MSC/M/47/2016
(Adopted at MSC-48)

Minutes
of the 47th Meeting of the Member State Committee (MSC-47)
25-29 April 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 47th meeting of the Member State Committee (MSC) (for the full list of attendees and further details see Part II of the minutes).

Item 2 - Adoption of the Agenda

The Agenda was adopted as modified by the MSC Secretariat to reflect the withdrawal of one dossier evaluation case (CCH-024/2016 – Penta-1,3-diene (EC No 207-995-2)) due to a cease of manufacture (final Agenda is attached to these minutes, Part III).

The Chairman also introduced a new concept to organise discussion groups in parallel to the plenary session such that these groups could prepare possible options for MSC agreement seeking.

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

Two members 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 Part IV. One of the members indicated that her alternate member, also present at the meeting, would take over any of her responsibilities for this agenda item. No other potential conflicts of interests were declared by any other members, experts or advisers with any other item on the agenda of MSC-47.

Item 4 - Administrative issues

- **Outlook for MSC-48**

The Chairman presented an outlook on the potential length of the next meeting using best available estimates on key parameters from dossier and substance evaluation, as well as SVHC identification and the MSC tasks related to recommending substances for inclusion in Annex XIV. Acknowledging the existing uncertainties, the June meeting is expected to require at least 6 plenary days. After exploring also alternative solutions, MSC concluded to split the meeting over two weeks, and to be held tentatively on 6-9 and 14-15 June.

Item 5 – Adoption of the minutes of the MSC-46 meeting

SECR informed the MSC that the minutes of the MSC-46 were adopted in written procedure and have been uploaded on MSC S-CIRCABC and ECHA website.

Item 6 - Substance evaluation

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

SECR introduced MSC with the outcome of the written procedure (WP) for agreement seeking on three substance evaluation cases (see Part VI for more detailed identification of the cases). WP was launched on 8 January 2016 and closed on 18 January 2016. By the closing date, unanimous agreement was reached on two draft decisions (DDs) with one abstention received for one draft decision. For one DD WP was terminated by the MSC Chair on the basis of Article 20.6 of the MSC Rules of Procedure as at least one MSC member requested meeting discussion of the case.

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

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

SEV-BE-003/2014 **4,4'-sulfonyldiphenol (EC No 201-250-5)**

Session 1 (*open*)

Three representatives of the Registrants participated in the initial discussion. In absence of specific confidentiality concerns in 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 by the BE-CA on the basis of the initial grounds for concern relating to Human health/Suspected CMR; Potential endocrine disruptor; Exposure/aggregated tonnage, MSC was guided through the information on the substance (including PfAs, Registrant(s) comments, and the eMSCAs responses to them).

Eleven proposals for amendments (PfAs) were received. In addition five PfAs were submitted as alternative options for four out of the eleven PfAs.

A request was made for Extended One Generation Reproductive Toxicity Study (EOGRTS) in rats, oral route according to test method OECD 443, with the developmental neurotoxicity and immunotoxicity (DNT/DIT) cohorts and with the extension of Cohort 1B to mate the F1 animals to produce an F2 generation. In this regards, one PfA proposed to clarify the concern related to its potential adverse effects on cognitive function of mammals by including learning and memory tests in the cohort 2A/2B and to specify that after receiving the results from DNT cohort in OECD 443, the eMSCA may consider further testing on DNT during the follow-up evaluation if necessary. A different PfA on the other hand, considered that there is sufficient information to classify the substance as Reprotox 1B (for fertility) and to identify it as a potential ED (oestrogenic activity – uterotrophic assay). In addition, they do not consider that information on other ED mode of actions is necessary. Therefore, the PfA submitter was not convinced that there was a need for the EOGRTS. They however, agreed that specific DNT investigations were justified and suggested to remove the request for an EOGRTS and instead request for a developmental neurotoxicity study (OECD TG 426). If this PfA could not be accepted, the PfA submitter proposed to request for EOGRTS basic design, in rats by oral route with inclusion of cohort 2 (DNT) only.

Requests for *in vivo* alkaline comet assay in rats by oral administration (gavage) (test method: OECD 489) and toxicokinetics (test method: EU B.36/OECD 417) were part of the decision that was circulated with the MSCAs and ECHA for PfA submission following the eMSCA assessment of several *in vitro* data and a negative *in vivo* micronucleus test (MN) conducted on mice.

Regarding the request made for toxicokinetics (TK) (test method: EU B.36/OECD 417), two PfAs were received expressing the opinion that it was unclear how the requested information would contribute to the risk management of the substance. One proposed to better substantiate this request by clarifying its purpose, whilst the other proposed to remove this study from the decision, but if the request for TK and comet assay were maintained, a tiered approach was proposed. A third PfA on this study proposed to conduct this study before the comet assay to establish optimum sampling times to ensure that any induced DNA strand breaks which may be short lived are recorded in the assay and to identify other target tissues to be investigated in the comet assay.

In one of the PfAs on the TK study, it was noted that this study would be warranted on rats. The Registrant agreed to perform the TK study in order to demonstrate that the MN study carried out on mice is a reliable negative. The PfA submitter, however, stated that demonstration of bone marrow exposure would only be possible if the TK study is carried out in the same or similar conditions as the available *in vivo* MN study. Hence, according to this PfA the negative result of the *in vivo* mouse MN assay would only be confirmed by the presence of either the parent compound or its metabolites in mouse blood. Since according to the same PfA the proposed TK study in rats does not seem relevant for the mouse to allow the validation of the *in vivo* MN hence the request of the comet to tackle the concern for clastogenicity of the parent compound on the basis of the *in vitro* data was still valid. Therefore, text suggestions to reflect this in the DD were provided in the PfA.

Another PfA on the comet assay, expressed the possibility for conducting the comet assay on non-validated tissues. Hence, it proposed to conduct the comet assay on liver, glandular stomach, duodenum/jejunum and other tissues if warranted by a concern or if demonstrated by the TK study which they proposed to be conducted before the comet

assay. Furthermore, it proposed that the Registrants may also consider sampling and examining gonadal cells to be able to conclude on germ cell mutagenicity and to optimise use of animals.

A final PfA on the comet assay, on the other hand expressed the view that the MN study gave a convincing negative result hence they proposed not to perform the comet assay. Alternatively, if both the comet assay and TK study are maintained, a tiered approach was proposed (comet assay conditional).

A request for a Fish Lifecycle Toxicity Test (FLCTT) (USEPA OPPTS 850.1500) to clarify endocrine disruption concern shown in published studies on sexual development and reproduction of zebrafish was included in the decision. PfAs submitted on this study included suggestions to establish the maximum test concentration; requested for a OECD test 240 describing the Medaka Extended One Generation Reproduction Test (MEORGT) instead of the FLCTT; requested to delete the FLCTT request and replace it with the fish sexual development test (FSDT) OECD 234 (using five concentrations) a level 4 test according to OECD guidance 150. Alternatively, if the latter PfA is not taken up, it was proposed to strengthen the justification explaining why a level 5 test was needed in this case rather than a level 4 study. In this PfA it was recognised that the Japanese Medaka extended one generation test is considered to be the most robust protocol for fish life cycle testing. However, in absence of a validated level 5 test guideline for zebrafish the PfA submitter welcomes the FLCTT but given the large number of animals involved, they proposed to include in the DD the possibility for eMSCA and ECHA to review the Registrant's test protocol before the study begins or else a more detailed study protocol to be appended to the DD.

The Registrants provided written comments on the PfAs which were reiterated during the discussion by the Registrants' representatives. With regards to EOGRTs the Registrants agreed to perform the test but considered the DNT cohort would be compromised with including additional testing for cognitive function. They agreed to conduct the TK study only in a tiered approach with the *in vivo* genotoxicity assay and expressed reservations about the inclusion of duodenum/ jejunum as additional tissues for comet assay arguing that shortage of historical control data for these tissues may result in problematic test interpretations. With regards to the fish test the Registrants' representatives preferred to stay with the FLCTT test because zebrafish is the fish species tested in both published studies on sexual development and reproduction and because they consider that the proposed test design addresses specifically the concerns on ED properties raised by the published studies. Additionally, there is no certainty that medaka will be as sensitive as zebrafish. In case the OECD 240 test on medaka would come out negative the concern related to zebrafish sensitivity would still remain Furthermore, they argued that few laboratories were involved in the validation of this MEOGRT and very little experience has been gained so far with a limited number of tested chemicals.

During the MSC discussion, questions were asked to the Registrants' representatives which allowed them to further clarify that based on their view further validation of cognitive assays is needed, which is currently being done by the US National Toxicology Program. Furthermore, the Registrants' representatives stated that the EOGRTS should best be performed with Wistar rats, since Sprague Dawley rats showed severe organ toxicity in the gastro-intestinal (GI) tract in repeat dose toxicity testing, and a correlation with the observed toxicity to reproduction cannot be excluded.

With regards to the most appropriate test to detect mutagenicity, the Registrants' considered that in general if significant bioavailability can be demonstrated then in their view the MN in mice is the assay to use to detect for both parent and metabolites mutagenicity. Furthermore, they mentioned that the MN was performed with a concentration of 2000 mg/kg body weight and, based on the current knowledge of high organ toxicity in the rat GI-tract, such high doses in the comet assay would not be possible.

With regards to the Fish test, the Registrants' representatives clarified that they would be able to carry out both the FLCTT and ZEOGRT, test but not the MEOGRT.

Session 2 (closed)

With regards to infertility concern of the substance there were initial divergent views on the amount of evidence required in order to justify the trigger of the F2 generation. However then it was recognised that if the effects in the parental and first generation would meet the criteria to classify the substance as reproductive toxicant 1B according to the CLP Regulation then the production of an F2 generation would not be required.

With regards to the rat strain to be used, it was agreed that the same rat strain used for the Reproduction/Developmental Toxicity Screening Test OECD 421 (Sprague-Dawley) should be tested to clarify the suspected concern for reproduction and avoid introducing differences in sensitivity between rat strains.

With regards to the additional parameters for cognitive function it was agreed to assess the cognitive function by including learning and memory test within the DNT cohort since, this possibility for such investigation in the DNT cohort is mentioned in the OECD 443 Test guidance (paragraph 50).

Hence MSC unanimously agreed to keep the request for Extended One Generation Reproductive Toxicity Study in rats, oral route, according to test method OECD 443, with the developmental neurotoxicity and immunotoxicity (DNT/DIT) cohorts using Sprague-Dawley rats (including testing for cognitive function) and with a conditional extension of Cohort 1B to mate the F1 animals to produce an F2 generation.

In relation to genotoxicity, MSC considered all the elements presented in the PfAs, the eMSCA's reactions to the PfAs as well as the Registrants' comments to the PfAs and unanimously agreed on a tiered approach by first requesting the TK study in rats in order to confirm the results from the available *in vivo* MN assay in mice. Members unanimously agreed that if the results of the toxicokinetics study demonstrate the presence of the parent substance in the plasma and if it is demonstrated by the Registrants that the results of this *in vivo* toxicokinetics study in rats can be used to confirm the results of the available *in vivo* micronucleus study in mice, the comet assay should not be conducted. Otherwise, the comet assay needs to be conducted to address this concern.

