MSC/M/50/2016
Adopted in MSC-51

Minutes
of the 50th Meeting of the Member State Committee (MSC-50)
25-27 October 2016

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 50th meeting of the Member State Committee (MSC) (for the full list of attendees and further details see Part II of the minutes).

The Executive Director of ECHA Mr Geert Dancet addressed the MSC members on the occasion of its 50th meeting.

Item 2 - Adoption of the Agenda

The Agenda was adopted as modified by the MSC Secretariat with addition of an item to the any other business (Item 10, AOB) on ECHA's preparations for a report on regulatory applicability of alternative and non-animal approaches and based on a request from a member for another addition to the AOB on the report on EOGRTS published on ECHA website (final Agenda is attached to these minutes).

The Chairman provided a status update on action points of the MSC-49 meeting regarding the Accredited Stakeholder review informing MSC that the teleconference with the Animal Welfare NGO representatives was held and a letter was received from NGOs covering part of the requested issues. This letter was distributed to the MSC for information. Other Accredited Stakeholder review related action points had been accomplished in due time as well.

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

One member declared a potential conflict of interest in respect to specific agenda items. Details of the declared potential conflicts and the mitigating measures are attached to these minutes as Section IV. No other potential conflicts of interests were declared by any other members, experts or advisers with any other item on the agenda of MSC-50.

Item 4 - Administrative issues

- **Outlook for MSC-51**

The Chairman presented an outlook on the potential length of the next meeting which is expected to require five plenary days. The Chairman also indicated that there will be a need for additional preparatory meetings due to the high number of dossier evaluation, substance evaluation and SVHC cases. The Chairman also presented an early stage estimation for the MSC-52 meeting in February which is expected to last five days.

- **Refresher on ethics and integrity rules**

The item was postponed to MSC-51 meeting.

Item 5 – Adoption of the minutes of the MSC-49 meeting

The minutes of MSC-49 were adopted as provided for the meeting.

Item 6 – Substance evaluation

1. Community Rolling Action Plan (CoRAP) & MSC opinion development

- **Introduction of the annual draft CoRAP update by ECHA**

SECR presented the draft CoRAP update for 2017-2019. As per previous years, each substance has an accompanying justification document. The draft CoRAP including the initial grounds for concern and contact details of the evaluating Member State Competent Authorities (eMSCA) was to be published on the ECHA's website during the MSC meeting week i.e. on 28 October. Substances on the CoRAP list were identified through the ECHA's common screening activities ACROSS, through IT pre-selection and then through manual screening performed by MSCAs. The draft CoRAP update for years 2017-2019 has a total of 112 substance, 21 new and 95 already included in the 2016-2018 CoRAP update – 23 substances for 2017, 49 substances for 2018 and 44 substances for 2019. The starting year for evaluation has been changed (postponed) for 53 substances mainly due to

ongoing compliance check of the substances. During the discussion it was explained that it is preferred that these substances remain in the CoRAP until the outcome of the compliance check is known. This might even lead to removal of the concern, and reducing the suitability of the substance as a good candidate for CoRAP.

The Rapporteur and working group already started reviewing the draft CoRAP update aiming to submit a first draft opinion to MSC for MSC-51 meeting in December.

2. Decision making process

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

SECR introduced the report on the outcome of the written procedure (WP) for agreement seeking on one substance evaluation case with one draft decision (DD) (see Section VI for more case-identifier information). WP was launched on 29 September 2016 and closed on 10 October 2016. By the closing date, unanimous agreement was reached.

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

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

SEV-FR-024/2014 Tert-butyl methyl ether (EC No. 216-653-1)

Session 1 (open)

One representative 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 France (FR-CA) presented the outcome of substance evaluation (SEv) of the above-mentioned substance (MTBE) which was performed by the FR-CA on the basis of the initial grounds for concern relating to human health/potential endocrine disruptor, exposure/wide dispersive use and aggregated tonnage.

The DD consulted with the Member State Competent Authorities (MSCAs) and ECHA had five requests for information. Proposals for Amendments (PfAs) were received on all five requests. One of the five requests for information received only an editorial PfA which the evaluating MSCA accepted hence this request was not discussed at the meeting.

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 transgenic rodent somatic and germ cell gene mutation assays (TGR) (test method OECD 488) (via inhalation route with sampling of liver, kidney, nasal tissue, Leydig cells and lymph node), PfAs were submitted suggesting for specification of the requests and for improvement of the reasoning, e.g. since testing on germ cells was conditional and not optional, the collection of these cells should be obligatory; the need to add considerations on how the requested information may improve the risk management; and clarification of the need to request for TGR.

Regarding the request for fish sexual development test (FSDT) (test method: OECD 234) PfAs suggested addition of considerations on how the requested information may improve the risk management and to delete the option to use stickleback as a test species, since this species has a low sensitivity for induction of a sex ratio change. Furthermore, a PfA to request for an extended one generation fish study according to OECD 240 with zebrafish instead of an FSDT was also submitted, since the latter does not cover the reproductive life stage of the fish, hence risking that not enough information on the Mode of Action (MOA) and adversity of MTBE is generated.

With regards to the request for simulation biodegradation test of MTBE in surface water under aerobic conditions (OECD 309) with surface water and sediment originating from a historically non contaminated site, it was proposed to either delete the request (questioning whether it is needed to refine the environmental risk assessment and to

identify potential degradation products) or else to provide additional justification on the concern, the likely risk management measure, further specifications on the test design in Section II, a better reflection of the Registrants' comments on the volatility of the substance, and also to increase the deadline.

The PfA on the request for clarification and detailed justification for each environmental exposure scenario proposed to clarify the potential risks that need to be clarified over and above what was identified in RAR (2002).

The Registrants provided written comments on the PfAs and the draft decision. In general, the Registrants seem to have put a different weight on the carcinogenicity and endocrine disruption related studies from ECHA when analysing them in a weight of evidence approach. This was reflected in their written and verbal comments on the PfAs for both the TGR request as well as on the request for FSDT. The Registrants did not agree with both requests, however, no PfAs had been received that suggested to delete those requests.

With regards to the request to assess in the TGR Leydig cells and lymph nodes, the Registrants provided written comments against the technical feasibility in using such cells/tissues. CROs (n=3) contacted had no experience with this cell type which implied a validation program would have to be run which would require much more than the deadline in the DD of 18 months. During the meeting, the Registrants' representative explained that this request hinges on two non-guideline *in vivo* common assays. In the view of the Registrants' representative, these should not be considered for risk assessment. He explained that it is not clear in DD what is being requested and the reasons for the concerns. He reiterated their view that the substance is not a mutagen hence it is not likely to be shown to be mutagenic in a TGR assay in any tissue or cell type. The Registrants' representative requested to further define the concerns, the study design and the species to address the concerns. The expert from the eMSCA explained again that they regarded the TGR as necessary to conclude on the potential mutagenicity and to analyse the relevance of the tumours described in the carcinogenicity database.

In his intervention at the meeting, the Registrants' representative reiterated the written comment that the OECD 309 will not bring any additional information to be used for risk assessment hence also agreed with the PfA to delete this request.

As for the request for clarification and detailed justification for each environmental exposure scenario, the Registrants referred to a 2015 CSR update and asked to inform them of the additional changes that need to be made if the information in the update is not enough.

The expert from the evaluating MSCA explained at the MSC meeting that following the Registrants' written comments on the PfAs they agreed to remove the request to isolate and test Leydig cells during TGR assay. She explained that there was no specific scientific justification in this case why Leydig cells would be more sensitive than others to genotoxicity. However, it should be noted that in the contrary to what claimed by registrant, this would be technically feasible if using other technics than LCM, gradient for example. Further, regarding lymphatic tissue the Registrant was given the option to choose between lymph node and bone marrow.

Regarding FSDT eMSCA agreed with the PfAs not to provide the option for testing on stickleback and not to request for OECD 309. Linked to the latter, the expert from the evaluating MSCA suggested specifying in the request for clarification and detailed justification for each environmental exposure scenario, the need to perform the environmental exposure assessment with the assumption of no degradation of the substance. The representative of the Registrants had no comments to the latter suggestion by the evaluating MSCA when the Chairman specifically asked for their views.

The MSC member of the PfA submitting Member State which requested to replace FSDT with OECD 240 explained that they agree with the justifications given by the evaluating MSCA for performing the FSDT in this specific case, and hence did not pursue further their PfA.

A discussion on the test concentrations took place in the context of vitellogenin induction in medaka or zebrafish when performing FSDT. For aquatic toxicity, effects that occur in

concentrations higher than 1 mg/L are not taken into consideration for chronic classification, and hence it was suggested not to use a concentration of 10 mg/L. However, it was recognised that establishing an upper limit for testing in relation to endocrine disruption was not discussed before and beyond the scope of the submitted PfAs, hence it was agreed to proceed with requesting also the test concentration of 10 mg/L.

Session 2 (closed)

During the closed session MSC requested clarification of whether the CSR updates from 2015 and 2016 were evaluated by the MSCA. It was explained that a targeted evaluation of the updates was carried out and the eMSCA considered that the adequacy between the described use and the applied SPERC are still missing. Therefore, ECHA cannot perform an exposure and risk assessment for the environment even when considering the last version of the registration dossier. As a consequence, clarification and justification for each environmental exposure scenario are still needed. Clarification was also sought regarding the biodegradation criteria used in the environmental risk assessment. The eMSCA explained that they did not consider the available data supported the registrant's assumption of "inherently degradable not meeting criteria".

