MSC/M/64/2019
Adopted at MSC-65

Minutes

of the 64th Meeting of the Member State Committee (MSC-64)

14-16 May 2019

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 64th meeting of the Member State Committee (MSC) (for the full list of attendees and further details see Part II of the minutes). The Chairman informed MSC that MSC Meeting will no longer be recorded from MSC-65 onwards.

Item 2 - Adoption of the Agenda

As regards the agenda the Chairman suggested including an item for discussion under item 6.4 on the status update of substance evaluation given the questions that the information document (slides from ECHA) had triggered. Based on requests from members the Chairman also suggested including any other business-items about reports commissioned by ECHA on the DNT/DIT cohorts, an update on the forthcoming Dutch workshop on possible triggers for these cohorts based on relationships between steroid hormones and developmental neuro- and immune-toxicity, and an update on the written comments received on the discussion document regarding the use of sterile controls in degradation simulation testing. The latter topic was suggested for a closed session. The Agenda was adopted with these modifications (final Agenda is attached to these minutes as Section III).

Item 3 - Declaration of specific interests to items on the Agenda

No potential conflicts of interests were declared by the Chairman, any members, experts or advisers with any item on the agenda of MSC-64.

Item 4 - Administrative issues

- *Refresher and update on ECHA's conflict of interest policy*

SECR provided to MSC a refresher on ECHA's conflict of interest policy explaining the main changes and highlighting that the main principles have remained unchanged.

- *Outlook for MSC-65*

The Chairman informed MSC that he has declared a specific interest on a substance likely to be on the agenda for MSC-65, and that the ECHA Executive Director has appointed a Chair and Co-Chair to replace him for the agreement seeking by MSC. The Chairman then presented an outlook on the potential length of the next meeting which is expected to require 3,5 plenary days. The Chairman also presented an early stage estimation for the length of the MSC-66 meeting in October 2019. One member raised a concern about the timing of the MSC referrals in summer. The Chairman noted this and informed MSC that he will arrange phone calls with members in July to see what possibilities there are to change MSC timings in the future and what the main hurdles would be.

- *Composition of MSC Working Group*

The Chairman reported as an outcome of written procedure that MSC had tacitly agreed to a change in the composition of the MSC Working group working on the 9th draft recommendation. This was a change of one of its members.

Item 5 – Minutes of the MSC-63 meeting

SECR informed the committee that the minutes of MSC-63 were adopted by MSC in written procedure and have been published in MSC S-CIRCABC and on ECHA's website.

Item 6 – Substance evaluation

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

SECR introduced the report on the outcome of the written procedure (WP) for agreement seeking on one substance evaluation (SEv) case (see Appendix to the final agenda in Section III for more detailed identification of the cases). WP was launched on 18 April 2019. By the closing date 29 April 2019, MSC reached unanimous agreement on this one SEv case.

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

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

SEV-DE-006/2017 Zinc oxide EC No 215-222-5

Session 1 (open)

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

The evaluating Member State Competent Authority (eMSCA) from Germany (DE-CA) presented the current status of this SEv case (SEV-DE-006/2017). The initial grounds of concern when placed on the Community Rolling Action Plan (CoRAP) were relating to the potential hazards of zinc oxide in nanoform and its wide dispersive use, consumer use and exposure of the environment. In the course of the evaluation, the evaluating MSCA identified additional concerns on Human Health - Insufficient justification for the applied read across/category approach with respect to most HH endpoints; Repeated dose toxicity (RDT): oral and inhalation route; Neurotoxicity; Genotoxicity of nano zinc oxide; Reproductive toxicity (fertility); Developmental toxicity and on potential additional effects on environmental organisms and different bioavailability of the nanoforms of zinc oxide.

MSC was guided by the experts from DE-CA through the information on the substance and through the proposals for amendment (PfAs) received from Member State Competent Authorities (MSCAs), ECHA, the Registrants' comments on the PfAs and the eMSCA's response to them.

Some of the PfAs submitted were accepted by the eMSCA and led to an amendment in the DD in advance of the meeting. The MSC agreed with these amendments and discussion focused on the unresolved PfAs.

In the registration dossier the registrants proposed a category approach for i) Zn-salts, ii) microsized (bulk) ZnO, iii) coated ZnO in nanoform (nano ZnO) and iv) uncoated nano ZnO, based on the assumption of toxicological equivalency of these zinc compounds/forms of ZnO, as they proposed that their toxicity is only driven by released zinc cations (Zn^{2+}) (in the following called 'ion-only hypothesis'). However, for ZnO nanoforms no evidence for this assumption was provided other than water solubility data and results of bioelution studies on some ZnO nanoforms.