If the comet assay is conducted, the MSC unanimously agreed to ask for glandular stomach, duodenum and liver. Even though the PfA requested for duodenum/ jejunum, in line with previous MSC agreements, it was acknowledged that the duodenum is the most appropriate part of the intestine to be tested, as it is the first part of the intestine and directly connected to the stomach. The duodenum tissue sampled may contain a small part of the jejunum, which is why MSC in earlier cases referred to duodenum/jejunum. The comments of the Registrants on lack of validation for duodenum were acknowledged, however, MSC considered that duodenum is now routinely analysed by test laboratories performing the comet assay.

With regards to the fish test, MSC carefully compared the different fish tests FLCTT, FSDT, MEOGRT and ZEOGRT – and considered protocol availability, the number of animals needed, the OECD validation status, the estimated costs, and the endpoints studied per test. Furthermore, MSC discussed the choice of species considering the ED effects revealed in previous studies, laboratory capacities and preference of the Registrants. Since for this substance it is already shown from other studies that fecundity and fertility are affected and FSDT (OECD 234) does not cover reproduction, MSC considered the FLCTT or MEOGRT/ZEOGRT more appropriate. Given that MEOGRT/ZEOGRT use less animals than FLCTT without effecting the statistical power of the test and the Registrants indicated to have capacity to also perform ZEOGRT, MSC unanimously agreed to request MEOGRT/ZEOGRT. MSC supported the preference of the Registrants to test with zebrafish as endocrine concern for 4,4'-sulfonyldiphenol in fish originated from two available literature studies which were performed with this species. However, given that OECD 240 is validated for medaka whereas it refers to possible adaptation for smaller fish like zebrafish, MSC unanimously agreed to leave the choice of species for the Registrants. If the zebrafish is chosen, the Registrants would need to follow the protocol attached to the decision, and discuss and agree possible technical deviations with the eMSCA prior performing the test.
MSC unanimously agreed on this decision, although one member expressed some reservations on the proposed non-validated test protocol for zebra fish and about the lack of genetic sex determination in zebra fish (genetic sex determination being highlighted as a

benefit of medaka in both OECD 234 and OECD 240). On this ground it was requested that MSC-S brings to the attention of the ECHA ED Expert Group the need for a general discussion on the scientific benefits of each of the level 5 fish test protocols, and zebra fish sex determination based on what is written in OECD 234 and 240.

SEV-FI-020/2014 Diuron (EC No. 206-354-4)

Session 1 (open)

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

The eMSCA from the Finnish CA (FI-CA) presented the SEv outcome of the above-mentioned substance based on the initial grounds for concern, i.e. relating to potential human health endocrine disruption, wide dispersive use and other exposure/risk-based concern.

The members were guided through the information requirements and explained that additional concern for environmental endocrine disruption (ENV ED) have been identified during the substance evaluation, thus, eMSCA has chosen to follow a tiered testing strategy with a focus first on ENV ED effects where Human Health (HH) effects are to be considered at a later stage. During the presentation of the case eMSCA explained that five PfAs were received from two MSCAs and the DD was modified for the meeting based on one of the PfAs received while the others are to be discussed at the meeting. It was clarified that regarding Fish Sexual Development Test (FSDT, test method OECD 234) one MSCA proposed to conduct the FSDT study with a defined fish species Japanese medaka (*O. latipes*) which is one of the three species mentioned in the guideline, due to the sensitivity of its secondary sexual characteristics to androgen or antiandrogen chemicals. The other MSCA also supported the information request but discussed in the PfA potential alternative approaches concluding that not only possible effects on sex hormone systems but also effects on the thyroid hormone system should be investigated. As the testing in fish does not address thyroid system, in their PfA this MS proposed to include a request for larval amphibian growth and development assay (LAGDA) (OECD TG 241) as effects on the thyroid system should be investigated in amphibians. Furthermore, this MS provided some general considerations regarding sequential versus parallel testing for endocrine disruption in rats, fish and amphibians and suggested considering possible ED effects in other species as well by requesting for parallel testing for human health and environmental effects in those cases where *in vivo* ED related testing is warranted based on the available information. In addition this MSCA proposed investigating possible ED effects preferably in an EOGRTS (OECD TG 443) including DIT and DNT, or alternatively to request a targeted *in vivo* study investigating prenatal developmental toxicity and ED activity with 20 animals per dose group and including substance specific ED related parameters of relevance.

eMSCA noted that there are currently three ongoing assessments of diuron under the PPP and BPR review programmes, as well as under the US EPA ED screening assessment programme (where diuron is included in list 2).

The Registrants provided written comments on all PfAs prior to the meeting and clarified these at the meeting. In their comments on the PfAs, the Registrants agreed to perform the requested FSDT (OECD 234) as a definite study needed to verify the initial concerns on potential endocrine disruption of diuron, although in their view, no trigger for ED mode of action (MoA) has been seen. However, they disagreed with the other PfAs on the need for further parallel or sequential testing, as well as with the proposed EOGRTS (OECD 443) and LAGDA (OECD 241) as, in their view, the available information does allow to conclude that no relevant adverse ED effects have been seen for human health, while the FSDT will clarify the potential concerns for the environment. Furthermore, the Registrants disagreed with the PfA as regards the most appropriate test species and are of the view that the selection of the test species should be left to the study-performing laboratory. At the meeting the Registrants requested MSC to consider longer deadline of 2 years if the DD is further modified to require FSDT testing with Japanese medaka only, to allow sufficient time to complete the test validation of the laboratory and to obtain the FSDT results.

During the MSC discussion, clarifying questions were asked to the Registrants' representatives where they mentioned that new information from 23 recently conducted screening studies has been generated in the US EPA ED screening programme (where all except one are giving negative results), as well as already known or recently published higher tier studies in rats and mice. The Registrants noted that all of them confirm their conclusion that neither evidence for adverse ED activities caused by diuron, nor triggers for further testing are found. However, not all of this information had been provided earlier and thus was not considered before by eMSCA and MSC.

eMSCA agreed that fish secondary sex characteristics should be recorded if possible with the test species.

In regard to the substance-specific testing strategy, the eMSCA indicated preference to assess the concern for the environment first based on the results of the FSDT and later on, taking into account the available information released also from the other review programmes, to consider the need for further testing, if triggered, for the environment and/or for human health. The member from the MS submitting the PfA to include LAGDA testing indicated that he reluctantly agreed in this particular case with the eMSCA's testing strategy proposal for sequential testing, i.e. initially to first consider the sex hormone related concerns for ED effects in fish. However, pointing out the uncertainty in species sensitivity when investigating endocrine disruption (in fish versus amphibians, as well as in different test species for FSDT), he suggested that the issue be brought to the attention of the ED expert group for their further discussion. As regards the concern for HH, he mentioned that in his view the current dataset sufficiently indicates the concern which should be addressed in an EOGRTS with DNT and DIT cohorts to then be considered in the follow up.

Session 2 (closed)

MSC discussed the issue of the test species selection for the FSDT, as well as the need to consider any further testing in amphibians or mammals at this stage of the substance evaluation.

MSC unanimously agreed with the request for FSDT (OECD TG 234) and that the test should be perform with either Japanese medaka (*Oryzias latipes*) or Zebrafish (*Danio rerio*) or Three-spined stickleback (*Gasterosteus acuelatus*), leaving it to the testing laboratory to select the specific test species. If possible, for the selected test species, the inclusion of the determination of the genetic sex and secondary sex characteristics should also be required.

MSC agreed with the eMSCA's testing strategy, as described above. No further information requests were found necessary at this stage of the substance evaluation.

MSC further agreed to extend the deadline for submission of the requested information of 18 months from the date of the final decision taken by ECHA for consistency reasons (allowing the Registrants 3 months to the contact a test laboratory that will conduct the test). In conclusion, some procedural modifications in the DD have been made to better clarify the follow-up evaluation.

MSC unanimously agreed on this SEv DD, as modified at the meeting, based on the above considerations.

SEV-NL-031/2014 Silver (EC No. 231-131-3)

Two representatives of the Registrants participated in the initial discussion. In absence of specific confidentiality concerns in draft decision (DD), an open session was held. Conflict of interest was declared by two MSC members (as specified in Part IV).

The evaluating Member State Competent Authority (eMSCA) from The Netherlands (NL-CA) presented the outcome of SEv of the above-mentioned substance which was performed by the NL-CA on the basis of the initial grounds for concern relating to Nanoparticles/Ecotoxicity of different forms of the substance; Environmental fate; Exposure/Wide dispersive use; aggregated tonnage. MSC was guided through the information on the substance (including PfAs, Registrant(s) comments, and the eMSCAs responses to them).

Twelve PfAs were received. Regarding the request for information on physico-chemical properties of each individual form or nanosilver PfA proposed to better justify or preferably remove the request. In the submitter's view it was not clear how the physico-chemical information would be used in relation to the new ecotoxicological information to clarify the potential risk and for the studies where information already exists on these properties the decision did not explain why the existing information was insufficient, why new information was necessary and the possible regulatory action following the submission of the information. If however, the request remained it was proposed to include guidance and criteria for grouping of the different nano forms.

Regarding the request for quantitative information on nanosilver particles in soil and information on the ecotoxicity of three different nanosilver forms representing the range of forms of nanosilver, the same PfA was submitted. The submitter agreed with the need to test the Registrant's hypothesis that silver ion was the main responsible factor for inducing adverse effects, as it was not clear how other parameters influenced the toxicity of the silver nanoparticles. Hence it was proposed to specify in the decision that the form(s) to be tested should represent the worst case.

Regarding the request on the uses of each individual form of nanosilver, it was proposed to allow the registrant to make grouping.

Furthermore, additional PfAs were submitted to reflect better the Registrants' comments related to the overlap between the requests on fate in soil and a recently EU funded project; scope of decision; scope of SEv versus the Biocidal Products Regulation; downstream users; and the small tonnage of silver used as nanosilver. It was also proposed to justify the reasoning of the extension of the deadline in the DD, and proposed to replace the definition of a nanoform in the decision.

The Registrant(s) provided written comments on the PfAs which were reiterated during the discussion by the Registrant(s) representatives. The Registrant(s) representatives informed MSC that only two registrants out of 59 registrants of silver, have registered nano silver in the range of 1-10 tons per year out of a total volume of >100,000 tons per year, with one nanoform per registrant. The main uses of nanosilver are in electronics and electroplating.

With regards to the definition of nanoforms, the Registrants appreciated to have a fixed definition for the course of the silver substance evaluation. The nanoforms registered fall within the operational definition as suggested by the eMSCA taking into account the specific shape, surface area, surface treatment and particle size distribution. Granulometric data and surface coatings included in the CSR suggested potentially more nanoforms, however, the Registrant(s) representatives clarified that these have been provided by all the different producers not differentiating between what was used in the EU and outside of the EU.