With regards to sampling of germ cells, it was recognised that testing on germ cells is conditional to any of the other tissues giving a positive result. However since the germ cells would have to be gathered at the same time as the other tissues, these cells would not yet have completed the full spermatogenic cycle. Therefore it was suggested to give the Registrants the option to include an additional sampling time after the end of the treatment on a voluntary basis, in order to accurately evaluate the effect of the treatment on those cells that were spermatogonial stem cells during the exposure period.

In conclusion, MSC agreed unanimously to keep the requests for 1) TGR (test method OECD 488) via inhalation route performed on liver, kidney, nasal tissue, lymphatic tissue (lymph node or bone marrow) and germ cells (with the option of an additional sampling time as explained above).
2) risk assessment of general population following indirect exposure of MTBE;
3) clarification and detailed justification for each environmental exposure scenario following the consideration by the evaluating MSCA of the relevant elements of dossier updates submitted in 2015 and 2016. MSC agreed to request the environmental exposure assessment to be performed with the assumption of no degradation of the substance in the environment compartment;
4) a FSDT (test method: OECD 234), deleting the option to use the stickleback as test species.

Furthermore, MSC agreed unanimously to remove the request for OECD 309.

d. General topics

- **Discussion on use of open and closed sessions in evaluation process (closed session)**

SECR presented the main points for MSC members' consideration and exchange of views based on the provided meeting documents and relevant legal and procedural documentation. MSC agreed that increasing the transparency to its evaluation work is an important issue. Further, members exchanged views on how this could be achieved, whether there is a need to change the relevant MSC procedural documents and/or the MSC established working practices in this regard and how this could be done.

Members concluded that the scientific discussions on DEV/SEv DDs should predominantly happen in open sessions (Session 1), while the DD text revision and the voting should remain in closed sessions. No need has been identified with regard to potential change in any of its SEv/DEv-related procedural documents, but only to adjust accordingly the current meeting practices.

In conclusion, MSC agreed to share with the MSC observers the meeting presentation and documents ECHA/MSC-50/2016/023-024 for their information.

- **Appeals update *(partly closed session)***

SECR gave an overview of the status of recent appeals on dossier and substance evaluation submitted to the Board of Appeal of ECHA (BoA). MSC took note of the information received. A brief update on new appeals was provided in a closed session to the members only.

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 twenty-two dossier evaluation cases (see Section VII for more detailed identification of the cases). WP was launched on 29 September 2016 and closed on 10 October 2016. By the closing date, unanimous agreement was reached on sixteen DDs[1]. One member abstained from voting on one case. For six DDs, MSC Chairman terminated the WP on the basis of Article 20.6 of the MSC Rules of Procedure.

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-066/2016 Turpentine oil (List No. 932-349-8)

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 explained that five PfAs to ECHA's DD were submitted. The first PfA on extended one-generation reproductive toxicity study (EOGRTS) suggested that the results from sub-chronic repeated dose toxicity study (90-day) results and any other relevant available information may lead to changes in study design.

The second and third PfA on EOGRTS requested the developmental neurotoxicity (DNT) cohorts 2A and 2B and developmental immunotoxicity (DIT) cohort 3, respectively. The PfAs considered there was scientific evidence on particular concerns, which justified the inclusion of these cohorts.

The fourth PfA on simulation test on ultimate degradation in surface water suggested some further text should be provided in the DD regarding the simulation testing in surface water (see reasons below on sediment simulation testing).

The fifth PfA on sediment simulation testing requested addition of some text referring to either PBT assessment or the results of risk assessment in order to clarify that the results of chemical safety assessment (CSA) indicated the need to investigate further the degradation of the substance and its degradation products. The PfA considered that the tests listed in Annex X, column 1 were only examples of tests that might be needed based on the results of CSA, and that further investigation on degradation should be requested in accordance with column 2 i.e. that the substance was not ready biodegradable and that the CSA indicated the need for testing (due to either risk for the environment or PB(T)-properties). As the registered substance was a UVCB, the PfA requested to elaborate whether it or its known or expected constituents should be used in the simulation test.

SECR modified the DD for the meeting based on the PfAs regarding EOGRTS-design (first PfA), simulation test on ultimate degradation in surface water and sediment simulation testing.

[1] See Section VI for details on case TPE-064/2016.

The Registrant provided written comments prior to the meeting and agreed with the first PfA on EOGRTS, on simulation test on ultimate degradation in surface water and on sediment simulation testing and disagreed with the second and third PfAs on *EOGRTS*.

The MSC expert representing the MSCA submitting PfA explained that several weak findings together should in combination be considered as strong enough to trigger DIT and DNT cohorts in the EOGRTS design. Although an individual MoA could not be identified, the overall weight of evidence was sufficient to support that multiple endocrine MoAs were likely and hence the cohorts should be included. Examples were presented of known endocrine disrupting chemicals where a blurred picture on *in vivo* effects were observed, too. Also, constituents of the substance have an endocrine disrupting MoA and, furthermore, they are shown to effect the immune system.

Several MSC members elaborated on the type of effects that would trigger DNT and DIT cohorts based on the studies on constituents of this UVCB substance.

SECR explained that recital 6 of REACH Regulation did not foresee DNT and DIT cohorts for most of the cases. Both legal text and guidance indicated that only severe and clear effects should be regarded as triggers. Therefore, weak and moderate triggers were not considered enough to trigger DIT and DNT cohorts in this case. SECR did agree that several weak lines of evidence taken together in principle could trigger these cohorts. It was also pointed out that the individual lines of evidence should meet a sufficient level of reliability, adequacy and relevance in order to be considered in a weight of evidence approach.

Session 2 (closed)

MSC did not conclude at the meeting whether the triggers for inclusion of DNT and DIT were met. A majority of MSC supported a proposal to await the 90-day study results before deciding on absence or presence of sufficient triggers for the DNT and DIT cohorts, since the 90-day study results may add further evidence.

MSC agreed unanimously the DD as amended during the meeting. Three members abstained from voting, which were the MSC members from the Netherlands, Denmark and Lithuania.

CCH-068/2016 N-[3-(dimethylamino)propyl]methacryl amide (EC No. 226-002-3)

Session 2 (closed)

SECR explained that agreement was initially sought in written procedure. The written procedure was terminated by the Chairman of MSC in accordance with MSC's Rules of Procedure Art 19(6).

A MSC member requested stopping the written procedure to allow a discussion on the PfA requesting for the EOGRTS an extension of the cohort 1B to produce a F2.

SECR had not modified the DD in advance of the written procedure based on this PfA.

The Registrant had provided written comments on the DD (not reflected here) and on the PfAs, disagreeing with this PfA.

The MSC member who requested for stopping the written procedure reiterated their consideration that both conditions were met to allow a request for the extension of Cohort 1B to produce the F2 generation. They included uses leading to significant exposure of professionals and indications for ED MoAs due to effects observed in endocrine sensitive reproductive organs (testis and epididymis) in an OECD TG 422 study.

A MSC member noted that some adverse effects were seen in a short-term screening study, while not visible in longer-term studies; and while EOGRTS was to be performed in any case, which will generate information on the F1 generation, there seemed no need for extending cohort 1B to produce the F2 generation. Some MSC members considered the results from long-term studies more reliable, and noted the possibility for the Registrant to continue EOGRTS with F2 extension if findings during the study would raise concern for it. Other MSC members considered that the REACH Annexes mention that the Agency may

require extension of Cohort 1B to produce the F2 generation when among others the condition is met that there are indications of one or more relevant MoAs related to endocrine disruption.

From the discussion it became clear no unanimous agreement on all information requirements could be reached, and thus MSC decided to split the DD in two decisions. MSC agreed unanimously on ECHA's split of the DD part B, as modified during the meeting with a change of the deadline for submission of the data due to the splitting of the DD.

MSC did not reach unanimous agreement on the DD addressing the extended one-generation reproductive toxicity study (part A), with one member voting against. Seven MSC members abstained from voting, including members from Belgium, Denmark, Greece, Lithuania, the Netherlands and Sweden. However, MSC agreed to modify the deadline due to the splitting of the DD. The Chairman invited the disagreeing MSC member to provide written justification for the disagreement (see Section VIII). SECR will refer the DD to the Commission, which will prepare a decision in accordance with the procedure of Article 133(3) of REACH.

CCH-070/2016 Diphenyl(2,4,6-trimethyl-benzoyl)phosphine oxide (EC No. 278-355-8)

Session 1 (open)

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

SECR explained that seven PfAs to ECHA's DD were submitted. Five PfAs were submitted on EOGRTS, one on simulation test on ultimate degradation in surface water and one on identification of degradation products.