The DD notified to the MSCAs had a total of eight requests – three human health related requests, one physchem request, three environmental requests and one exposure request, all on nanoforms of the zinc oxide.

The PfAs received on the three human health requests were resolved in advance of the meeting leading to the removal of one of the three requests, i.e. request for OECD TG 422 was removed but the request for OECD TG 413 was combined with a study according to OECD TG 421.

Request 4 asked for information on transformation, dissolution and dispersion stability of the manufactured and imported nanoforms of zinc oxide that are covered by the registration dossier by performing a 24 hour screening test (4a) as per OECD GD 29 TDp

and further on an OECD TG 318 test (4b). This request was to enable the Registrants to group nanoforms based on these parameters and select nanoforms with which they shall perform the environmental toxicity tests.

One of the PfAs proposed to delete the dissolution and dispersion stability request and the three environmental toxicity study requests. Such information requests (4a and 4b) will become standard information requirements for any substance in nanoform once the REACH annexes for nanomaterials enter into force. However, in case the environmental requests (4.b) remain, a text was proposed to respond to the Registrant's comment that the request for OECD TG 318 seemed to be a research issue. Furthermore, the PfA argued that the environmental toxicity requests did not appear proportionate in relation to the planned risk management measures as zinc oxide already appeared to have the strictest harmonised classification as aquatic acute 1 and aquatic chronic 1. Specifically the importance for the derivation of the M-factor for this substance was not clearly expressed in the decision; and 2) for reasons of legal certainty, which and how many nanoforms are to be tested should have been specified.

One of the three environmental toxicity study requests (fish testing) was removed from the DD in advance of the meeting, based on PfAs received, which MSC agreed to.

On request 8 asking for information on supported use conditions and characteristics of the nanoforms in their different uses, one of the PfAs proposed to delete this request as: 1) it appeared wide and imprecise; 2) it may go beyond the control of the Registrants; 3) the recommendations included in this request appeared not to be enforceable and 4) it was not clear if the information requested was needed to conclude on the need for regulatory risk management actions.

The Registrants submitted written comments on the PfAs, the main points of which they reiterated during the MSC meeting by the Registrants representatives.

Regarding requests 4a and 4b the Registrants supported the PfA to delete both requests. They planned to conduct the request 4a on all EU marketed forms of nano zinc oxide during 2019 to anticipate completion of the registration files. They requested for the dispersion stability test to be carried out at environmentally relevant pH 7.6 but only if request 4b stays in the decision. They further explained their view that dissolution TG 29 of nanomaterial provided a worst case, and that the results of the additional dispersion test (TG 318) would have limited value for predicting the fate of nanoparticles during a chronic ecotoxicity test. Furthermore, performing the dispersion test at three pHs would require a very high number of samples. An industry stakeholder representative suggested that if the transformation, dissolution demonstrates that the nanoforms dissolve very quickly and completely then the dispersion test (TG 318) is completely irrelevant hence not needed therefore the requests could be performed in a tiered way.

The Registrants supported the PfAs to delete the environmental toxicity requests. They argued there was no reason for testing from a risk management view due to the, in their view, very large ecotox data sets on the worst case soluble zinc forms and that the current observed difference in toxicity between the nanoform of zinc oxide and the zinc ion is a factor of 2. Any change in M-factor would, however, require a factor of 10. If environmental toxicity requests would remain the Registrants suggested to conduct ecotoxicity testing on algae and invertebrates, as fish were proven to be less sensitive to Zn^{2+} ions.

Regarding request 8, the Registrants supported the PfA proposing its deletion. The Registrants' representatives explained that they received some information on uses during the last year and they intended to update the dossier with that information.

The PfA submitter proposing to delete the environmental requests explained, after having heard the discussions, that they could support the environmental requests provided the concern was sufficiently justified and streamlined in the decision.

The registrants confirmed general agreement with the Human Health requests but indicated few unclear specificities on test conditions. They recognised that such are outside the PfAs and hence outside the scope of the MSC discussion.

Session 2 (closed)

Regarding the transformation, dissolution and dispersion stability study, MSC acknowledged that the REACH Annexes will be updated in January 2020 making these obligatory information requirements for nanoforms. As at the time of the decision making phase this was not yet a legal obligation under REACH, MSC agreed to request this information. With regards to the suggestions of conducting the study in a stepwise manner, it was recognised that there was no PfA in this regards which would allow introduction of this change in the decision. With regard to the M-factor, MSC acknowledged that a possible risk management measure as a consequence of the information requests in this decision would be derivation of higher M factors than those currently used for specific ZnO nanoforms. It was agreed to further explain in the decision text why M-factor matters in terms of further risk management.