During the discussion the Registrant(s) representatives were requested whether it was possible to say the type of surface treatment of the two registered silver nanoforms. They promised to check with the Registrant(s) concerned for confidentiality and will send that information to the eMSCA.

The DD requests for further aquatic toxicity data to test the hypothesis presented by the Registrant(s) in their registration dossiers that the silver ion is more toxic than any silver nanoform. The Registrant(s) agreed to the need to test their hypothesis and suggested to use as test material the nanoform with the smallest particle size and highest surface area since they expect that the smallest size would have the highest dissolution rate. The Registrant(s) representatives originally requested for an extension of the deadline from 12 months to 30 months due to the required aging time for the soil experiment. While it was appreciated that the deadline had been amended to 24 months, in the view of the Registrant(s) representatives the decision should build in a reasonable time contingency as this request is research focused and not a standard information requirement, therefore, the laboratories to undertake this work are limited and significant time will be needed for study preparation due to lack of clear test guidelines.

The Chairman pointed out that following future dossier updates or new registrations this could result in more nanoforms being registered. However, for this substance evaluation process, it was specified that MSC would discuss only the two nanoforms present at that

point of time, and if in the future more nanoforms are introduced the identified concern may also apply to those additional forms. In such case, there might be a need for those registrant(s) at the registration phase to ensure that the hypothesis applies to their specific nanoform(s).

The eMSCA agreed with many of the the PfAs submitted, hence the discussion focused on clarifying the testing strategy in the DD in particular on providing better guidance to the Registrant(s) on the choice of test material, as well as on better linking of the requests with the concern identified.

Session 2 (Closed)

For the purpose of this substance evaluation, the eMSCA distinguished two broad (groups of) forms (which may be divided in subgroups): the nanoforms, and the bulk forms (*i.e.* larger than nanoform). A nanoform of a substance is a form that would fulfil the definition in the Commission Recommendation (2011/696/EU). Different nanoforms of silver are further characterised by a specific size, shape and surface chemistry. The specific surface chemistry can be due to deliberate modification (e.g. surface treatment or coating), or the absence of surface modification (no surface treatment).

With regards to the choice of the test material industry fully recognised the need to do a proper characterisation of the nanoform. Due to the limited amount of information currently available to MSC on different parameters like particle size, surface area and surface treatment and their correlation with toxicity, and acknowledging that the request needed to be proportionate, the choice of the test material was left to the Registrant(s).

In conclusion, based on the PfAs and discussions at the meeting MSC unanimously agreed to drop the request for information on the physico-chemical properties of each individual form of nanosilver manufactured, imported and/ or placed on the market. It decided to keep the request for information on ecotoxicity (on algae, long term toxicity on aquatic invertebrates and on soil microorganisms) specifying that only the smallest of the two nanoforms of silver with the highest specific surface area shall be tested. Furthermore, the test material shall be sufficiently characterised, by providing information on physico-chemical properties. MSC decided to make the request for the quantitative information on the fate of nanoparticles of silver in soil pore water and the soil solid fraction conditional to the results on ecotoxicity (such information is required if a higher toxicity is found in any of the ecotoxicity tests performed for the nanoform as compared to the ionic silver). The request for information on the uses of each individual nanoform of silver that is registered was maintained.

Consequently the decision has two deadlines. If the environmental fate information is not to be generated the deadline for the ecotoxicity and use information is 12 months, otherwise the deadline to submit the information on all three requests is 30 months.

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

SEV-FR-021/2014 Methyl methacrylate (EC No. 201-297-1)

Session 1 (*open*)

One representative of the Registrants participated in the initial discussion. In absence of specific confidentiality concerns in the DD, an open session was held. Conflict of interest was declared by two MSC members (as specified in Part IV).

The eMSCA from France (FR-CA) presented the SEv outcome of Methyl methacrylate (MMA) which was performed on the basis of the initial grounds for concern relating to Human health: sensitiser, wide dispersive use, consumer use, exposure of sensitive populations, high risk characterisation ratio (RCR) and high (aggregated) tonnage, and on the additional concern identified during evaluation relating to mutagenicity. MSC was guided through the information on the substance (including PfAs, Registrant(s) comments, and the eMSCAs responses to them).

Three PfAs were received in total. Regarding the request for *Mammalian Erythrocyte Micronucleus assay in rodent via the most appropriate route (MN; OECD 474),* one PfA suggested eMSCA to reflect in section III the Registrants' comments in the decision why

there is a need for requesting the same type of test. In particular, it proposed clarification to be provided on the reason why a weight of evidence approach could not be applied, referring to specific toxicokinetic considerations and results of the available *in vivo* MN and dominant lethal test.

Also related to this request another PfA suggested to change the request *for a MN* into an *in vivo mammalian alkaline comet assay (OECD 489), in rats via inhalation* with the assessment of DNA damage in lung, liver, and bone marrow. A MSCA agreed that the current data for *in vivo* cytogenicity are not suitable to conclude on the absence or presence of the genotoxic potential and one of the shortcomings of the available MN test data is the lack of clarity on whether the substance reaches the bone marrow. It was specified that due to the rapid metabolism the concern for this substance consists mostly on possible genotoxicity at the site of first contact, and comet assay is the best way to address a site of first contact concern. Furthermore it was suggested that the relevant route of administration by inhalation should be specified in the DD, as lungs are a sensitive tissue and can be reached more quickly by this substance than the intestines, and the parenteral route requested in the draft decision is not relevant for human risk assessment of industrial chemicals.

An additional PfA was submitted, introducing an information request related to *further information regarding available data for skin sensitisation in order to evaluate the potency and to suggest sub-categorisation in category 1A or 1B as appropriate*. The PfA suggested the Registrants to provide the (re)-assessment of available data for skin sensitisation and possibly an update of the harmonised classification (currently skin sensitising Category 1). A MSCA referred to available human data and mentioned that a classification as a strong sensitiser in category 1A may be justified based on that human evidence.

The Registrants provided written comments on the PfAs which were reiterated during the discussion by the Registrants' representatives. With regards to the MN test the Registrants' representatives expressed the view that due to the corrosivity of one of MMA (methyl methacrylate)'s metabolites (i.e. methyl acrylate), testing via inhalation as well as subcutaneous or intraperitoneal routes are not a viable option.

Regarding the route of administration Registrants' representatives reiterated their opinion that gavage is the most relevant parenteral route and specified the high dose that could be tested. They further justified this route by highlighting the disadvantages of the other exposure routes.
The Registrants' representatives also questioned the relevance of the new to be generated data for further assessment of risk management measures (RMM) as they considered that, the available information on MMA and the other substances in the category "Lower Alkyl (C1-C8) Methacrylates" is sufficient to prove that this class of chemicals is not mutagenic, irrespective of the new results.

Regarding the PfA for *skin sensitisation* Registrants' representatives indicated that recent data correspond for including MMA in the subcategory of sensitisers of weak potency (CLP subcategory 1B) and they agreed to update the MMA (methyl methacrylate) registration dossier to address more clearly the sensitising potency.

During the discussion, clarifying questions were asked to the Registrants' representatives. In the context of the mutagenicity concern they hypothesized that positive *in vitro* results generated so far are an artefact related to pH-issues in the assays and they mentioned that additional *in vitro* testing will be considered to substantiate that view. With regard to the inhalation studies the Registrant(s) representatives further explained the method to derive exposure concentrations which led them to conclude that tissues were destroyed mainly due to acid exposure as a result of hydrolysis, and which allowed them to specify the limit value for dosing of the substance via inhalation testing.

Session 2 (closed)

The PfA on skin sensitisation was not further pursued since the eMSCA indicated a willingness to prepare a proposal for harmonised classification under Regulation (EC) No 1272/2008.

With regards to the request of performing a comet assay instead of a MN test there were initial divergent views, and also there was further discussion on the amount of existing data reflecting positive, false positive or negative results related to the mutagenicity concern. MSC considered that insufficient data were available in the registration dossier to clarify the mode of action (MoA) of MMA regarding human health concerns, and that with regards to the additional information that the Registrants intends to provide supplementary, MSC considered it was limited in its judgement of the relevance of such new data at this stage of the decision making process. However, the eMSCA considered the Registrants' clarifications brought in the open session and MSC discussion and presented the option to follow a different approach on the basis of their assessment of the available information, not necessarily requesting for further information on mutagenicity for MMA at this stage, and instead also to include a proposal for a harmonised classification relating to respiratory sensitisation, skin sensitisation and carcinogenicity. Using such an approach, the Registrants could still deliver additional *in vitro* information to strengthen their case that mutagenicity is of no concern for this substance. In case RAC decides there is insufficient information for a harmonised classification then substance evaluation may be initiated again to address remaining or new concern(s).

By dropping the request for mutagenicity testing no further information would be requested in the context of this substance evaluation. Hence MSC decided to prepare a draft agreement document, discussed its content and the procedural and legal aspects to be covered.

Subsequently, MSC agreed unanimously on the draft agreement document which records that there is no need to request for further information on mutagenicity for Methyl methacrylate at this stage.

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

SEV-FR-025/2014 2-ethyl-2-[[(1-oxoallyl)oxy]-methyl]- 1,3-propanediyl diacrylate (EC No. 239-701-3)

Session 1 (*open*)

One representative of the Registrants participated in the initial discussion. In absence of specific confidentiality concerns in 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 which was performed on the basis of the initial grounds for concern relating to human health: sensitiser; exposure: wide dispersive use, exposure of workers, high RCR, and on the additional concern identified during evaluation: carcinogenicity, genotoxicity, environment. MSC was guided by the eMSCA's representative through the information on the substance (including PfAs, Registrant(s) comments, and the eMSCAs responses to them).

Ten PfAs were received in total.

In the DD a request was made for an *in vivo* mammalian erythrocyte micronucleus assay in mice (MN; OECD 474), via parenteral route. In this regard one PfA suggested either 1) the introduction of a tiered testing strategy starting with an *in vitro* assay on liver metabolism to assess the extent of first pass elimination followed by a MN in mice with intravenous administration and analysis of liver and bone marrow, or 2) directly asking for the latter MN assay.

In another PfA it was considered that the MN assay may clarify a concern which needs to be resolved regarding the mode of action (MoA) for carcinogenicity in case the substance reaches the bone marrow in sufficient amounts, or if the test substance fails to reach the bone marrow there will still be a residual concern for a genotoxic carcinogenic effect in other organs/tissues. Therefore the PfA proposed to request a comet assay (OECD 489) instead of a MN assay, indicating the species (mice), possible ways of administration (parenteral or another route if evidence of adequate systemic exposure is provided), and different tissues to be sampled and analysed in function of the administration route.

As regard to the requested *Fish, Acute Toxicity Test (EU TM C:C.1; OECD TG 203) a* PfA indicated that it cannot be excluded that the other aquatic species may be more sensitive

than fish and suggested to also request acute toxicity testing for algae (*EU TM C:3;* OECD TG 201) and aquatic invertebrates (*EU TM C:2;* OECD TG 202), it is suggested to take into account the surface active property of TMPTA and to determine exposure concentrations at multiple time points during the test, or to consider a possible alternative the OECD 236 Zebra fish embryo toxicity test (ZFET) on the basis of animal welfare considerations.