Regarding EOGRTS one PfA requested an editorial modification and to refer to consumer and professional uses. A second PfA requested to improve the justification for production of F2 generation also referring to professional uses. Another PfA requested the inclusion of DNT cohorts 2A and 2B based on information for an ED MoA from repeated dose toxicity studies. Furthermore, two other PfAs requested inclusion of DNT cohorts 2A and 2B and DIT cohort 3 referring to (a) one or more endocrine disruptive (ED) mode(s) of action (MoA) and that the registered substance may act through androgenic or anti-estrogenic and anti-androgenic MoAs; (b) validation report of the OECD studies to update OECD TG 407; and specifically used the examples of findings for tamoxifen and prochloraz which are known endocrine disrupting chemicals where a blurred picture on *in vivo* effects are observed too. Additionally it is requested that if inclusion of DNT and/or DIT cohorts is not agreed by the MSC then to include internal triggers, and if the results from investigation of one or more of the internal triggers provide information on ED activity the Registrant(s) should include the relevant cohorts.

Regarding the PfA on simulation test on ultimate degradation in surface water (OECD TG 307) it is requested to substantiate more clearly why persistence in the aquatic environment should be investigated and why the substance is a potential PBT/vPvB substance, by reference to the results of a PBT assessment.

Regarding the PfA on identification of degradation products it was requested to further clarify in the DD why the column 2 requirements i.e. the "CSA indicates the need to investigate further the degradation of the substance and its degradation products" are fulfilled, and combine this request with those for the simulation degradation testing.

The Registrant provided comments on the DD (not reflected here) and the PfAs regarding the inclusion of DNT and DIT cohorts, and agreed with SECR that these are not triggered at present. He highlighted that there is no structural relation between prochloraz and the registered substance, and there is no evidence linking hypothetical endocrine disruption properties of the registered substance to developmental toxicity

Furthermore the Registrant's representative detailed the data from repeated dose studies which, in their view, can be sufficient for self-classification as a Reproductive toxicant Cat

1B, as atrophy of seminiferous tubuli with reduced spermatogenesis and oligospermie in the epididymis grade 4 up to azoospermia was present in all evaluated animals in two 90-day studies.

The Registrant's representative did not provide specific comments on the PfAs regarding simulation test on ultimate degradation in surface water and on identification of degradation products.

The MSC member of the PfA submitting country of these PfAs appreciated SECR responses to those PfAs and the amended DD text.

Regarding the PfAs on EOGRTS an MSC member of the PfA submitting country clarified the fact that tamoxifen and prochloraz were named not for read-across, but only as examples of substances that act through many different modes of endocrine action (prochloraz) or induce estrogenic effects in some tissues and anti-estrogenic effects in other tissues (tamoxifen), and thus give a blurred picture of *in vivo* effects. In analogy, the available repeated dose studies for the registered substance provide information on ED MoA, and is therefore adequate to trigger the inclusion of DIT/ DNT cohorts.

SECR had amended the DD before the meeting based on some of the PfAs, but did not include the request for DIT and DNT cohorts.

One MSC member considered that interpretation of the REACH annexes on inclusion of the DNT and DIT cohorts (e.g. "specific MoA with association to (developmental) neurotoxicity and/or developmental immunotoxicity") has to be done on case by case basis taking into account all relevant data in the dossier, but that this text was more stringent than in regards extension of Cohort 1B to produce the F2 generation (e.g. "there are indications of one or more relevant modes of action related to endocrine disruption"). This member supported ECHA not to include the DNT and DIT cohorts on the basis of the available data. Another MSC member questioned whether at this stage of the evaluation process a self-classification for Repr Cat 1B, can be applied as a waiver for the testing requested.

Registrant's representative responded that they intend to submit a harmonised classification proposal first, but the problems they encounter is that the evaluation process is ongoing.

Registrant's representative also highlighted the technical difficulties in conducting an EOGRTS with this substance. In particular .given the severe testicular toxicity observed in repeated-dose studies they were not sure there would be sufficient pups to conduct the required investigations.

Session 2 (closed)

In response to the discussion on the interpretation of the REACH annexes, SECR referred to the paragraph in the guidance where it is specified that standard information requirements are limited to the basic configuration of the EOGRTS and that available information has to show a particular concern for the inclusion to be clearly justified. In some evaluation DDs SECR considered these triggers are met but not in most of the cases. ECHA and COM views are that the triggering of the supplementary cohorts in all or most cases will go beyond the intention of the legislator.

MSC noted that it appeared that the harmonised classification in place (currently Repro Cat 2) was in essence based on the same data as the Registrant(s) took into consideration. MSC agreed that the intention of the Registrant(s) to apply for a revision of the harmonised classification would not obviate the need to request the study, also considering that associated risk management measures have already to be in place

The MSC members also discussed in detail the scientific arguments for inclusion of DIT/DNT cohorts, the specificity of the effects for the registered substance, the advantages of inclusion of DIT/DNT cohorts. Due to significant practical limitations associated with

internal triggering the EU had decided in general not to follow such an approach when requesting the EOGRTS. However, due to the case-specific circumstance MSC could support the inclusion of considerations on internal triggering for DIT and DIT in the decision.

Based on the above considerations MSC agreed unanimously the DD as amended during the meeting. Four members abstained from voting, which were the members from the United Kingdom, the Netherlands, Germany and Belgium.

CCH-071/2016 3,5-dimethylpyrazole (EC No. 200-657-5)

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 explained that one PfA to ECHA's DD was submitted on extended one-generation reproductive toxicity study (EOGRTS). It requested (a) F2 generation as the conditions were met (exposure of professionals, indications for endocrine disruptive (ED) modes of action (MoA)); and (b) to include DNT cohorts 2A and 2B due to non-impaired hearing combined with lack of a startling response.

SECR had modified the DD based on the first part of the PfA in advance of the meeting.

The Registrant had not provided comments on the PfAs.

One MSC member explained that the test results as reported indicated that the animals could hear, although they did not respond to auditory stimulus. As full details of the test were not available a possible explanation could be that the a set of fibres carrying reflex signals was not functioning, perhaps due to the test substance, while the other set of fibres carrying sounds was working normally. Several MSC members supported the request for DNT cohorts as the results were raising concern. Some members considered SECR could have requested from the Registrant the full study report in order to better assess the reported findings before inclusion of a request for the DNT-cohort.

Session 2 (closed)

MSC concluded that the test results with a failure to react to the auditory stimulus was a particular concern leading to the need to request DNT cohorts, whereas the Registrant still retained the possibility to more transparently describe the findings of the earlier study in the registration dossier

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

CCH-082/2016 Diethoxymethane (EC No. 207-330-6)

Session 2 (closed)

SECR explained that agreement was initially sought in written procedure. The written procedure was terminated by the Chairman of MSC in accordance with MSC's Rules of Procedure Art 19(6). A MSC member requested stopping the written procedure to discuss the PfA on exposure assessment requesting background information on the specific environmental release classes (SPERC) and their applicability for the exposure scenarios to determine whether the risk management measures (RMM) are adequate to control the risk. For a number of the exposure scenarios the SPERC-related emission factors (EF) were without further explanation on their derivation and their applicability for the process and the specific substance.

SECR had not modified the DD in advance of the written procedure based on this PfA.

The Registrant had provided written comments on the DD (not reflected here) and on the PfAs, agreeing with this PfA.

The MSC member who requested for stopping the written procedure reiterated their view that the registrant used a SPERC instead of the default emission rate without proper justification and considered such requests being within the scope of the compliance check.

He additionally referred to re-calculations indicating that the risk characterization ratios would rise significantly if default values were used.

SECR explained that the compliance check strategy as agreed with ECHA's Management Board and CARACAL concentrates on eight super-endpoints. Only in exceptional cases the Chemical Safety Report is assessed as there could be other more effective ways to address lacking information or justifications, including informal interactions with Registrants. Several MSC members noted that when exposure-based waiving of the hazard information is used by Registrants the CSR would need to be checked and inquired which approach would be most efficient and effective. A MSC member also raised concern that there is limited knowledge in countries on how SPERCs are developed and documented, and emphasized the crucial role of exposure in risk assessment.

In the discussion in the meeting, SECR confirmed it was committed to solve CSR-related issues by contacting the Registrant by telephone or informal letter, and if necessary, sending requests for available information based on Article (36) or further CCH decisions. It also drew attention to follow-up activities on a project on SPERCs which was finalised two years ago.

MSC agreed unanimously to the DD as circulated for the written procedure. One MSC member abstained from voting.

CCH-083/2016 1,1'-[methylenebis(oxy)]dibutane (EC No. 219-909-0)

Session 2 (closed)

SECR explained that agreement was initially sought in written procedure. The written procedure was terminated by the Chairman of MSC in accordance with MSC's Rules of Procedure Art 19(6).

The Chairman of MSC stopped this case as several information requirements in the DD were linked with those in CCH-082/2016 through a read across.

SECR explained that MSC would first have to agree on all aspects of CCH-082/2016 including possible discussions on PfAs where the read across was implied. Two PfAs had been received but not on aspects relating to exposure assessment or read across.

SECR had not modified the DD in advance of the meeting.

The Registrant had not provided any comments on the PfAs.

MSC concluded that no more discussion was necessary on this case following its agreement on the decision for CCH-082/2016.

MSC agreed unanimously to the DD as circulated for the written procedure.