Regarding the choice of pH for the dispersion stability test according to OECD TG 318, MSC discussed whether the Registrant could perform the test at only one pH (7.6) as they requested. The MSC acknowledged that the aim of the request 4a and 4b was to identify similarities and differences of the registered ZnO nanoforms allowing to group the nanoforms with respect to their behaviour under environmentally relevant conditions. Besides grouping, the information on all pHs (including pH 4 and pH 9) is also relevant to extrapolate results from the environmental toxicity studies to all (groups of) nanoforms covered by the registration. Hence MSC concluded to leave the request for the dispersion part of the test in accordance with OECD TG 318 i.e. requesting 3 pHs. As the OECD TG 318 states that the extended test does not need to be performed for those nanoforms which show either low dispersion stability or high dispersion stability under all conditions of the screening test, this could potentially reduce the number of samples needed for this test.

The text of the decision was further clarified with regard to the testing conditions of dispersion stability.

Regarding the test material for the environmental requests, MSC agreed that a maximum of 3 nanoforms based on request 4.a. and a maximum of 3 nanoforms based on request 4.b. are to be tested. Hence the test substance for each request is the nanoform of zinc oxide a) with the highest, lowest and a mean dissolved Zn^{2+} concentration based on the results from the 24 hr screening test and b) one representative nanoform from the sets of nanoforms with low dispersion stability, high dispersion stability and with condition-depending dispersion stabilities based on the results from OECD TG 318. Regarding the exposure request, the PfA submitter proposing its removal, explained that it had discussed in advance of the MSC meeting with the eMSCA and that they now understood that the request is not wide and imprecise, what the further risk management measures could be, and that the request does not go beyond the control of the Registrant. The PfA submitter could therefore accept the amendments to the decision text proposed by the eMSCA. The same applied for the revision of the text related to the environmental requests.

The MSC unanimously agreed on the decision as further amended in the meeting.

SEV-FR-004/2017 Potassium titanium oxide ($K_2Ti_6O_{13}$) EC No 432-240-0

Session 1 (open)

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

The evaluating Member State Competent Authority (eMSCA) from France (FR-CA) presented the current status of this SEv case (SEV-FR-004/2017). The initial grounds of concern when placed on the Community Rolling Action Plan (CoRAP) were relating to carcinogenicity and exposure of workers. In the course of the evaluation, the evaluating MSCA identified additional concerns on exposure of the general population and potassium titanium oxide toxicity on sediment-dwelling organisms.

MSC was guided by the experts from FR-CA through the information on the substance and through the proposals for amendment (PfAs) received from Member State Competent Authorities (MSCAs), ECHA, the Registrants' comments on the PfAs and the eMSCA's response to them.

Some of the PfAs submitted were accepted by the eMSCA and led to an amendment in the DD in advance of the meeting. The MSC agreed with these amendments and discussion focused on the unresolved PfAs.

The human health concern about this substance stems from its potential to be produced in a fibrous form, which gives rise to a classification as Carc 2. Fibres expected to raise the highest concern regarding carcinogenicity are fibres fulfilling the WHO definition in length, diameter and aspect ratio. The requests for human health (1) and exposure (2) were relevant if there is an exposure potential to WHO fibres either through the presence of WHO fibres in the registered compositions or through possible formation of WHO fibres during handling and use. Hence the draft decision contained an exemption from conducting the requests 1 and 2 for Registrants with registered compositions that contain less than 1% w/w of WHO fibres and which do not generate WHO fibres above 1% w/w.

Request 1 asked for a subchronic inhalation toxicity 90-day study (OECD TG 413) with WHO fibres of the registered substance to be performed in rats via the inhalation route with additional specifications, and integration of an OECD TG 489 (*in vivo* mammalian alkaline comet assay) with specific modification to detect oxidative stress. PfAs received proposed 1) to apply additional parameters in case the test material includes a significant portion of granular particles which would also induce lung fibrosis when administered in high concentrations; 2) to specify the inclusion of a recovery group in request 1, as it is not a default requirement for OECD TG 413; 3) to clarify whether the recovery group is also subject to the comet assay and 4) to specify that OECD TG 413 is to be performed by nose only inhalation to prevent ingestion of test material through grooming.