As regard to the request of *Evaluation of bioaccumulation potential: Refinement of log Kow based on CMC determination and on refined solubility of TMPTA in octanol and QSAR evaluation of the bioaccumulation potential with unequivocal justification and documentation that the approach is valid for TMPTA,* or *Bioaccumulation in Fish-Aqueous and Dietary Exposure (EU TM C:13; OECD TG 305)*, a PfA suggested: 1) deletion of this request, as the substance is readily biodegradable so the remaining concern-driven reason for a fish BCF would be to assess secondary poisoning risks; 2) to maintain the request but to amend the draft decision bringing clarification on the concern addressed, and the impact on the risk management of the substance; 3) to postpone the BCF (bio-concentration in fish) test pending receipt and assessment of the exposure data; and 4) to request only a 'weight of evidence' analysis at this stage, and the need for the test determined following receipt of this and of the exposure data.

Also related to the request for an evaluation of bioaccumulation potential it was suggested that all the existing data on Kow and BCF are discussed and explanations/additions provided why further long-term aquatic toxicity testing might be needed, to substantiate the risk of potential secondary poisoning, and to address that the respective request leads to improved risk management measures, with the alternative to drop the request if it cannot be justified. In case the request would be maintained the PfA suggested to define the conditions needed for QSAR prediction of a fish BCF needs to meet if no measured results are submitted.

As regard to the request for a *Detailed description and justifications for each contributing scenarios and revision of spraying scenarios with appropriate methods* two editorial PfAs related to the update of the dossier were submitted.

Another PfA was submitted introducing an information request related to *Further information regarding available data for skin sensitisation in order to evaluate the potency and to suggest sub-categorisation in category 1A or 1B as appropriate,* suggesting to add in the draft decision explicitly a request the Registrant re-assesses the available data for skin sensitisation and classify accordingly, which may involve submitting a proposal for a revised harmonised classification (including sub-categorisation) as appropriate.

The Registrant(s) provided written comments on the PfAs which were reiterated during the discussion by the Registrant(s) representatives. With regard to the requested MN test, the Registrant(s) agreed to this test using intravenous (i.v.) administration, since preliminary results from an *in vitro* metabolism study indicated fast biotransformation, while they questioned the relevance of a comet assay. In their view the substance would reach the bone marrow in the MN test (mortality and clinical signs related to TMPTA observed in males), whereas in the comet assay any potential DNA damage observed would be due to the irritative properties of the substance and not because of DNA damage. Moreover, no alerts of gene mutation were observed in the in vitro tests available on TMPTA (Ames test and HPRT).

In regard to *Detailed description and justifications for each contributing scenarios and revision of spraying scenarios with appropriate methods* the Registrant indicated this had been addressed in the latest submitted update of the registration dossier.

In regard to *Fish, Acute Toxicity Test* the Registrant(s) agreed to perform fish testing but were of the opinion there is limited added value by repeating the algae and crustacean toxicity studies. An MSC member emphasised that the TMPTA's intrinsic properties and physical-chemical parameters (such as absorption-desorption processes) and the variations of algae biomass could lead to fluctuations of concentration during the tests. During the discussion one MSC member queried whether it was possible to mention the use of OECD TG 236 study (FET, fish embryo acute toxicity) in an approach to adapt the standard information requirements (in line with what was done in an earlier DD on a SEv case) and

one stakeholder observer noted that OECD TG 236 has been validated and the option could be provided for the Registrant to consider.

As regard to *Evaluation of bioaccumulation potential* the Registrant(s) representatives specified that they will perform the CMC-refined log Kow and report the calculations with a detailed explanation and justification of the result, which will be backed by justification for the applied QSAR equation considering the application domain and the reliability for estimating BCF for the substance.

As regard the reassessment of skin sensitisation data the Registrants agree to review this set of information and determine the subcategory in the next update.

Session 2 (closed)

In relation to genotoxicity, MSC considered all the elements presented in the PfAs, the eMSCA's reactions to the PfAs as well as the Registrants' comments to the PfAs and unanimously agreed to drop the request for MN test (OECD 474) in mice and to request for a comet assay in mice (OECD 489). If the comet assay is conducted, the MSC unanimously agreed to ask for using appropriate injection administration techniques to diminish irritation and to analyse bone marrow and liver. In particular administration volume and dosing rate (slow rate of injection) need to be carefully selected in order to minimise local reaction and to achieve sufficiently high dosages.

With regard to the possibility of requesting to test Zebra fish and/or algae instead of requesting Acute Toxicity Test on Fish, MSC discussed the uncertainity that could affect the results from tests on Zebra Fish and/or algae due to surfactant properties of TMPTA. Furthermore, MSC recognised that the applicability domain of OECD TG 236 in a regulatory REACH context was not yet concluded by ECHA's evaluation and also that ECHA could not build all possible adaptation arguments for a Registrant. Due to all these aspects, MSC agreed not to specify the OECD TG 236 as a possible part of an approach to adapt the standard information requirement under the "Note for the consideration of the Registrant" in this case. One member commented that no published data can be found indicating why the FET test should not be offered as an option in this case. Therefore, the fish embryo acute toxicity test (FET), as a validated OECD test guideline (OECD 236) should also be offered to the registrant as an option as there are animal welfare benefits by preferring the FET.

With regard to the evaluation of bioaccumulation potential MSC agreed to request for the refinement of the estimation of log Kow based on appropriate determination of CMC and solubility of TMPTA in octanol. It was discussed on the limitations of the test and it was established that if the refined log Kow ≥3, it is needed to request an update of secondary poisoning risk assessment based on QSAR evaluation of the bioaccumulation potential with appropriate justification and documentation that the approach is valid for TMPTA. The limitations and technical aspects of the test will require that if it is not technically possible to refine the log Kow, or risk of secondary poisoning is identified further to the risk assessment update, Bioaccumulation in Fish: Aqueous and Dietary Exposure (OECD TG 305) is requested.

MSC also agreed unanimously to keep the remainder of the information requests with some further modification of the decision text to improve on its structure and clarity of the requests.

MSC unanimously agreed to the DD as modified at the meeting. A member abstained from voting.

<u>SEV-UK-037/2014</u> Climbazole (EC No. 253-775-4)

Session 1 (*open*)

Two representatives of the Registrant were present during the initial discussion, however, they were not given the floor to comment on the PfAs as they had not commented on those during the Registrant's commenting period. In absence of specific confidentiality concerns in DD, an open session was held.

The eMSCA from the United Kingdom (UK-CA) presented the SEv outcome of the above-

mentioned substance which was performed by the UK-CA on the basis of the initial grounds for concern relating to human health / suspected CMR (reproductive toxicity) and human exposure (wide dispersive use, consumer use). During this evaluation additional concerns had been identified regarding worker exposure, environmental risks and potential environmental endocrine disruption. MSC was guided through the information requests on the substance (including PfAs and the eMSCAs responses to them).

During the consultation of MSs and ECHA eight PfAs were received and, in addition, three PfAs had been submitted as an alternative to one of these eight.

Regarding the request *for combined repeated-dose toxicity study with reproduction/developmental toxicity screening test (in rats, oral route)* (OECD 422) additional investigations and some changes in the study design to better clarify the concern (reproductive and possible ED concerns) were proposed. The two-week premating period was proposed to be extended to ten-weeks and inclusion of hormonal parameters investigation in parental animals was also suggested to be included for consideration by the registrant.

One PfA suggested requesting an EOGRTS (OECD TG 443) without F2 but including DNT and DIT cohorts instead of the currently proposed combined repeated-dose toxicity study. This inclusion was proposed since the current database raise a potential concern not only to for wildlife but also for human health. The PfA requesting EOGRTS brought forward arguments that the EOGRTS is to be requested instead of OECD TG 422 as in this case the number of animals used in the two tests would be equal, and EOGRTS would be preferable for detecting endocrine disruption. Additionally, the available rodent toxicity database, even if quite comprehensive, does not assess the range of endocrine sensitive endpoints. Three alternative PfAs related to the further requirements for OECD 422 request were withdrawn during the discussion and are not further explained here. The points in favour of requesting for an adapted OECD 422 with additional number of animals per dose group and measurements and other points arguing in favour of requesting for an OECD 443 study instead were brought forward in the discussion.

In the context of the inclusion of the ED concern, there was a discussion about the reliability and robustness of the read across. As stated by the eMSCA the current data do not give clear indication for an ED action *in vivo*. A suggested read across had not been fully substantiated as part of the PfA.

As regards the *testing strategy* described, one PfA proposed to amend the strategy to describe inclusion of results from investigation of ED relevant endpoints in the requested rat study so that they are included in the weight of evidence analysis regarding endocrine disruption, and that they will be used in deciding whether to request a study in fish later on. Another PfA proposed to delete the possibility that the Registrant may recommend additional RMMs, as an alternative to *in vivo* testing, in case the provision of new *in vitro* data indicates a potential for endocrine disruption.

Regarding the request for *in vitro endocrine disruption screening studies* an editorial PfA and a PfA suggesting including measurement of progesterone in the steroidogenesis assay, as well as a recommendation to better explain why the original testing strategy was modified, had been made.

One PfA suggested to clarify that the Fish Sexual Development Test (OECD 234) will have to be performed in case of positive *in vitro* screening studies, or positive rodent *in vivo* study results.

The Registrant had not provided any comments on the PfAs.

eMSCA had modified the DD to reflect partly or in full most of the PfAs in advance of the meeting, and hence most of those did not require much further discussion at the meeting. With regard to the PfA for requesting EOGRTS instead of an extended screening study (OECD TG 422) some members expressed a concern that after performing an OECD TG 422 a follow-up request for EOGRTS might still be needed in order to clarify any remaining concerns related to reproductive toxicity classification and labelling. Further discussion on this PfA took place in a closed session.

Session 2 (closed)

MSC exchanged views on how to best follow-up on the identified concern for prolonged parturition *i.e.*, a reproductive toxicity (fertility) concern which could lead to classification.

One MSC member whose CA submitted PfAs indicated that the additional investigations in the *combined repeated-dose toxicity study with reproduction/developmental toxicity screening test (in rats, oral route)* (OECD 422) (two-week premating period and hormonal parameters investigation in parental animals) could be made mandatory for the registrant if added to the DD.

The eMSCA originally had opted to request a screening study with many adaptations and additional measures, whereas at the meeting it was argued that a basic EOGRTS design would provide more robust information for classification purposes. An additional argument discussed was that RAC recently came to the opinion that a structurally related azole (triadimenol (EC 259-537-6)) should be classified repro cat 1B. Further incentive to request the basic EOGRTS design was that the expanded screening study and the basic EOGRTS design were using approximately similar number of animals.

On the basis of results obtained with other azole compounds it was discussed whether to include an additional human health related ED concern related to developmental toxicity. Divergent views remained whether this was of potential concern and whether triggers for inclusion of DNT and DIT cohorts in the EOGRTS were met.

MSC agreed unanimously on the request for an EOGRTS using the basic design (no additional cohorts), as well as with the other requests as modified at the meeting. MSC found unanimous agreement on ECHA's DD as amended at the meeting.