CCH-089/2016 Bis(2-propylheptyl) phthalate (EC No. 258-469-4)

Session 1 (open)

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

SECR explained that one PfA to ECHA's DD was submitted to request long-term toxicity on fish since the substance is poorly water soluble and the short-term toxicity test for fish was not valid. The PfA considered the structural and physical-chemical properties of the registered substance (DPHP) similar to DEHP, which has been identified as SVHC and ED for the environment. Furthermore, it was argued that DPHP has indications for possible estrogenic and thyroid MoAs. Therefore, the PfA requested a fish sexual development test (FSDT; OECD TG 234) covering potential ED effects on aquatic organisms.

SECR agreed to the long-term toxicity data gap and had modified the DD for the meeting based on the PfA. It had included a request for a Fish Early Life Stage test (FELS; OECD TG 2010) as it did not support the arguments about potential ED properties of the registered substance.

The Registrant provided written comments and disagreed with both aspects of the PfA.

The representative of the Registrant explained that they consider OECD TG 203 study (short-term toxicity on fish) as a valid study with no effects up to 10 mg/l although the water solubility of the substance was below 0.1 µg/l. In their opinion there was no need for a long-term toxicity on fish study based on the results of the long-term toxicity to daphnia. Furthermore, he explained that their substance was structurally and toxicologically different from DEHP, and also considered that the thyroid effects observed with the registered substance were only secondary and not relevant for humans/mammals. Hence, they did not consider there was any need for long-term fish test targeting ED properties. The Registrant further elaborated that the substance had not been found in environmental samples, where the limit of detection (LOD) was 0.1 µ/l. Finally, the Registrant explained that they had contacted several test laboratories which had confirmed in writing there was no lab capacity available, and hence they would need more time (up to 26 months) to perform pre-natal developmental toxicity study (PNDT).

SECR explained that the test concentration applied in the fish short-term toxicity test was well above the water solubility limit, that the concentrations in the study were only nominal while the OECD TG 203 requires proof for the tested concentrations.

The MSC member of the PfA submitting country agreed with SECR response to the PfA.

Session 2 (closed)

MSC concluded to add the additional request for a long-term toxicity study on fish (OECD 210) and to extend the deadline from 18 months to 26 months due to the documented laboratory unavailability to perform the PNDT study.

MSC found unanimous agreement on ECHA's DD as amended at the meeting.

CCH-092/2016 3-isocyanatomethyl-3,5,5-tri-methylcyclohexyl isocyanate homopolymer, isocyanurate type (List No. 931-312-3)

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 explained that one PfA to ECHA's DD was submitted requesting sufficient and appropriate information on the chemical name and manufacturing process of the registered substance. This PfA was triggered by some remarks on these aspects in the read-across argumentation of the DD. However, SECR clarified that this text was a left-over from a request in the original DD send to the Registrant(s) to further clarify the chemical structure in section 1.2 of the dossier covering different isomers of the constituents. In their comments to the initial DD and a registration dossier update this issue had been sufficiently addressed.

SECR had modified the DD in advance of the meeting removing the left-over text from the DD, which the MSC member from the PfA submitting country considered sufficient to address the PfA.

The Registrant provided written comments on the PfA (and the DD not reflected here) prior to the meeting and disagreed with the PfA.

Session 2 (closed)

MSC concluded that no more discussion was necessary on this case as there were no open issues remaining from open session.

MSC found unanimous agreement on ECHA's DD as provided for the meeting.

TPE-046/2016 m-(2,3-epoxypropoxy)-N,N-bis(2,3-epoxypropyl)aniline (EC No. 275-662-9)

Session 1 (open)

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

SECR explained that six PfAs to ECHA's DD were submitted, the first four being on EOGRTS. The first PfA requested, firstly, amending text to use non-irritant and non-corrosive dose levels and to perform oral substance administration by feeding and not by gavage, i.e. "oral route, via the diet"; and secondly, including DIT cohort 3 based on effects noted in the 28-day study in rats. The second PfA requested (a) DNT cohorts 2A and 2B as there was information on one or more ED MoAs from a repeated-dose toxicity study; and (b) DIT cohort as there is information on blood-cell counts and effects on endocrine sensitive reproduction organs from a repeated-dose toxicity study, and the substance is self-classified as skin sensitiser. The third PfA requested text change to indicate that the substance is self-classified as Muta 2 and that the extension of cohort 1B (F2) must be included if the Registrant indicates the presence of exposure for consumers or professionals. The fourth PfA requested DNT and DIT cohorts 2A, 2B and 3 as there was information on one or more ED modes of action and on immunotoxicological effects from a 28-day study in rats.

The fifth PfA, on PNDT, requested to perform oral substance administration by feeding and not by gavage, i.e. "oral route, via the diet" and suggests amending text to clarify to use non-irritant and non-corrosive dose levels. The sixth PfA, on grouping of substances and read across approach, requested amending text to reflect that the absence of information on human health toxicity prevents accepting the proposed read across approach.

SECR had modified the DD based on the first part of the first PfA on EOGRTS and on the fifth PfA on PNDT in advance of the meeting.

MSC was satisfied with ECHA's response on the fifth and sixth PfA, whilst MSC discussed all other PfAs at the meeting.

The Registrant had provided comments on the DD (not reflected here) and on several PfAs. In his comments the Registrant disagreed with most PfAs, but agreed with the statement in the last PfA on lack of toxicity data. The representative of the Registrant further referred to new data available and supported pragmatic approach to testing to limit the use of animals.

Some MSC members reasoned that the pattern of effects seen in available repeated dose toxicity study indicate concern on ED MoAs, and that the effects on lymphatic tissues were to be considered primary response to the substance. Another member supported ECHA and argued that lymph node effects observed only in the vicinity of the gastrointestinal tract would be a direct impact of the gastrointestinal tract being eroded, and hence were to be considered secondary response to other toxic effects by the substance.

Session 2 (closed)

MSC concluded that lymphatic tissue effects seen in the available study may have been a secondary consequence of severe gastrointestinal irritation/corrosion. Thus evidence for triggering DNT and DIT cohorts may not be strong enough.

MSC agreed unanimously to the DD as provided for the meeting.

TPE-047/2016 Reaction mass of bis(2,3- epoxypropyl) terephthalate and tris(oxiranylmethyl) benzene-1,2,4-tricarboxylate (List No. 940-592-6)

Session 1 (open)

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

SECR explained that two PfAs to ECHA's DD were submitted, both on EOGRTS, suggesting to include a request for the DIT cohort 3, the justification being (a) one or more endocrine disruptive mode(s) of action of the substance; (b) expressing a particular concern for DIT (Skin Sens. 1). Additionally in one PfA reference was made to the validation report of the OECD studies to update OECD TG 407; and specifically used the examples of findings for tamoxifen and prochloraz which are known endocrine disrupting chemicals where a blurred picture on *in vivo* effects are observed too. Furthermore, this PfA requested that if MSC does not agree with inclusion of DIT cohort, it was proposed to include a note on internal

triggering. In the other PfA it was specified that tests on two parent substances of the reaction mass might substantiate the findings from the studies with the reaction mass.

SECR did not modify the DD in advance of the meeting based on the PfAs.

The Registrant provided written comments on the PfAs prior to the meeting disagreeing to include the DIT Cohort in the study as minor and isolated effects related to the endocrine system were seen as secondary response to stress, not due to inherent toxicity of the registered substance. In their view the tested substance produced necrotic effects and not endocrine disruption effects, and the sensitisation mechanism of the substance is related to protein alkylation by active cyclic agents.

The Registrant's representatives highlighted that there is no structural relation between prochloraz and the registered substance, and there is no evidence linking hypothetical endocrine disruption properties of the registered substance to developmental toxicity.

In addition the Registrant's representative detailed that inclusion of the DIT Cohort is also not supported as it is known that chemicals that have a molecular weight less than 500, and possess a cyclic structure without a hydroxyl or amino group are reported to be non-binders to the estrogen receptor. Furthermore he emphasized that the effects noted for each compound individually bis(2,3-epoxypropyl) terephthalate and tris(oxiranylmethyl) benzene- 1,2,4-tricarboxylate were observed at high dose levels and that both compounds separately were tested in a range of purity (80-90%) which is notably higher than their respective concentration in the reaction mass registered substance.

The expert to the Member of the PfA submitting country explained that their intention when they used tamoxifen and prochloraz was misunderstood as they used them not for read-across but as examples for nonspecific endocrine disruption effects.

Registrant representative further explained their interpretation of the results in relation to the necrotic effects and the reasons why those are not seen as having endocrine disruption mode(s) of action.

SECR repeated that indeed the testicular weight increase and reduced seminal vehicle can be related to ED, however they are a weak indication and do not lead them to conclude that the substance possesses ED properties.

Session 2 (closed)

SECR referred to the paragraph in the guidance where it is specified that standard information requirements are limited to the basic configuration of the EOGRTS and that available information has to show a particular concern for the inclusion to be clearly justified. In some evaluation DDs SECR considered these triggers are met but not in most of the cases. ECHA and COM views are that the triggering of the supplementary cohorts in all or most cases will go beyond the intention of the legislator.

MSC did not amend the draft decision as provided for the meeting.

