-phenylene diisocyanate	218-485-4
CCH-032/2017	1,1'-(methylenedi-p-phenylene)bismaleimide	237-163-4
CCH-033/2017	1,1,3,3-tetramethylbutyl 2-ethylperoxyhexanoate	244-894-2
CCH-035/2017	Reaction products of ethylene glycol, urea and paraformaldehyde	700-934-5
CCH-040/2017	1,3-propanediol, 2-ethyl-2-(hydroxymethyl)-, polymer with (chloromethyl)oxirane	608-489-8

Testing proposal examinations (TPE)

MSC ID number	Substance name used in draft decision	EC or List number
TPE-010/2017	1,1,3,3-tetramethylbutyl 2-ethylperoxyhexanoate	244-894-2
TPE-011/2017	Phosphoric acid, mixed esters with Bu alc. and ethylene glycol	284-716-0
TPE-012/2017	Reaction mass of methyl dihydrogen phosphate and orthophosphoric acid and dimethyl hydrogen phosphate	908-996-7

VII. Statements of MSC members on SEv decisions

Statement of member from FR regarding SEV-BE-003/2015

The MSC member from France abstained from voting regarding SEV-BE, because of the deletion of one of the registrant for the reason he has registered the substance as a “Transport Isolated Intermediate” (TII).

One of the concern was that the registrant changed his type of registration from a full registration to a TII registration while the procedure of substance evaluation was already going on. Moreover, this registrant claimed to ECHA that there was now no exposure with the use as TII. Finally, ECHA has published its views regarding TII registration, considering that they have to be excluded if there is now no exposure.

First, FR-MSCA does not agree with ECHA’s view which was neither agreed or discussed as a general issue before in MSC, CARACAL or with the Commission. Indeed REACH Regulation excludes “On-Site Isolated Intermediate” and not TII of the Title VI on Evaluation of the REACH Regulation. This is why FR-MSCA considers that this question has to be brought to CARACAL in order to harmonize the case of TII in the evaluation procedure.

Secondly, the change of type of registration by the registrant during the process of evaluation is also questionable. For FR-MSCA, this registrant didn’t provide enough proof during the discussion on the Draft Decision (DD) or during the MSC meeting that its fulfill the “Strictly Controlled Conditions” (SCC) for use as TII. FR-MSCA recognizes that MSC doesn’t have the responsibility to verify the condition neither to launch enforcement. But in the opinion of FR-MSCA, the default position should have been to include the registrant in the addresses of the decision, in the absence of evidence.

Finally, the respect of SCC conditions is also a matter of enforcement. FR-MSCA strongly encourages ECHA to work on a procedure between MSC, FORUM and NEA (National Enforcement Authorities), in order to provide sufficient elements (such as letter stated that there is no exposure in this case) to NEA to verify the allegation on site.

Statement of MSC member from UK regarding SEV-NL-029/2015

The UK member abstained from the vote on SEV–NL-029/2015 due to concerns over the parallel testing strategy proposed for P and B testing. This is different to the sequential approach in the REACH guidance, and whilst we appreciate the arguments made for this specific case, we remain of the view that the primary focus of this evaluation should be the PBT assessment in the first instance. One of the drivers for this parallel testing was the time needed to conclude however we think the test deadline in this case would be unaffected by performing P and B testing sequentially. We think this is particularly important where two vertebrate bioaccumulation tests are potentially being sought.

VIII. Statement of MSC members from FI and UK regarding the SVHC identification of 4,4'-isopropylidenediphenol (bisphenol A) as a SVHC substance with endocrine disrupting properties to human health

The members of the MSC for FI and UK support the identification of BPA in accordance with Article 57(f) based on effects on the reproductive function that are linked to an ED MoA. The effects on reproductive function induced by BPA in relation to its ED MoA are considered serious adverse effects for human health. The identification is further supported by data showing effects on the mammary gland development, cognitive function and metabolism through pathways that are linked to ED MoA. However, there are considerable uncertainties regarding both the relevance of these effects to human health and the connection between the observed effects and the proposed possible serious effects on human health (i.e. breast cancer, neurobehavioural disorders and diabetes). Therefore, the current evidence is considered insufficient to conclude whether these effects have probable serious impact on human health that could give rise to an equivalent level of concern to those of other substances listed in paragraphs (a) to (e) of Article 57 and should be used only as supporting information. As this was not reflected in the Support Document, the members of the MSC for FI and UK decided to abstain from voting.