SEV-SE-030/2013 Trimethoxy(methyl)silane (EC No. 214-685-0)

Session 2 (closed)

The written procedure for MSC agreement seeking on this SEv draft decision prepared by the SE CA (eMSCA) had been terminated by the MSC Chair on request of a MSC member and the case was brought to the meeting to further discuss and clarify the proposed removal of the information request for a *Local lymph node assay (LLNA) (OECD 429 or OECD 442A or OECD 442B),* as requested in two PfAs received.

In the following discussion, the eMSCA's expert and the MSC members exchanged views on the validity of the results of the positive Buehler test and the potential ways forward. The eMSCA proposed to drop the requests for LLNA and information on human experience from the DD and proceed based on the available information with a CLH proposal under the CLP Regulation such that RAC may assess its applicability for CLP-purposes. eMSCA further clarified that in the follow-up evaluation, after obtaining the information on mutagenicity testing and possibly taking into account the outcome of the CLH process, the eMSCA will re-assess whether the concern for skin sensitisation remains and whether further studies should be requested.

MSC supported the eMSCA's strategy to proceed with a CLH dossier first based on the currently available dataset and to assess further information needs in the follow-up evaluation stage.

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

d) General topics

- **Status update on substance evaluation**

SECR updated MSC about the consistency screening observations, the new template for SEV decisions, reminded the CAs (via MSC) to plan and book the 2015 substances, latest by December this year to be in line with the 6 months deadline to book the appropriate CA consultation round (or to communicate if there is a justified reason to deviate).

Also information was provided on small corrections in the draft CoRAP, learnings from consistency screening on qualitatively and quantitatively aspects of the draft decisions issued, learnings for CSR related requests and potentially outcomes versus expectancies of

the final eMSCA submissions, including the number of DDs/ conclusions/ suspensions. Also PBT, vPvB and ED concerns on human health and environment addressed and preferred ways of addressing them in the DD were specified.

SECR informed MSC on the main decision issued from the Workshop on Substance Evaluation that it is considered, specifically that any request issued in the decision should be enforceable, as the decision taken in MSC is the most appropriate and generally agreed solution to address the issues.

SECR provided information to MSC on the new SEv DD template including the reasoning for the new structure and advantages for the clarity of the DD. New steps for efficient processing and finalisation of the substance evaluation dossiers were also introduced.

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

SECR gave an overview of the status of some recent appeals on evaluation submitted to the Board of Appeal of ECHA (BoA) and pending cases submitted to the European Court of Justice relating to the authorisation process. This was much appreciated by the MSC.

- **Fish Embryo Acute Toxicity (FET) project – outcome report**

SECR presented the project that ECHA started in 2015 with the assistance of an external contractor, to assess the relevance and adequateness of using OECD 236 to fulfil the information requirements under REACH, Classification Labelling and Packaging of substances and mixtures and Biocidal Products Regulations.

The aim of ECHA project was to assess the capability of the FET test in predicting acute fish toxicity and to define its applicability domain for regulatory purposes. The existing fish embryo data (acute - 96h LC50) were compared to the data available on the adult fish toxicity (acute - 96h LC50). The database was filtered to remove FET studies of low reliability by applying quality criteria on several test conditions that were considered as most influential on the determination of the reliable LC50 in the fish embryo test. Wrongly conducted studies or studies where the test concentrations could not be maintained can over- or underestimate the toxicity due to data reliability and bioavailability issues. After filtration of the database the final dataset for comparative analysis was limited therefore it was not possible to conclude on several aspects in relation to the applicability domain of FET. Further analysis will be possible when more valid FET studies are available.

The general conclusion of this project is that FET data can be used as part of a weight of evidence approach together with relevant information on the substance chemistry and other supporting information on fish toxicity (e.g. valid and well documented QSAR information, well-justified read-across evidence, etc.). The complete report will be published on the ECHA website once finalised. Furthermore, SECR informed that as part of the OECD test guideline program, an ad hoc working group is analysing the incorporation of the FET test in the toxicity threshold approach and that ECHA is seeking to be part of this working group to contribute with the results of the ECHA project.

MSC appreciated the work performed and acknowledged the complexity of such an analysis however, a number of members felt it was difficult to have a meaningful discussion without seeing the full report and underlying data. One representative expressed some reservations since in his view insufficient details on the substance selection criteria were provided to MSC and also that the outcome of this project does not encourage the use of OECD 236. He raised a number of questions on points and claims made in the presentation, which he could not verify in the absence of the report. These included substance selection criteria (and the database that resulted), the significance of interspecies sensitivity when comparing ZFET results to acute fish test data, and whether some highlighted limitations of the FET tests also apply to standard acute fish tests. He expressed this reservation given that the outcome of the presentation does not appear to encourage the use of OECD 236.

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 six dossier evaluation cases (see Part VII for more detailed identification of the cases). WP was launched on 1 April 2016 and closed on 12 April 2016. By the closing date, unanimous agreement was reached on five DDs. By the closing date, one member abstained from voting on four cases. For one DD, WP was terminated by the MSC Chairman on the basis of Article 20.6 of the MSC Rules of Procedure as at least one MSC member requested meeting discussion of the case at the MSC-47 meeting.

b. Introduction to and preliminary discussion on draft decisions on compliance checks and testing proposals after MS-CA reactions *(Session 1, tentatively open session)*

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

Compliance checks (CCH)

CCH-002/2016 - Benzaldehyde (EC No. 202-860-4)

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 two PfAs were submitted to ECHA's DD on extended one-generation reproductive toxicity study (EOGRTS; OECD TG 443).

The first PfA suggested requesting sequential testing in order to extend cohort 1B to include the F2 generation. It described that uses might lead to significant exposure of consumers or professionals, that available data indicate that benzoic acid, a metabolite (oxidisation product) of benzaldehyde, significantly increased the chromosomal aberration, sister chromatid exchanges and micronucleus frequency; and that the likelihood to meet Muta2 classification criteria was high. The PfA suggested waiting for the results of *in vitro* testing and follow-up *in vivo* testing before deciding on the final design of the EOGRTS, and requesting sequential testing with indication that, unless the F2 was added, a clear view on mutagenic properties needed to be available. The PfA continued to suggest requesting to include cohorts 2A and 2B (developmental neurotoxicity, DNT) based on benzaldehyde being a metabolite of toluene, a neurotoxicant, and available data to raise concern that the registered substance might affect the developing nervous system.

The second PfA, in its first part, suggested including DNT, considering that benzaldehyde is a metabolite of toluene, a neurotoxicant, and that benzaldehyde might contribute to the overall neurotoxicity of toluene because of reactive oxygen species (ROS) production. It referred to data on a proposed analogue substance, methyl benzoate, as a possible metabolite of benzaldehyde. It was of the view that available results indicated a neurotoxic effect of the registered substance in adult animals at high doses, where also systemic toxicity is observed, thus adding to the concern on effects on the developing nervous system. The PfA continued to suggest requesting to integrate cognitive testing of the animals in the DNT, explaining that for toluene both motor and cognitive/learning effects had been observed.

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

The Lead Registrant and a member of the joint submission had provided comments on the original DD (not reflected here) and the PfAs. In their written comments the Registrants noted (a) that it was not feasible to include DNT as direct developmental neurotoxicity could not be distinguished from effects due to maternal toxicity at the dose levels needed, and (b) that the integration of cognitive testing was deemed unnecessary as the inclusion of DNT is unjustified.

The representative of the Registrant explained at the meeting that they felt strongly that the developmental toxicity of the substance had been evaluated within the well-established benzoate category, and that the substances had been well studied and evaluated by other regulatory agencies. He further mentioned that although they acknowledge not being able

to address the original DD at the appropriate stage of the procedure, they had updated their dossier with a read-across justification for the benzoates category and read-across with benzyl alcohol.

SECR noted in general that all registrants of substances which are part of a category should include any relevant (new) category information in their dossiers without undue delay, and that they should not wait for ECHA to send a DD or any other form of reminder.

MSC was satisfied with ECHA's response not to amend the DD to include a request for cognitive testing, whilst MSC discussed all other aspects of the PfAs at the meeting.

One MSC member justified that the testing should be sequential for mutagenicity properties, in particular in view of the forthcoming substance evaluation of the registered substance and the significant exposure to consumers and professionals.

A MSC member's expert raised several arguments to support their views: as benzaldehyde is a metabolite of toluene, it is hypothesised to have effects, however, scientific literature appears to have contradicting results that could be interpreted in different manners; lesion was found at high doses in available studies, including ROS formation; further metabolisation to benzoic acid would not exclude that fetus was exposed to benzaldehyde, and evidence indicates that it reaches the brain when exposed to high doses; and ECHA Guidance on triggers and their interpretations would indicate the need to include DNT cohort.

Session 2 (closed)

SECR invited MSC to discuss first the sequential testing and F2 cohort issues, and provided the view that based on available results the evidence appeared weak, given also that benzoic acid was classified without genotoxicity concerns. One MSC member was of the view that even when evidence was weak the concern still existed. Another MSC member noted the difficulties in studying aldehydes and that F2 was generally insensitive measure of reproductive toxicity in rats. A MSC member's expert explained that two available studies did not raise any concerns on carcinogenicity. Overall, MSC felt that there was not enough evidence to support the request for sequential testing, first having the mutagenicity *in vitro* testing, and then potentially including the F2 cohort.

On the DNT cohort inclusion, several MSC members and their experts exchanged views on how to interpret research results and how the substance behaves, especially when it is a metabolite of toluene and further metabolises into benzoic acid, and in general the solvent neurotoxicity that would be relevant for DNT. COM reminded that the legal text was thoroughly discussed before the approach was agreed to be a trigger-based system, with credible hypotheses on concern, to include DNT. One MSC member argued the evidence would seem to be enough for a trigger, while several others doubted that. Eventually, the view of MSC was that DNT cohort would not be requested in the DD.

As for the category approach presented in the comments of the Registrants, SECR concluded based on its review that the proposed category read-across could not be accepted due to inconsistent effects in repeat dose studies; higher reactivity of benzaldehyde in comparison to other category members, where the worst case was benzaldehyde; and, studies were not adequate for read-across purposes. SECR considered that the weight-of-evidence approach would fail for similar reasons, and that it was unclear what weight was put on presented studies to overcome the identified deficiencies. MSC took note of SECR's assessment on the information provided and decided there was no need to further changing the DD as similar issues with analogue approach were also identified in the category approach.

MSC agreed unanimously to the DD as provided for the meeting. One MSC member from France abstained from voting.

CCH-004/2016 - 5-methylhexan-2-one (EC No. 203-737-8)

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 one PfA was submitted to ECHA's DD on *e*xtended one-generation reproductive toxicity study (OECD TG 443). It suggested requesting to include cohorts 2A and 2B (DNT), explaining that the registered substance had been shown to induce an acute sedative effect on the central nervous system (CNS) in rats after exposure to whole-body inhalation to vapour. Also, it considered the substance structurally similar to methyl isobutyl ketone, which was also observed to induce a sedative effect on the CNS, leading to a concern that it could affect developmental neurotoxicity.