The MSC members from the PfA submitting countries maintained that the effects observed were targeted on the reproductive organs and should not be ignored, and their policy is then to request inclusion of the DIT cohort 3. However since they did were not supported by MSC for this request they would prefer to abstain.

Based on the above considerations MSC agreed unanimously the DD as provided for the meeting. Four members including the members from Denmark, Lithuania and the Netherlands abstained from voting.

TPE-070/2016 Cashew (*Anacardium occidentale*) nutshell extract, decarboxylated, distilled (List No. 700-*991-6);*
***TPE-071/2016 Cashew (Anacardium* occidentale) nutshell extract, decarboxylated, distillation residue (List No. 941-212-1) and**
TPE-072/2016 Cashew (*Anacardium occidentale*) nutshell extract, decarboxylated (List No. 941-216-3)

Session 2 (closed)

SECR explained that agreement was initially sought in written procedure. The written procedure was terminated by the Chairman of MSC in accordance with MSC's Rules of Procedure Art 19(6).

A MSC member requested stopping the written procedure to further discuss the PfAs expressing a general concern how aquatic toxicity testing of UVCB's should be approached, and whether a long-term fish toxicity test using OECD TG 234 could be requested (as part of these TPEs) to address an ED concern for some of the constituents of the three registered UVCB substances.

SECR had not modified the DD's in advance of the written procedure based on these PfA's.

The Registrant had provided written comments on the DD (not reflected here) and on the PfAs, disagreeing with these PfA's.

SECR explained that when initiated this DD had used a, by now outdated, TPE policy line where first a daphnia test was requested and the integrated testing strategy (ITS) was indicated as an option. Application of the most recent TPE policy line would lead to an acknowledgement that there is a data gap for fish long-term toxicity, and to an inclusion of this endpoint into a TPE public consultation and the DD. Originally, the registrant had planned to test one substance to cover the information requirements for all three UVCB's, however, the read-across approach between these three substances had been rejected by SECR as not all the constituents of three different substances would have been covered. Therefore, testing few constituents from these UVCB's would contradict the read-across rejection since no information on the (absence of) toxicity of the other constituents was available. It was additionally noted that constituents of the substance are structurally similar to nonylphenol, which is a well-known environmental endocrine disruptor and thus these registered substances could have an endocrine disruption potential.

A MSC member raised a concern that while using a water accommodated fraction (WAF) method in aquatic toxicity testing of UVCBs may be appropriate for CLP purposes, it is not currently covered by guidance for risk assessment. Guidance does not address potential differences in fate and behaviour of the UVCB constituents and its impact on the PNEC derivation. The need for a general discussion and possible guidance update in this matter was supported by other MSC members as well.

Furthermore, it was argued by an MSC member that both fish early life stage (FELS, OECD TG 210) and fish sexual development test (FSDT, OECDTG 234) meet the information requirement for early life stage tests, Annex IX, Section 9.1.6.1. Hence, the latter test guideline, that would address the additional ED concern, could be requested. It was acknowledged that in standard cases the FELS test would be requested, but ECHA was invited to prepare for a MSC discussion in one of its next meetings and propose criteria when to request a FELS or FSDT test under dossier evaluation. The alternate possibility of a MSC working group on this matter was mentioned.

For the specific DDs, SECR proposed that an assessment of the need for further studies (i.e. on long-term toxicity to fish) could be taken up in the follow up process, e.g. after submission of the information on daphnia toxicity and the other information requirements, which include the bioaccumulation study. At that moment also the MSC discussion on the possibility for requesting an OECD TG 234 would take place. SECR explained further that the changes implemented in the DDs to flag the concern raised with testing with WAF are the same in all three DDs.

MSC unanimously agreed on all three DD's as amended at the meeting.

d. Decision making process general topics

- **Discussion on use of open and closed sessions in evaluation process (see under 6.2d)**

Covered under item 6.2d.

- **Appeals update (Partly closed session)**

See item 6.b.

Item 8 – ECHA's recommendations of priority substances to be included in Annex XIV

Setting Latest Application Dates (LADs) – Practical implementation

SECR shared with MSC a draft approach which could be used at practical level in setting latest application dates (LADs) when substances are recommended for inclusion in Annex XIV. The proposed methodology is aimed at increasing transparency of that process and how the time needed to prepare applications for authorisation (AfA) could be assessed. It was emphasised that the "General approach for preparation of draft Annex XIV entries" provides the generic basis for defining the Annex XIV entries and that the proposed new methodology concerns the practical implementation of one aspect of setting LADs. It does not take into consideration other aspects that are relevant when setting LADs, such as processing capacity by authorities or number and length of possible LAD slots in one recommendation round. Instead, it aims at assessing the time needed to prepare an AfA more transparently. Based on registration data (that can be further refined) it gives consideration to factors such as vertical and horizontal complexity of supply chain, number of sites and registration requirements. Each factor is given a score to facilitate easier comparison between substances and to give similar weight to the different factors. It was stressed that there are further factors that also influence the time needed to prepare an AfA (e.g. how sectors organise themselves, how experienced potential consortia are, etc.), however those are not considered in this methodology as they cannot be assessed at the time of recommending substances. SECR emphasised that the purpose of the system would be to provide a comparison of a limited number of substances with the aim to assign them to LAD slots in one recommendation round, and further aspects (described in the general approach) still would need to be considered in the slot assignment. Some examples were presented to exemplify the methodology and how it could be used.

To provide an insight into practical experiences, SECR also presented a summary of results from a survey among 112 AfA applicants carried out by ECHA on the time need to prepare an application. Main findings indicated that the time constraints faced were mainly related to how to organise in-house and external expertise and how to get information from the supply chain, as well as how to conclude on suitability and availability of alternatives.

Several members welcomed the proposed methodology among others due to its contribution to increased transparency. It was seen to provide an impartial way to the assessment work, and as such something that could shape future recommendations. As a further suggestion one member suggested using expert judgement on the top of the proposed scoring approach.

Responding to some questions SECR welcomed also any further ideas and indicated its openness to reconsideration, for example for grouping or cut-off to different scores but was hesitant to becoming overly detailed, noting that only a relative assessment is possible.

Many of the stakeholders welcomed the approach and took the opportunity to voice their initial views and provide some further suggestions. One of those was a consideration how and when best to try to get the type of information which is not available in the registrations but which would be used for setting the LADs. An observer from IND suggested to do it early on, e.g. during the year the substance is added on the Candidate List, or during the RMOA stage. He also commented on two new factors suggesting using also the number of countries as a factor for complexity of the supply chain, and secondly the use of process complexity did seem crucial in his view, not necessarily the supply chain complexity as such. In one of his comments he also questioned why recycling was not accounted for in the number of life-cycle stages for the vertical complexity. As regards the SMEs, he suggested that it is mainly an awareness issue.

Another observer from IND also highlighted the potential difficulties in gathering information, which is not in dossiers in a controllable way, and questioned during which public consultation that information gathering is expected to happen. He also reminded that continuously new companies become involved with authorisation applications, including downstream users, and they will need to start their learning process from

scratch. SECR in its response agreed that availability of uniform information is indeed a challenge, and that the aim of the approach is to find a system that applies even and equal treatment between different uses of substances.

The discussion was concluded with an invitation for some further contributions in writing following the meeting. Taking account of the comments, it is currently planned to try-out the proposed methodology for the 8th recommendation.

Item 9 – MSC Manual of decisions (MoD)

SECR presented a proposal for an entry for inclusion in the Manual of Decisions and Opinions (MoD). It comprised standardized text on targeted evaluation of the 90-day repeat dose toxicity study data for further informing on the design of the extended one-generation reproductive toxicity study (EOGRTS) in decisions, which contained requests for both studies and the study design was not yet fully expanded. The text was first presented and discussed at MSC-49. Thereafter it was modified based on a suggestion from an MSC member and ECHA. The proposal for MSC-50 also included some further minor (editorial) revisions. MSC agreed to include this entry in section 3.1.9 of the MoD, as revised at the meeting.

Item 10 – Any other business

- **Use of webforms in dossier evaluation**

An MSC member had in the previous meeting (MSC-49) asked for an explanation on how to improve the usability of the webforms in the dossier evaluation. The member explained that their MSCA faced several difficulties while submitting the PfA's via webform as it does not allow text editing or use of text formatting (e.g. boldface, overstrike).

SECR explained that they are aware of the difficulties. However, this issue would probably not be solved in the near future but would be taken into consideration in the later updates. SECR also informed of an ongoing ECHA project internally identified as Interact, which may provide further possibilities for an enhanced interface in the coming years.

- **Report on Regulatory Applicability of Alternative and Non-animal Approaches (ANAA)**

SECR presented a brief overview of the new ECHA's project for the development of the above report and clarified its aim, envisaged report content and project timelines.

A MSC member requested for clarifications about the purpose of the project, if this project is going to be used for updating or making a new guidance, and its relation to the existing guidance.

SECR explained that the document follows the adaptation rules from REACH, and weight of evidence (WoE) as stated in guidance document and it is for screening purpose. The aim of the project was to include consideration of alternative methods that can be used in testing in an easy to understand non-scientific way.

One stakeholder reflected the view that the project as presented shows clearly the promotion of non-animal testing.