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

The Registrant had provided written comments on the PfA considering that solvent-related sedation and narcosis were dose-related phenomena common to low-molecular weight organic solvents and related to short-term reversible effects. Thus, there was no trigger for inclusion of DNT. In addition, he considered that the one carbon atom difference in the carbon chain between the ketone and methyl group should not be assumed to have no difference in developmental neurotoxicity, as ECHA had not accepted read-across between substances with one carbon difference for nephropathy. The representative of the Registrant further justified their view that overall there were no findings to justify the triggering of neurotoxicity, and that there was no evidence that narcosis would produce neurotoxicity.

One MSC member argued that concern was raised by the scientific literature which showed neurotoxicity for solvents like toluene, xylene and ethanol, as well as the high vapour pressure of the substance.

Session 2 (closed)

SECR noted that available studies indicated effects only at levels close to lethality, and that the mode of action was narcosis. One MSC member reminded of the sluggish behaviour effects at lower doses. SECR referred to the legal text which details the options to trigger additional cohorts, which it felt were not fulfilled in this specific case. One MSC member argued there was in general scarce information on mechanisms/mode of action and chronic effects on solvents, and therefore it was not considered straightforward to find justifications besides reference to narcosis to request DNT in such cases. Several MSC members hold the view that the other volatile solvents with narcotic effects after short-term exposure and chronic or DNT effects after longer term exposure like toluene, xylene, styrene or ethanol were structurally too dissimilar as compared with the registered substance to provide sufficient evidence.

MSC agreed unanimously to the DD as provided for the meeting. Seven MSC members with voting rights abstained from voting, including members from Austria, Denmark, France, Germany, Lithuania, the Netherlands, and Sweden. The member from Norway supported these members.

CCH-019/2016 - Sodium sulphamidate (EC No. 237-572-8)

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 was submitted to ECHA's DD on skin sensitisation. It suggested to delete word "scientific" in "ECHA also reminds you that the scientific justification to be provided needs to be substance specific and adequately documented". It reasoned that the justification for performing the Guinea pig maximisation test instead of the local lymph node assay (LLNA) may be regulatory rather than scientific in this particular case.

SECR had modified the DD for the meeting based on the PfA.

The Registrant had not provided comments on the PfA.

Session 2 (closed)

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

CCH-023/2016 - Calcium dipropionate (EC No. 223-795-8)

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 one PfA was submitted to ECHA's DD on *s*kin irritation. It requested the Registrant to explain, firstly, why results of the bovine corneal opacity and permeability test method (BCOP) could be used to assess skin corrosion/irritation. Secondly, it considered that insufficient scientific evidence was provided to explain how information on *in vitro* and *in vivo* studies on the metal carboxylates and the inorganic metal salt could be used to justify *in vivo* testing for the registered substance, and requested providing more detailed information on the three model substances to support the justification.

SECR had not modified the DD based on the PfA.

The Registrant had provided comments on the PfA reasoning why the BCOP test could be used as a surrogate to assess skin corrosive properties, however, he had not provided additional information about the three model substances used to support the testing strategy.

During the meeting the representative of the Registrant agreed that further information on three model substances could have been provided. He also emphasized that the composition of the registered and three model substances were similar, two comprising a metal cation and organic anion and the third being an inorganic metal salt.

One MSC member noted that in his view no links had so far been established between eye and skin irritation and therefore using results from BCOP appeared problematic. He further emphasized that not only more information was necessary on the three model substances but also scientific support as to why those substances show that the Registrant's argument that *in vivo* testing in this case is appropriate for the registered substance.

Session 2 (closed)

One MSC member commented that the Registrant had claimed having done a read-across to three model substances, however, not providing sufficient documentation on this. Another MSC member doubted the validity of *in vitro* testing and applicability to the registered substance. SECR reminded that the Registrant had already provided further justification of his testing strategy in his comments to the PfA. MSC members agreed to request the Registrant to include further justification to the testing strategy in the technical dossier, and that ECHA in its follow-up would assess the information after the deadline in the decision has passed.

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

TPE-003/2016 - SDA Product (desulphurization of exhaust gases by semi-dry absorption method from the coal fired power plants) (List No. 931-259-6)

Session 1 (open)

Two representatives of the Registrant were present during the initial discussion, however, they were not given the floor to comment on the PfAs as they had chosen not to comment on those during the formal registrant's commenting period. In absence of specific confidentiality concerns in DD, an open session was held.

SECR explained that two PfAs to ECHA's DD were submitted on the mutagenicity request which was for Transgenic rodent somatic and germ cell gene mutation assays (TGR, OECD TG 488) or *in vivo* mammalian alkaline comet (single cell electrophoresis) assay (OECD TG 489).

Both PfAs suggested an alignment in the request for the tissues to be analysed in case comet assay is used by suggesting three tissues (liver, glandular stomach and duodenum/jejunum) instead of the two required in the DD submitted to MS consultation.

The other PfA also suggested an addition to Section II to add spermatozoa to be harvested in the TGR assay. It further specified that the germ cell samples shall also be analysed in case the analysis of any of the somatic tissues indicates that the substance is a somatic cell mutagen.

SECR had modified the DD for the meeting based on PfAs, however, inserting in Section II only collection and storage of germ cell samples (spermatozoa) in the TGR but not a request for its analysis which was left for the Registrant to consider once the results of the somatic cells are available.

MSC considered it also needed some further discussion in closed session mainly whether the DD should actually specify the third tissue for the comet assay as 'duodenum/jejunum' or rather simply as 'duodenum'.

Session 2 (closed)

MSC supported the way the request for Transgenic Rodent assay (TGR) had been amended based on the PfA to include a request for sampling and storage of germ cells in Section II. MSC agreed to specify the storage time for germ cells as up to 5 years, in line with what is specified in the OECD guideline. This time would allow not only the registrant but also authorities to consider the need to analyse the stored germ cells after the results for the somatic cells become available, avoiding the need to require any further animal testing afterwards.

As regards the tissues for comet assay SECR explained that the intention is to sample duodenum as the first site of contact and hence it would be clearer to indicate duodenum only in the DD. It was acknowledged that the duodenum is the most appropriate part of the intestine to be tested, as it is the first part of the intestine and directly connected to the stomach. The duodenum tissue sampled may contain a small part of the jejunum. MSC supported this change to be incorporated to this decision but also other decisions under finalisation.

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

Based on the agreement for inclusion of sampling and storage of germ cells in Section II SECR informed MSC it will apply this now as a feasible approach in other TPEs or CCHs where a TGR is requested.

CCH-003/2016 - Thiophene, tetrahydro-, 1,1-dioxide, 3-(C9-11-isoalkyloxy) derivs., C10-rich (EC No. 800-172-4)

Session 2 (closed)

SECR explained that agreement was initially sought in written procedure. The written procedure was terminated by the Chairman of MSC on request of one MSC member suggesting MSC discussion on this DD.

SECR introduced the PfA that was received to ECHA's DD. The PfA on the *Worker Exposure assessment and risk management measures, Wearing gloves for more than 4 hours* which suggests requesting the Registrants to demonstrate the safe use of the substance by reducing the risk arising from wet work situations and to clearly state in the exposure scenario (ES) if the gloves are only required for special activities during the task.

Following the PfA did not modify the DD.

The MSC member who requested for termination of the written procedure explained that there was limited information providing evidence that the use of gloves more than 4 hours in wet conditions does not produce an additional risk for workers.

SECR explained that the proposed level of information suggested to be provided by the Registrants cannot be included in the DD on the overall scope of CCH under REACH regulation.

During the discussion MSC members supported the opinion that even if the additional risk identified fails to be included in the requirements of a CCH dossier, Registrant have to demonstrate that the substance is used safely and this can still be addressed through further communication on these issues, which should be handled through other instruments, i.e. the national legislation. Also the additional risks related to gloves, protecting clothing and other PPE (Personal Protective Equipment), and the conditions that can bring additional risks (i.e. substance specificity, temperature, time of wearing) what needs to be

documented in the CSR (Chemical Safety Report), can be addressed in the CSR after on-going updating stage of the guidance documents on CSR and ES.

MSC agreed unanimously to the DD as circulated for the written procedure, while the MSC member who requested for the written procedure termination abstained from voting.

d) General topics

- **New draft decision template in dossier evaluation**

MSC was provided with information on the new decision template for dossier evaluation which was already in use for some of the decisions in this round of MSC meeting. The efficiency benefits from the implementation of the new template in comparison with the previous way of drafting the decisions were underlined. Feedback from StO on the clarity of the new draft template was provided and also the request for explanation on the reasoning for providing information in the annex or in the decision. In response ECHA explained the confidentiality aspects that have to be taken into account when drafting the decision and what information should be included in the appendix.

- **Implications of Article 13(1) for compliance checks**

SECR introduced the background for two pilot cases (CCH-019 and CCH-023), which were opened due to European Ombudsman (EO) decision of 11 December 2014 (1568/2012/(FOR)AN). EO had considered that the inclusion of Article 13 of the REACH Regulation in the parameters for compliance checks (CCH) under Article 41(1)(a) of the REACH Regulation, shows that such CCHs were also meant to verify whether the information provided in the registration dossier was generated in compliance with the last resort principle relating to the use of animals in testing as laid down in Article 13. ECHA has explored how to meaningfully assess the compliance according to Art. 13(1) under CCH, with two pilot cases relating to performance of an *in vivo* study without prior performance of *in vitro* testing (irritation) and justification for not performing the first choice *in vivo* study (skin sensitisation). Issues arising from these two pilot cases were: inadequate scientific justification for performing an *in vivo* study and justification related to "global responsibilities".

One MSC member inquired whether this would apply only to *in vitro* tests, or also to *in vivo* endpoints where one test would offer animal welfare benefits over other available tests. . Another MSC member noted that scientific and legal rationales are not always the same. SECR reminded that the two pilot cases could have been addressed directly to enforcement authorities, but were brought to MSC as test cases. One MSC member remarked that CCH could be a slow and heavy process, and that any guidance would preferably need to be translated. Several MSC members were of the view that an ECHA decision, or guidance, or authoritative statements, would facilitate the work of national enforcement authorities, as inspectors may not have the opportunity to check the technical dossier or screen scientific data; at any rate, each case would have its specificities. However, one MSC member emphasized that it would be practical also not to have too much information, and inspectors can contact CAs to prepare a clear mission. SECR noted that the Forum will also be informed in its June meeting on the pilot cases, and that lessons learned from the two pilot cases will be provided when cases have been finalised.

- **Appeals update**

See under 6.2d

Item 8 - ECHA's 7th draft recommendation of priority substances to be included in Annex XIV

- **Presentation by secretariat on summary of issues raised in public consultation**
- **Work plan of MSC Rapporteur and Working Group for opinion drafting**
- **Discussion on elements for the draft opinion on ECHA's 7th draft recommendation for Annex XIV**

SECR gave a status update and an introduction to the main issues raised in the comments per substance or substance group (all together 11 substances). Responses to the comments received in public consultation will be for discussion in the next meeting, and are to be structured in the similar manner as in the previous round. All draft responses were already made available to MSC, however it was stressed that the work on them continues until the June MSC meeting, and even beyond. SECR also indicated its appreciation to the commenters for providing consolidated comments, in particular as regards comments submitted by industry.

The Rapporteur presented the timeline for 2016 recommendation work in MSC, a brief overview of comments received during the public consultation, and an initial assessment of potential MSC discussion items for this or later meetings. Members of the Working Group for the MSC opinion forming on the draft 7th recommendation had provided their input to the Rapporteur, and the summary was based on this joint assessment.

The Rapporteur invited for any feedback or comments from members as an input to producing the first draft opinion for discussion in MSC-48.

In the following discussion one industry stakeholder observer acknowledged that the responses are now made available by ECHA one meeting earlier than during the previous rounds, providing more time to reflect them, and he also appreciated the improved clarity and comparability of responses with the current structure of response-documentation. However, he expressed a concern that the release of responses this early may jeopardise any independent review of the public consultation comments by MSC by providing an ECHA view on them early on. As an example he mentioned ECHA's assessment on exemptions which could easily be seen as influencing MSC. One of the other more general items he raised was a concern over the potential structuring of latest application dates (LADs), reminding also on the proposal submitted earlier by him. Furthermore, in his view different substances to be listed in Annex XIV (referring there also to substances not yet identified as SVHC) but with the same use (batteries as an example) should not have different LADs in order not to distort/interfere the application for authorisation process.

In responding to the first critique raised both the Rapporteur and SECR assured that MSC will provide its independent opinion to ECHA, and transparency of the process with full inclusion of stakeholder observers further helps to ensure that. Furthermore, it was reminded that the MSC opinion on the ECHA recommendation has a somewhat different status than in other processes where Committees are involved. SECR in responding to the concern over LAD setting reconfirmed that they are working to develop a more systematic approach even if it is not yet ready to be presented. However, the approach currently in place is the one that is applied until revised.

An observer from a sectoral organisation in his intervention confirmed that indeed the use of lead as a stabilizer in PVC has been voluntarily phased out for use on the EU market by the end of 2015, however legacy lead stabilizers will still be found in PVC recyclate obtained from post-consumer waste. ECHA is now developing a restriction dossier related to those uses. Another point he made was that registration updates for the epoxy hardeners HHPA and MHHPA indicate that only industrial uses exist for those substances and, he informed that the supply chain using those hardener joined together in a project to assess exposure of workers, for which results should be available in July.

The Chairman reiterated in his concluding remarks that at the next meeting a first discussion on the draft MSC opinion is foreseen.

Item 9 – SVHC identification

● Secretariat's preliminary analysis whether comments received in the ongoing public consultation trigger MSC referral and agreement seeking

SECR introduced to MSC the preliminary observations on the public consultation comments received on the four SVHC proposals in the ongoing SVHC 02/2016 round, the identified triggers for MSC involvement and the way considered for addressing them later on.

Members also took note of the time schedule for MSC agreement seeking for this SVHC round.

Item 10 – Any other business

● A short summary of an industry led project on interpretation of intermediate status under REACH and its main outcomes

An observer presented to MSC a short summary of the industry-led project on the interpretation of the intermediate status under REACH and its main outcomes. It was explained that this initiative was supported by Eurometaux and Cefic and aimed to clarify the intermediate status of such materials towards downstream users and manufacturers where difficulty has been identified in assessing the intermediate status in specific complex cases (e.g. inorganic matrix materials).

SECR commented that expert workshops give opportunities for industry to provide further information on their substances and/or processes, and for ECHA to explain how such information could be assessed in the regulatory work, thereby allowing for a constructive dialogue. However, such exchange or, the attendance of workshops by ECHA staff, should not be perceived as providing a formal ECHA-position, nor should a presentation to MSC be construed as an endorsement of the workshop's findings.

MSC highly appreciated this industry initiative towards the downstream users and the summary provided on the project outcomes.

● References to EU test methods and OECD test guidelines in evaluation decisions

SECR provided MSC with an outline on development and approval of the test guidelines and on the priority to be applied in referring to the EU Test Method Regulation (TMR) as a default. SECR made a suggestion that the reference is made to new/updated OECD Test Guidelines for methods which are not yet in EU TMR. The analysis was restricted to human health and environmental fate and hazard endpoints, and did not cover physical-chemical methods agreed at UN-level.

SECR explained the actors, procedures and timings affecting the updating process of the test methods at EU level and OECD level, and provided clarifications on principles and practicalities linked to the two systems.

It was suggested to request ECHA to share its approach with (e)MSCAs for their implementation in SEv DDs and when submitting Proposals for Amendments, and for MSC-S to prepare a draft entry for the MSC Manual of decisions.

Item 11– Adoption of conclusions and action points

The conclusions and action points of the meeting were adopted at the meeting (see Part V).

II. List of attendees

Members/Alternate members
ALMEIDA, Inês (PT)
ANDRIJEWSKI, Michal (PL)
BORG, Ingrid (MT)
COCKSHOTT, Amanda (UK)
COSGRAVE, Majella (IE)
DE KNECHT, Joop (NL)
DEIM, Szilvia (HU)
DIMCHEVA, Tsvetanka (BG)
DUNAUSKIENE, Lina (LT)
FINDENEGG, Helene (DE)
HUMAR-JURIC, Tatjana (SI)
JANTONE, Anta (LV)
KREKOVIĆ, Dubravka Marija (HR)
KOUTSODIMOU, Aglaia (EL)
KULHANKOVA, Pavlína(CZ)
LONDESBOROUGH, Susan (FI)
LUNDBERGH, Ivar (SE)
MANSUY, Patrick (FR)
MARTÍN, Esther (ES)
MIHALCEA UDREA, Mariana (RO)
REIERSON, Linda (NO)
RUSNAK, Peter (SK)
STESSEL, Helmut (AT)
TYLE, Henrik (DK)
VANDERSTEEN, Kelly (BE)
VESKIMÄE, Enda (EE)
WAGENER, Alex (LU)
Representatives of the Commission
GARCíA-JOHN Enrique (DG GROW)
KOBE, Andrej (DG ENV)
Observers
ANNYS, Erwin (Cefic)
HÖK, Frida (ChemSec)
KERÄNEN, Hannu (CONCAWE)
LEROY, Didier (CEPE)
REGO, Laura (ECEAE)
STODDART, Gilly (PISC)
TILLIEUX, Geoffroy (EuPC)
WAETERSCHOOT, Hugo (Eurometaux)

ECHA staff
AJAO, Charmaine
ANASTASI, Audrey Anne
BERCARU, Ofelia
BERNASCONI, Giovanni
BICHLMAIER, Ingo
BROERE, William
CALEY, Jane
CARLON, Claudio
CARTON DE TOURNAI, Laure-Anne
CARTLIDGE, George
CESNAITIS, Romanas
DELOFF-BIALEK, Anna
DE WOLF, Watze
DEYDIER, Laurence
DREVE, Simina
FABJAN, Evelyn
HALLING, Katrin
HAUTAMÄKI, Anne
HOFFSTADT, Laurence
HUUSKONEN, Hannele
JOHANSSON, Matti
KARKOLA, Sampo
KLOSLOVA, Zuzana
KORJUS, Pia
KREUZER, Paul
KUITTINEN, Marko
LE CURIEUX, Frank
LOUEKARI, Kimmo
MÜLLER, Birgit
NAUR, Liina
PELLIZZATO, Francesca
QUINN, Bernadette
ROCKE, Timo
RODRÍGUEZ-IGLESIAS, Pilar
ROSSI, Laura
RÖNTY, Kaisu
SCHOENING, Gabriele
SCHULTHEISS, Christian
SOBANSKA, Marta
SUMREIN, Abdel
VAHTERISTO, Liisa
VASILEVA, Katya
WOLLENBERGER, Leah
YLÄ-MONONEN Leena

Proxies

- BORG, Ingrid (MT) also acting as proxy of PISTOLESE, Pietro (IT)
- KOUTSODIMOU, Aglaia (EL) also acting as proxy of PALEOMILITOU, Maria (CY)
- DUNAUSKIENE, Lina (LT) also acting as proxy of GAIDUKOVS, Sergejs (LV) on 25 April
- STESSEL, Helmut (AT) also acting as proxy of MIHALCEA-UDREA, Mariana starting from the afternoon of 28 April
- TYLE, Henrik also acting as proxy of DUNAUSKIENE, Lina (LT) in the afternoon of 26 April

Experts and advisers to MSC members

BARTHELEMY-BERNERON, Johanna (FR) (expert to MANSUY, Patrick)
BLOM, Cécile (NO) (adviser to REIERSON, Linda)
BOEL, Els (BE), (adviser to VANDERSTEEN, Kelly)
BOUWMAN, Tialda (NL) (expert to DE KNECHT, Joop)
BUDASOVA, Jana (EE) (expert to VESKIMÄE, Enda)
FREY, Sabine (BE), (adviser to VANDERSTEEN, Kelly)
GRACZYK, Anna (PL) (expert to ANDRIJEWSKI, Michal)
GREGOROVIĆ, Gordana (HR) (expert to KREKOVIĆ, Dubravka Marija)
GRINCEVICIUTE, Otilija (LT) (expert to DUNAUSKIENE, Lina)
HEESCHE-WAGNER, Kerstin (DE) (adviser to FINDENEGG; Helene)
HOLMER, Marie Louise (DK) (expert to TYLE, Henrik)
INDANS, Ian (UK) (expert to COCKSHOTT, Amanda)
KOZMIKOVA, Jana (CZ) (expert to KULHANKOVA, Pavlina)
MALKIEWICZ, Katarzyna (SE) (expert to LUNDBERGH, Ivar)
MEYS, Catherine (BE) (expert to VANDERSTEEN, Kelly)
NYITRAI, Viktor (HU) (expert to DEIM, Szilvia)
PAPPONEN, Hinni (FI) (adviser to LONDESBOROUGH, Susan)
PRIHA, Maarit (FI) (adviser to LONDESBOROUGH, Susan)
RISSANEN, Eeva (FI) (adviser to LONDESBOROUGH, Susan)
ROSENTHAL, Esther (DE) (expert to FINDENEGG, Helene)
TALASNIEMI, Petteri (FI) (adviser to LONDESBOROUGH, Susan)

MSCA Experts for SEV cases
ARABI, Azadeh (SE)
BLEEKER, Eric (NL)
KOSHY, Lata (UK)
LORI, Julia (FR)
PASQUIER, Elodie (FR)
RÖHL, Martine (BE)

By WEBEX/phone connection:
During the agenda item 6: Sjur ANDERSEN (NO), Béatrice CHION (FR), Agnieszka DOBRAK-VAN BRELO (BE), Ian DOYLE (UK), Marius GUDBRANDSEN (NO), Hélène LECLOUX (BE), Audrey PEARSON (UK)
During the agenda items 8, 9 and 10: Valentina BERTATO (DG GROW)
During the whole meeting: Maila PUOLAMAA (DG GROW)