One MSC member expressed his view on the necessity of updates of the guidance documents, and that this project could be a good start for this.

The Chairman of MSC announced that the ANAA report will be submitted for consultation and commenting to MSC members.

- **Suggestions from members**

One MSC member referred to a document published in September 2016 on ECHAs website relating to how ECHA identifies the design for the extended one-generation reproductive toxicity study (EOGRTS) under dossier evaluation, and asked for clarifications if it is meant to be a guidance document.

SECR explained that the document is a technical report and not a guidance document, published on ECHAs website for transparency reasons, clearly triggered from the need to

update stakeholders and to clarify how far ECHA goes in scanning the literature for the assessment of a substance. It was clarified that the document was commented upon by the advisory expert working group on EOGRTS in its draft form before publication.

The MSC member considered that the title of the document should clarify that it originates from the ECHA secretariat and not create potential confusion with guidance documents which go through a consultation round by all MSC members.

Item 11– Adoption of conclusions and action points

The conclusions and action points of the meeting were adopted in the meeting (see Section V).

II. List of attendees

Members/Alternate members
ALMEIDA, Inês (PT)
ANDRIJEWSKI, Michal (PL)
BORG, Ingrid (MT)
COCKSHOTT, Amanda (UK)
COSGRAVE, Majella (IE)
DEIM, Szilvia (HU)
DUNAUSKIENE, Lina (LT)
FINDENEGG, Helene (DE)
FRANZ, Michel (FR)
GYMNAOU, Panagiotis (CY)
HERMES, Joe (LU)
HUMAR-JURIC, Tatjana (SI)
KOUTSODIMOU, Aglaia (EL)
KREKOVIĆ, Dubravka Marija (HR)
KULHANKOVA, Pavlína(CZ)
LONDESBOROUGH, Susan (FI)
LUNDBERGH, Ivar (SE)
MARTÍN, Esther (ES)
MIHALCEA UDREA, Mariana (RO)
PISTOLESE, Pietro (IT)
REIERSON, Linda (NO)
STESSEL, Helmut (AT)
TYLE, Henrik (DK)
VANDERSTEEN, Kelly (BE)
VESKIMÄE, Enda (EE)
WIJMENGA, Jan (NL)
Representatives of the Commission
SCHUTTE, Katrin (DG ENV)
Observers
ANNYS, Erwin (Cefic)
DROHMANN, Dieter (ORO)
HYNES, Jarlath (HSI)
HÖK, Frida (ChemSec)
KERÄNEN, Hannu (CONCAWE)
REGO, Laura (ECEAE)
WAETERSCHOOT, Hugo (Eurometaux)

ECHA staff
AJAO, Charmaine
ANASTASI, Audrey Anne
BERCARU, Ofelia
BICHLMAIER, Ingo
BROERE, William
CALEY, Jane
CARLON, Claudio
CONSTANTIN, Camelia
DANCET, Geert
DE BACKER, Liisi
DE WOLF, Watze
DREVE, Simina
FEDTKE, Norbert
HALLING, Katrin
HOFFSTADT, Laurence
HUUSKONEN, Hannele
JAAGUS, Triin
JOHANSSON, Matti
KARHU, Elina
MÜLLER, Birgit
NICOT, Thierry
NAUR, Liina
RAHKONEN, Olli
ROBERTS, Julian
ROOVERS, Nicolai
RYAN, Paul
RÖCKE, Timo
RÖNTY, Kaisu
SCHOENING, Gabriele
SOBANSKA, Marta
TRNKA, Jan Peter
VAHTERISTO, Liisa
VASILEVA, Katya
VERSONNEN, Bram
VOM BROCKE, Jochen
WALKER, Lee

Proxies

- COSGRAVE, Majella (IE) also acting as proxy of DEIM, Szilvia (HU)
- KULHANKOVA; Pavlina (CZ) also acting as proxy of DIMCHEVA, Tsvetanka (BG)
- VESKIMÄE, Enda (EE) also acting as proxy of JANTONE, Anta (LV)
- ALMEIDA, Inês (PT) also acting as proxy of MARTIN, Esther (ES) in the late afternoon of 27 October
- GYMNAOU, Panagiotis (CY) also acting as proxy of KOUTSODIMOU, Aglaia (EL) on 25 October and in the morning of 26 October
- LONDESBOROUGH, Susan (FI) also acting as proxy of COCKSHOTT, Amanda (UK) in the late afternoon of 27 October
- TYLE, Henrik (DK) also acting as proxy of DUNAUSKIENE, Lina (LT) in the afternoon of 25 October and during short periods on 26 and 27 October
- VANDERSTEEN, Kelly (BE) also acting as proxy of COSGRAVE, Majella (IE) in the late afternoon of 27 October
- VANDERSTEEN, Kelly (BE) also acting as proxy of HEESCHE-WAGNER, Kerstin (DE) for the cases CCH-068/2016 and CCH-092/2016

- VANDERSTEEN, Kelly (BE) also acting as proxy of FINDENEGG, Leni (DE) for the case SEV-FR-024/2014

Experts and advisers to MSC members
ATTIAS, Leonello (IT) (expert to PISTOLESE, Pietro)
BUDASOVA, Jana (EE) (expert to VESKIMÄE, Enda)
COPOIU, Oana (RO) (expert to MIHALCEA UDREA, Mariana)
DE KNECHT, Joop (NL) (expert to WIJMENGA, Jan)
DOBRAK-VAN BERLO, Agnieszka (BE) (expert to VANDERSTEEN, Kelly)
GRACZYK, Anna (PL) (expert to ANDRIJEWSKI, Michal)
GRINCEVICIUTE, Otilija (LT) (expert to DUNAUSKIENE, Lina)
HOLMER, Marie Louise (DK) (expert to TYLE, Henrik)
INDANS, Ian (UK) (expert to COCKSHOTT, Amanda)
KOZMIKOVA, Jana (CZ) (expert to KULHANKOVA, Pavlina)
MALKIEWICZ, Katarzyna (PL) (expert to LUNDBERGH, Ivar)
NYGREEN, Beryl. C. (NO) (adviser to REIERSON, Linda)
NYITRAI, Viktor (HU) (expert to DEIM, Szilvia)
RISSANEN, Eeva (FI) (adviser to LONDESBOROUGH, Susan)
ROSENTHAL, Esther (DE) (expert to FINDENEGG, Helene)
ZELJEZIC, Davor (HR) (expert to KREKOVIĆ, Dubravka)

MSCA experts for SEV cases
MICHEL, Cécile (FR)

By WEBEX/phone connection:
During the agenda item 6: Ian DOYLE (UK), Pierre LECOQ (FR), Mandy LOKAJ (DE), Franziska WITTMANN (DE) and Kerstin HEESCHE-WAGNER (DE)
During the agenda item 7: Mandy LOKAJ (DE), Franziska WITTMANN (DE), Kerstin HEESCHE-WAGNER (DE)
During the agenda item 7 for CCH-066/2016, CCH-070/2016, CCH-071/2016, TPE-046/2016 and TPE-047/2016: Minne HERINGA (NL) and Marjolijn WOUTERSEN (NL)
During the whole meeting from DG GROW: Valentina BERTATO, Enrique GARCÍA-JOHN, Maila PUOLAMAA and Jacek ROZWADOWSKI

Case owners:
Representatives of the Registrants were attending under the agenda item 6b for SEV-FR-024/2014, under the agenda item 7b for CCH-070/2016, CCH-089/2016, TPE-046/2016 and TPE-047/2016,

Apologies:
DIMCHEVA, Tsvetanka (BG)
JANTONE, Anta (LV)
PALEOMILITOU, Maria (CY)
RUSNAK, Peter (SK)
WAGENER, Alex (LU)

III. Final Agenda

MSC/A/050/2016

Agenda
50th meeting
of the Member State Committee

25-27 October 2016
ECHA Conference Centre
Annankatu 18, in Helsinki, Finland

25 October: starts at 9 am
27 October: ends at 4 pm

Item 1 – Welcome and Apologies

- Opening address by Geert Dancet, Executive Director of ECHA

For information

Item 2 – Adoption of the Agenda

MSC/A/050/2016
For adoption

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

Item 4 – Administrative issues

- Outlook for MSC-51
- Refresher on ethics and integrity rules

ECHA/MSC-50/2016/027
For information

Item 5 – Minutes of the MSC-49

- Draft minutes of MSC-49

MSC/M/49/2016
For adoption

Item 6 – Substance evaluation

Tentative timing: Item 6.2b Day 1
Closed session for 6.2c

3. Community Rolling Action Plan (CoRAP) & MSC opinion development

- Introduction of the annual draft CoRAP update by ECHA

ECHA/MSC-50/2016/027
For information and discussion

4. Decision making process

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

ECHA/MSC-50/2016/001
For information

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

For discussion followed by agreement seeking under 6.2c:

ECHA/MSC-50/2016/022

MSC code	Substance name	EC number	Documents
SEV-FR-024/2014	Tert-butyl methyl ether	216-653-1	

ECHA/MSC-50/2016/002-003
For discussion

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

Cases as listed above under **6.2b**

For agreement

d. General topics

- Discussion on use of open and closed sessions in evaluation process *(closed session)*

ECHA/MSC-50/2016/023
For discussion
ECHA/MSC-50/2016/024
For information

- Appeals update[2]

For information

Item 7 – Dossier evaluation

Tentative timing: Item 7b Day 1-2
Closed session for 7c, partly closed session for 7d

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

ECHA/MSC-50/2016/004
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)*

[2] A combination of Appeal updates for Substance and Dossier Evaluation may be introduced, if appropriate.

For discussion followed by agreement seeking under 7c:

ECHA/MSC-50/2016/021

Compliance checks

MSC code	Substance name	EC No.	Document
CCH-066/2016	Turpentine oil	932-349-8	ECHA/MSC-50 /2016/007-008
CCH-070/2016	Diphenyl(2,4,6-trimethyl-benzoyl)phosphine oxide	278-355-8	/2016/009-010
CCH-071/2016	3,5-dimethylpyrazole	200-657-5	/2016/011-012
CCH-089/2016	Bis(2-propylheptyl) phthalate	258-469-4	/2016/013-014
CCH-092/2016	3-isocyanatomethyl-3,5,5-tri-methylcyclohexyl isocyanate homopolymer, isocyanurate type	931-312-3	/2016/015-016

Testing proposal examinations

MSC code	Substance name	EC No	Document
TPE-046/2016	m-(2,3-epoxypropoxy)-N,N-bis(2,3-epoxypropyl)aniline	275-662-9	ECHA/MSC-50 /2016/017-018
TPE-047/2016	Reaction mass of bis(2,3-epoxypropyl) terephthalate and tris(oxiranylmethyl) benzene-1,2,4-tricarboxylate	940-592-6	/2016/019-020

For discussion

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** and cases returned from written procedure for agreement seeking in the meeting[3]:

MSC code	Substance name	EC/List No
CCH-068/2016	N-[3-(dimethylamino)propyl]methacrylamide	226-002-3
CCH-082/2016	Diethoxymethane	207-330-6
CCH-083/2016	1,1'-[methylenebis(oxy)]dibutane	219-909-0
TPE-070/2016	Cashew (Anacardium occidentale) nutshell extract, decarboxylated, distilled	700-991-6
TPE-071/2016	Cashew (Anacardium occidentale) nutshell extract, decarboxylated, distillation residue	941-212-1
TPE-072/2016	Cashew (Anacardium occidentale) nutshell extract, decarboxylated	941-216-3

For agreement

d. Decision making process general topics

- Discussion on use of open and closed sessions in evaluation process *(see under 6.2d)*
- Appeals update[1] *(Partly closed session)*

For information

[3] Documents for stopped cases are available in substance specific folder in MSC S-CIRCABC under dossier evaluation.

Item 8 – ECHA's recommendations of priority substances to be included in Annex XIV

Setting Latest Application Dates (LADs) – Practical implementation

ECHA/MSC-50/2016/025-026

For information and discussion

Item 9 – MSC Manual of decisions (MoD)

- Suggestion for a possible new entry to the MoD

ECHA/MSC-50/2016/006

For discussion and decision

Item 10 – Any other business

- Use of webforms in dossier evaluation
- Suggestions from members

For information

Item 11 – Adoption of main conclusions and action points

- Table with conclusions and action points from MSC-50

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 dossier evaluation work (presentation slides)
- Status report on on-going substance evaluation work (presentation slides)
- Report from other ECHA bodies (ECHA/MSC/I/2016/028)

IV. The following participants declared potential conflicts of interest with the indicated agenda items (according to Art 9 (2) of MSC RoPs)

AP/Dossier	MSC Member	Reason for potential CoI/ mitigating measures
AP 6 b&c: SEV-FR-024/2014 AP 7 b&c: CCH-068/2016 CCH-092/2016	Helene Findenegg	Annual declaration as published on the ECHA website. No participation in the Committee's deliberation and voting.

V. Main Conclusions and Action Points

Main conclusions and action points
MSC-50, 25-27 October 2016
(adopted at MSC-50)

CONCLUSIONS / DECISIONS / MINORITY OPINIONS	ACTIONS REQUESTED
Item 4 – Administrative issues • Outlook for MSC-51 • Refresher on ethics and integrity rules	
Refresher on ethics and integrity rules was post-poned to MSC-51.	**MSC members** to ask their colleagues in the eMSCA to indicate the preferred webex for their SEv cases – 30 November or 7 December. **MSC-S** to put it in the agenda for MSC-51
Item 5 – Minutes of the MSC-49	
MSC adopted the draft minutes as provided for the meeting	**MSC-S** to upload final version of the minutes on MSC S-CIRCABC by 28 October 2016 and on ECHA website without undue delay.
Item 6 - Substance evaluation **1. Community Rolling Action Plan (CoRAP) & MSC opinion development** • Introduction of the annual draft CoRAP update by ECHA	
	MSC-WG to take into account the changes introduced in the draft CoRAP following the referral.
Item 6 - Substance evaluation **2. 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.
Item 6 - Substance evaluation **2. Decision making process** **b. Introduction to and preliminary discussion on draft decisions on substance evaluation after MS-CA's/ECHA reactions** **c. Seeking agreement on draft decisions when amendments were proposed by MS-CA's/ECHA**	
SEV-FR-024/2014 Tert-butyl methyl ether (EC Nr. 216-653-1) MSC reached unanimous agreement	**MSC-S** to upload on MSC S-CIRCABC the final ECHA decision of the agreed case.
Item 6 - Substance evaluation **d. General topics** • Discussion on use of open and closed sessions in evaluation process	
MSC took note of the meeting documents and the references presented by SECR on use of open and closed sessions in the evaluation process. Members agreed that for increasing the	**MSC-S** to share the meeting presentation and documents ECHA/MSC-50/2016/023-024 with MSC ASO observers' for

CONCLUSIONS / DECISIONS / MINORITY OPINIONS	ACTIONS REQUESTED
transparency to the MSC evaluation work, its scientific discussions on DEV/SEv DDs should predominantely happen in open sessions (session 1), while the DD text revision and the voting should remain in closed sessions. MSC saw no need to change any of its SEv/DEv-related procedural documents, but only to adjust accordingly the current working practices. In conclusion, MSC agreed to share with the MSC observers the meeting presentation and documents ECHA/MSC-50/2016/023-024 for their information.	information **MSC-S** and **MSC members** to follow these working practices for and during open/closed evaluation sessions as agreed
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 compliance checks and testing proposals when amendments were proposed by MS-CA's** **c. Seeking agreement on draft decisions on compliance checks and testing proposal examinations when amendments were proposed by MS-CA's**	
MSC reached unanimous agreement on the following ECHA draft decisions (as modified in the meeting): **<u>Compliance checks:</u>** CCH-066/2016 Turpentine oil (List Nr. 932-349-8) CCH-068/2016 N-[3-(dimethylamino)propyl] methacrylamide (EC Nr. 226-002-3) *(part B on endpoints other than EOGRTS)* CCH-070/2016 Diphenyl(2,4,6-trimethyl-benzoyl)phosphine oxide (EC Nr. 278-355-8) CCH-071/2016 3,5-dimethylpyrazole (EC Nr. 200-657-5) CCH-082/2016 Diethoxymethane (EC Nr. 207-330-6) CCH-083/2016 1,1'-[methylenebis(oxy)]dibutane (EC Nr. 219-909-0) CCH-089/2016 Bis(2-propylheptyl) phthalate (EC Nr. 258-469-4) CCH-092/2016 3-isocyanatomethyl-3,5,5-tri-methylcyclohexyl isocyanate homopolymer, isocyanurate type (List Nr.931-312-3) **<u>Testing proposal examinations:</u>** TPE-046/2016 m-(2,3-epoxypropoxy)-N,N-bis(2,3-epoxypropyl)aniline (EC Nr. 275-662-9) TPE-047/2016 Reaction mass of bis(2,3-epoxypropyl) terephthalate and tris(oxiranylmethyl) benzene-1,2,4-tricarboxylate (List Nr. 940-592-6) TPE-070/2016 Cashew (Anacardium occidentale) nutshell extract, decarboxylated, distilled (Lis Nr. 700-991-6) TPE-071/2016 Cashew (Anacardium occidentale) nutshell extract, decarboxylated, distillation residue (List Nr. 941-212-1) TPE-072/2016 Cashew (Anacardium occidentale) nutshell extract, decarboxylated (List Nr. 941-216-3)	**MSC-S** to upload on MSC S-CIRCABC the final ECHA decisions of the agreed cases.
MSC could not reach unanimous agreement on the following draft decision, as submitted to the meeting after stopping in written procedure:	**MSC-S** to refer the decision (part where MSC did not reach agreement) to the Commission for further decision making,

CONCLUSIONS / DECISIONS / MINORITY OPINIONS	ACTIONS REQUESTED
CCH-068/2016 N-[3-(dimethylamino)propyl] methacrylamide (EC Nr. 226-002-3) *(part A on EOGRTS)*	without undue delay once minutes of MSC-50 are agreed.
Item 7 – Dossier evaluation **d. Decision making process - General topics** • Discussion on use of open and closed sessions in evaluation process	
See Item 6	
Item 8 – ECHA's recommendations of priority substances to be included in Annex XIV Setting Latest Application Dates (LADs) – Practical implementation	
MSC took note of the proposed approach.	MSC to provide comments by 10 November 2016
Item 9 – MSC Manual of decisions (MoD) • Suggestion for a possible new entry to the MoD	
MSC agreed to include one existing entry (under 3.1.9), in the MSC Manual of Decisions and Opinions (MoD), as revised at the meeting.	**MSC-S** to update on MSC S-CIRCABC the MoD as revised by 4 November 2016.
Item 10 – Any other business • ANAA[4] report	
	MSC-S will invite MSC to review and comment on the draft version of the ANAA project document(s), prior to external consultation planned by December 2016.
Item 11– Adoption of main conclusions and action points	
MSC adopted the main conclusions and action points of MSC-50 at the meeting.	**MSC-S** to upload the main conclusions and action points on MSC S-CIRCABC by 28 October 2016.