Case owners:
Representatives of the Registrants were attending under the agenda item 6b for SEV-BE-003/2014, SEV-FI-020/2014, SEV-NL-031/2014, SEV-FR-025/2014, SEV-FR-021/2014 and SEV-UK-037/2014; under the agenda item 7b for TPE-003/2016, CCH-002/2016, CCH-004/2016 and CCH-023/2016

Apologies:
PALEOMILITOU, Maria (CY)
PISTOLESE, Pietro (IT)
WIJMENGA, Jan (NL)

III. Final Agenda

MSC/A/047/2016 Final

Agenda
47th meeting of the Member State Committee

25-29 April 2016
ECHA Conference Centre
Annankatu 18, in Helsinki, Finland
25 April: starts at 9 am
29 April: ends at 1 pm

Item 1 – Welcome and Apologies

Item 2 – Adoption of the Agenda

MSC/A/047/2016
For adoption

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

Item 4 – Administrative and procedural issues

- Outlook for MSC-48

For information

Item 5 – Minutes of the MSC-46

- Final minutes of MSC-46

MSC/M/46/2016
For information

Item 6 – Substance evaluation

Closed session for 6c

Decision making process

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

ECHA/MSC-47/2016/001
For information

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

For discussion followed by agreement seeking under 6c:

ECHA/MSC-47/2016/017

MSC code	Substance name	EC number	Document
SEV-BE-003/2014[1]	4,4'-sulfonyldiphenol	201-250-5	ECHA/MSC-47/2016/002-003
SEV-FI-020/2014[1]	Diuron	206-354-4	ECHA/MSC-47/2016/006-007
SEV-NL-031/2014[1]	Silver	231-131-3	ECHA/MSC-47/2016/004-005
SEV-FR-021/2014[2]	Methyl methacrylate	201-297-1	ECHA/MSC-47/2016/014-015
SEV-FR-025/2014[2]	2-ethyl-2-[[(1-oxoallyl)oxy]-methyl]- 1,3-propanediyl diacrylate	239-701-3	ECHA/MSC-47/2016/010-011
SEV-UK-037/2014[2]	Climbazole	253-775-4	ECHA/MSC-47/2016/008-009

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 b** and a case returned from written procedure for agreement seeking in the meeting:

SEV-SE-030/2013	Trimethoxy(methyl)silane	214-685-0	ECHA/MSC/D/2016/035-036

For agreement

d) General topics

- Status update on substance evaluation
- Appeals update[3]

For information

- Fish Embryo Acute Toxicity (FET) project – outcome report

ECHA/MSC-47/2016/031

For information and discussion

Item 7 – Dossier evaluation

Closed session for 7c

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

ECHA/MSC-47/2016/016

For information

b) Introduction to and preliminary discussion on draft decisions on compliance checks and testing proposals after MS-CA reactions *(Session 1, tentatively open session)*

For discussion followed by agreement seeking under 7c:

ECHA/MSC-47/2016/018

Compliance checks

MSC code	Substance name	EC/List No.	Document
CCH-002/2016[5]	Benzaldehyde	202-860-4	ECHA/MSC-47/2016/019-020

[1] To be addressed during 25-27 April
[2] To be addressed during 27-29 April
[3] A combination of Appeal updates for Substance and Dossier Evaluation, if appropriate.

CCH-004/2016[5]	5-methylhexan-2-one	203-737-8	ECHA/MSC-47/2016/021-022
CCH-019/2016[4]	Sodium sulphamidate	237-572-8	ECHA/MSC-47/2016/023-024
CCH-023/2016[4]	Calcium dipropionate	223-795-8	ECHA/MSC-47/2016/025-026

Testing proposal examinations

MSC code	Substance name	EC/List No.	Document
TPE-003/2016[5]	SDA Product (desulphurization of exhaust gases by semi-dry absorption method from the coal fired power plants)	931-259-6	ECHA/MSC-47/2016/029-030

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 a case returned from written procedure for agreement seeking in the meeting:

CCH-003/2016	Thiophene, tetrahydro-, 1,1-dioxide, 3-(C9-11-isoalkyloxy) derivs., C10-rich	800-172-4	ECHA/MSC/D/2016/022-023

For agreement

d) General topics

- New draft decision template in dossier evaluation
- Implications of Article 13(1) for compliance checks
- Appeals update[3]

For information

Item 8 – ECHA's 7th draft recommendation of priority substances to be included in Annex XIV

Tentatively on 28th April

- Presentation by secretariat on summary of issues raised in public consultation[5]
- Work plan of MSC Rapporteur and Working Group for opinion drafting
- Discussion on elements for the draft opinion on ECHA's 7th draft recommendation for Annex XIV

For information and discussion

Item 9 – SVHC identification

- Secretariat's preliminary analysis whether comments received in the ongoing public consultation trigger MSC referral and agreement seeking

For information

Item 10 – Any other business

- A short summary of an industry led project on interpretation of intermediate status under REACH and its main outcomes

For information

[4] To be addressed on 28-29 April
[5] First draft responses are available in the Recommendation folder in MSC S-CIRCABC

- References to EU test methods and OECD test guidelines in evaluation decisions

ECHA/MSC-47/2016/012

For discussion

Item 11 – Adoption of main conclusions and action points

- Table with conclusions and action points from MSC-47

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

- *Dossier evaluation status report (presentation slides)*

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: SEV-FR-021/2014	Helene Findenegg	Annual declaration as published on the ECHA website. No participation in the Committee's deliberation and voting.
AP 6 b: SEV-FR-021/2014 SEV-NL-031//2014	Alex Wagener	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-47, 25-29 April 2016
(adopted at MSC-47)

CONCLUSIONS / DECISIONS / MINORITY OPINIONS	ACTIONS REQUESTED
Item 4 – Administrative and procedural issues	
Outlook for MSC-48	**SECR** to send the next meeting invitation for MSC-48 meeting scheduled for 6-9 June and 14-15 June.
Item 6 - Substance evaluation - Decision making process **a) Written procedure report on seeking agreement on draft decisions 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.
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)***	
MSC reached unanimous agreement on the following ECHA draft decisions as modified in the meeting: SEV-BE-003/2014 4,4'-sulfonyldiphenol (EC No. 201-250-5) SEV-FI-020/2014 Diuron (EC No. 206-354-4) SEV-NL-031/2014 Silver (EC No. 231-131-3) SEV-FR-025/2014 2-ethyl-2-[[(1-oxoallyl)oxy]- methyl]- 1,3-propanediyl diacrylate (EC No. 239-701-3) SEV-UK-037/2014 Climbazole (EC No. 253-775-4) SEV-SE-030/2013 Trimethoxy(methyl)silane (EC No. 214-685-0) For SEV-FR-021/2014 Methyl methacrylate (EC No. 201-297-1) it was unanimously agreed in MSC that no further information is necessary at this stage.	**SECR and eMSCA** to complete the decision for SEV-UK-037/2014 as per the editorial mandate given by MSC. **MSC-S** to upload on MSC S-CIRCABC the final ECHA decisions of the agreed cases. **MSC-S** to upload on MSC S-CIRCABC the agreement document on SEV-FR-021/2014 **MSC** mandated **ECHA-S** to editorial changes to implement references to test guidelines and test methods, including their recent corrections, in case agreed and those in preparation for MSC, as well as editorial changes on defining duodenum instead of duodenum/jejunum.
Item 6 - Substance evaluation - Decision making process **d) General topics** • Fish Embryo Acute Toxicity (FET) project – outcome report	
MSC took note of the FET project outcome report. The final report that was used for the assessment will be made available to MSC once published to be discussed at the appropriate forum within OECD.	**MSC-S** to inform MSC when the FET project report is published on ECHA website.
Item 7 – Dossier evaluation **a. Written procedure report on seeking agreement on draft decisions on dossier evaluation**	

CONCLUSIONS / DECISIONS / MINORITY OPINIONS	ACTIONS REQUESTED
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 decisions (as modified in the meeting, where appropriate): CCH-002/2016 Benzaldehyde (EC No. 202-860-4) CCH-003/2016 Thiophene, tetrahydro-, 1,1- dioxide, 3-(C9-11-isoalkyloxy) derivs., C10-rich (EC No. 800-172-4) CCH-004/2016 5-methylhexan-2-one (EC No. 203-737-8) CCH-019/2016 Sodium sulphamidate (EC No. 237-572-8) CCH-023/2016 Calcium dipropionate (EC No. 223-795-8) TPE-003/2016 SDA Product (desulphurization of exhaust gases by semi-dry absorption method from the coal fired power plants) (EC No. 931-259-6) ECHA-S informed that due to a cease of manufacture one case was withdrawn from MSC decision making: CCH-024/2016 Penta-1,3-diene (EC No.207-995-2)	**MSC-S** to upload on MSC S-CIRCABC the final ECHA decisions of the agreed cases. **MSC** mandated **ECHA-S** to editorial changes to implement references to test guidelines and test methods, including their recent corrections, in case agreed and those in preparation for MSC, as well as editorial changes on defining duodenum instead of duodenum/jejunum.
Item 8 – ECHA's 7th draft recommendation of priority substances to be included in Annex XIV	
• Presentation by secretariat on summary of issues raised in public consultation • Work plan of MSC Rapporteur and Working Group for opinion drafting • Discussion on elements for the draft opinion on ECHA's 7th draft recommendation for Annex XIV	
MSC took note of the summary of issues raised in the public consultation and the review of the comments as presented by the Rapporteur.	**MSC** to consider any issues which they would like to flag to the Rapporteur and the WG from the comments and issues presented by 9 May 2016. **Rapporteur,** with support of the working group, to submit the first draft opinion for discussion at MSC-48.
Item 11– Adoption of main conclusions and action points	
MSC adopted the main conclusions and action points of MSC-47 at the meeting.	**MSC-S** to upload the main conclusions and action points on MSC S-CIRCABC by 29 April 2016.

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 number
SEV-SE-031/2013	Trimethoxyvinylsilane	220-449-8
SEV-IT-029/2014	Benzene, mono-C10-13-alkyl derivs., distn. residues	284-660-7

VII. Dossier evaluation cases addressed for MSC agreement seeking in WP

Draft decisions unanimously agreed by MSC in WP:

Compliance checks (CCH)

MSC ID number	Substance name used in draft decision	EC number
CCH-001/2016	N,N'-ethylenebis(3,4,5,6-tetrabromophthalimide)	251-118-6
CCH-020/2016	Potassium 1,2-bis(2-ethylhexyloxycarbonyl)ethanesulphonate	231-308-5
CCH-021/2016	3-ethoxy-4-hydroxybenzaldehyde	204-464-7

Testing proposal examinations (TPE)

MSC ID number	Substance name used in draft decision	EC or List number
TPE-015/2016	Octene	246-920-8
TPE-019/2016	Bis(2-chloroethoxy)methane 1,15-dichloro-3,5,8,11,13-penta-oxa pentadecane 1-(2-chloroethoxy)-2-(2-chloroethoxymethoxy)ethane	940-783-4