[4] Applicability of alternative and non-animal approaches

VI. Substance evaluation cases addressed for MSC agreement seeking in written procedure (WP):

Draft decision unanimously agreed by MSC in WP

MSC ID number	Substance name used in draft decision	EC No.
SEV-DE-011/2015	bis(2-ethylhexyl) 4,4'-{6-[4-tert-butylcarbamoyl) anilino]-1,3,5-triazine-2,4-diyldiimino} dibenzoate	421-450-8

VII. Dossier evaluation cases addressed for MSC agreement seeking in the written procedure (WP)

MSC unanimously agreed on dossier evaluation draft decisions in the written procedure:

Compliance checks (CCH)

MSC ID number	Substance name used in draft decision	EC or List number
CCH-067/2016	2,4,6-tris(dimethylaminomethyl)phenol	202-013-9
CCH-074/2016	2,6,10-trimethyldodecane	622-542-2
CCH-075/2016	2,3-epoxypropyl o-tolyl ether	218-645-3
CCH-076/2016	Bis(2-ethylhexyl) tetrabromophthalate	247-426-5
CCH-077/2016	Bis(dibutyldithiocarbamato-S,S')copper	237-695-7
CCH-084/2016	Hexadecyl 3,5-bis-tert-butyl-4-hydroxy benzoate	267-342-2
CCH-085/2016	3-isocyanatomethyl-3,5,5-trimethyl cyclohexyl isocyanate, oligomers, allophanate type	933-047-9
CCH-086/2016	p-tert-butylstyrene	217-126-9
CCH-094/2016	3-(trimethoxysilyl)propylamine	237-511-5
CCH-096/2016	Triisotridecyl phosphite	278-758-9

Testing proposal examinations

MSC ID number	Substance name used in draft decision	EC or List number
TPE-053/2016	OO-tert-butyl O-(2-ethylhexyl) peroxycarbonate	252-029-5
TPE-056/2016	N,N'-(methylenedi-p-phenylene)bis [hexahydro-2-oxo-1H-azepine-1-carboxamide]	258-981-8
TPE-057/2016	Formaldehyde, reaction products with ethylenediamine	281-928-5
TPE-060/2016	Phosphoric acid, octadecyl ester	254-466-7
TPE-061/2016	N-{2-[(phenylcarbamoyl)amino]phenyl} benzenesulfonamide	806-543-7
TPE-064/2016[5]	1,10-decanediyl diacrylate	235-922-4

[5] *Post meeting note*: This agreement is to be considered void. An amended DD for agreement seeking in written procedure for MSC-52 (6-10 February 2017) will be resubmitted due to technical issues in processing Registrant's comments.

VIII. Statement to the minutes on CCH-068A/2016 from the MSC member from France

Statement reasoning for France to vote NO on the draft decision from ECHA on N-[3-(dimethylamino)propyl]methacrylamide, EC number: 226-002-3

The representatives on the Member State Committee for the country named above do not agree with the draft decision from ECHA on N-[3-(dimethylamino)propyl]methacrylamide, EC number:226-002-3, CAS number: 5205-93-6

Context:

In the original draft decision sent to the registrant, ECHA-S requested the study including the Cohort 1B (Reproductive toxicity) with extension to mate the Cohort 1B animals to produce the F2 generation. Indeed, the exposure criteria is fulfilled : the use of the registered substance is leading to significant exposure of professionals during uses such as mixing or blending in batch processes for formulation of preparations and articles (multistage and/or significant contact) (PROC 5); Treatment of articles by dipping and pouring PROC 13, transfer of substance or preparation (charging/discharging) from/to vessels/large containers at non-dedicated or dedicated facilities and Roller application or brushing (respectively PROCs8a, 8b and 10). Moreover, it has been described by NTP, that DMAPMA is used for the synthesis of polymers which have many uses, including paint resins, dispersions/emulsions, performance products, paper and water products, hair care products, and reactive systems. Hence there is potential worker exposure in multiple industries that have different degrees of process enclosure and worker protection. Some uses, e.g., automotive coatings, weather-resistant house paints, and textiles, might result in widespread worker exposure and consumer use. In addition, the monomer may be found in food contact substances (Source Dissemination website ECHA and NTP website).

In addition, there are indications for endocrine-disrupting modes of action because of clear effects in endocrine sensitive reproductive organs (testis and epididymides) are observed in high dose group in the combined screening reproductive/ repeated dose toxicity studies. Testicular atrophy associated with oligospermia was observed in 3/5 high dose group animals. Irregular seminiferous tubules were observed in 2 animals/5 treated with 200mg/kg bw/d (10 animals treated but only 5 fixed tissues were analysed).

Therefore, ECHA originally concluded that Cohort 1B must be extended to include mating of the animals and production of the F2 generation because the uses of the registered substance is leading to significant exposure of professionals and there are indications of modes of action related to endocrine disruption from available studies (OECD Guideline 422 (Combined Repeated Dose Toxicity Study with the Reproduction / Developmental Toxicity Screening Test), 2002).

After having obtained the Registrant´s comments however ECHA revised this view and proposed to endorse the Registrant's comments, who considered that "the testicular effects observed in the OECD TG 422 study, are reversible and not constituting a real alert because similar findings were not observed in the 90-day study". Indeed, ECHA notes that there is lack of consistency between the findings in the OECD TG 422 study and the OECD TG 408 study. Indeed, ECHA now claims that the lack of consistency cannot be explained by differences in these two studies, i.e. the different dose levels (i.e. highest dose level of 300 mg/kg bw/d in the OECD TG 408 study as opposed to 400 mg/kg bw/d in the OECD TG 422 study), routes of administration, animal species or strains, life stages tested, or parameters investigated. ECHA argues that the results from the OECD TG 408 reflect the toxicity after a longer exposure duration (13 weeks as opposed to a exposure duration of 4 weeks for the males in the OECD TG 422 study) which more than compensated that the highest dose level was only 75 % of that in the OECD TG 422 study. Based on these explanations, the majority of the MSC decided that the results from the OECD TG 408 study in this case should supersede the results of the OECD TG 422 study. Therefore,

ECHA-S did not request for extension of Cohort 1B to mate the Cohort 1B animals to produce the F2 generation.

Justification:

The FR representatives in the Member State Committee do not dispute the seemingly conflicting scientific discrepancies of the two particular studies described above. Indeed, neither ECHA-S nor any MSC member had access to the study reports to be able to check for details which might explain these discrepancies. The registrant did also neither explain them further in the registration dossier nor in their response to the initial draft decision document or to the Proposals for Amendments. Moreover, the FR MSC reprensentative believes that it is not the responsibility of MSC nor ECHA to evaluate thouroughly such detailed data to distinguish between false positive or false negative at this stage. Indeed, this kind of work would be done while setting up a CLH or restriction dossier by the dossier submitter and would latter be judged by RAC.
As needed information was not provided by the registrant to substantiate his attempt to explane the differences in results regarding testes toxicity in the OECD TG 408 and TG 422 study, FR representative believe that sufficiently evidence has not been provided by the registrant to disregard the findings in the OECD TG 422 study but rather that those findings constitute „indications of relevant modes of action related to endocrine disruption from available in vivo studies", and hence that this together with the avalable human exposure data according to the provisions of Annex X of REACH triggers the need for extension to mate the Cohort 1B animals to produce the F2 generation.

At that point of the decision making processes, MSC tasks is namely to ensure the Annex X dossier is compliant. Indeed, the column 2 paragraph 8.7.3. of annex X states that An Extended One-Generation Reproductive Toxicity Study with the extension of cohort 1B to include the F2 generation shall be proposed by the registrant or may be required by the Agency in accordance with Articles 40 or 41, if:
(a) the substance has uses leading to significant exposure of consumers or professionals, taking into account, inter alia, consumer exposure from articles, and
(b) any of the following conditions are met:
- the substance displays genotoxic effects in somatic cell mutagenicity tests in vivo which could lead to classifying it as Mutagen Category 2, or
- there are indications that the internal dose for the substance and/or any of its metabolites will reach a steady state in the test animals only after an extended exposure, or
- there are indications of one or more relevant modes of action related to endocrine disruption from available in vivo studies or non-animal approaches.

As both point (a) and (b) third bullet are fulfilled, FR MSC representative does not agree with ECHAs conclusion and believes that a F2 generation is triggered and therefore should be requested.