Some PfAs proposed alternative ways to conduct the testing. One proposal was to request for two separate OECD TG 413 and OECD TG 489 studies, due to the possible technical challenges associated when combining both tests. Another proposed a long term (2 years) intraperitoneal (IP) animal model to discriminate between effects of granular particles and fibres. In their view the IP test is relatively cost-effective, simple to perform, sensitive to detect a fibre-like carcinogenicity and a large number of fibrous materials have been tested in this assay. If the IP test would be requested it was proposed to set the deadline to 45 months.

Another PfA on request 1 proposed to delete the request due to uncertainties on what was to be tested and concerns that the results would be uninterpretable and instead, as a first step, ask the registrant to provide the composition of their registered substance and the dustiness test (as specified in the exemption conditions), and to report the presence of WHO fibres at 0.1% w/w. As a follow-up the eMSCA might then either prepare a CLH proposal for Carc Cat 1B if appropriate or if animal testing were to be required a different study might be more appropriate taking into consideration the characteristics of the substance.

Regarding the test material, a PfA proposed to clarify: i) the selection of test material if the exemption criteria listed in the DD are not met, and ii) what constitutes a "sufficient amount of WHO fibres" in the test material.

Regarding the threshold to conduct the fibre-related requests, a PfA proposed to use a WHO fibre content of 0.1% (based on classification as Carc. Cat. 1) instead of 1% (based on classification as Carc. Cat.2).

Request 2 (on exposure) asked for characterisation of the risks related to potassium titanium oxide fibres covering the use of the substance in brake pads through fibre-specific exposure assessment, and the derivation of a fibre-specific DNEL and a fibre-specific RCR. One PfA proposed to remove this request as this was already an obligation of the registrants to comply with the information requirements of Annex I of REACH. Furthermore, the option under this request to test brake pads in a brake dynamometer

assay could be beyond the Registrants' control since Registrants cannot oblige their downstream users to provide specific data related to their products. Additionally, it was insufficiently clarified how the testing should be performed to be representative of the variety of brake pads in the market.

Request 3 asked for a long-term toxicity to sediment organisms (OECD TG 225) with the registered substance. A PfA proposed to delete this request, as it was considered i) premature and ii) better to wait for the results of the ongoing chronic aquatic ecotoxicity tests with the parent substance. Furthermore, if the request was kept it proposed to clarify the level of environmental exposure, from which substance (parent, ion) and why this is of concern.

Another PfA proposed to explain the approach taken to calculate the tiered deadline.

The Registrants submitted written comments on the PfAs, the main points of which they reiterated at the meeting. The representatives of the Registrants presented few slides to characterise the different types of fibres, introduce their complexities, and explained the substances on the market.

Regarding request 1 the Registrants proposed to either remove from the DD the exemption related to non-fibrous forms of the substance or keep the existing exemption with a threshold of 1% WHO fibres, while disagreeing with the 0.1% threshold. They preferred that all the addressees are involved in the inhalation study (considering that all Registrants acknowledge to have fibrous materials on the market at the moment) and considered it more appropriate to have the possibility for an exemption in a later stage e.g. if the carcinogenicity study would be requested.

The Registrants agreed to characterise the different (sub)forms of the substance before starting the testing. They also agreed to test the substance fibrosity based on both thresholds of 0.1% and 1%. Furthermore, they asked to have the most appropriate technique for measuring the fibre amount clarified and unequivocally identified.

Following the results of the materials characterisation, the Registrants requested a meeting with eMSCA to agree on the fibre size and all the relevant parameters of the test material, before performing the 90 day inhalation study, as the fibre size requested does not match with all the real fibre length. Due to the uncertainties associated with combining the 90 day study with the comet assay, the Registrants requested for a detailed protocol to be also discussed with the eMSCA after obtaining the results of the materials characterisation. Regarding the proposed alternative long term test with IP application, the Registrants did not oppose.

Regarding request 2, the Registrants agreed with the PfA to remove the request. They intend to update the CSR to the best of their knowledge while at the same time improving and merging the different dossiers into a single consolidated joint registration dossier.

Regarding request 3, the Registrants agreed with the PfA that the request was premature. They clarified that at the time of the meeting they were testing both daphnia and fish chronic toxicity with the parent substance.

The Registrants in their comments on the PfAs requested for an extension of the deadline from 30 months to 39 months. The extra 9 months were to be able to carry out the characterisation of the different subforms of the substance.

During the discussion the eMSCA expert explained that considering the PfAs received and the comments of the Registrants on the PfAs they suggested to revise the requests, by first requesting characterisation of the fibres. They also suggested to remove the exemption criteria from the DD and replace it with a condition setting a threshold of WHO fibre content of 0.1% (based on classification as Carc. Cat. 1) to conduct the fibre-related requests. Such a condition would make the request in the DD more proportionate.

MSC discussed which is the better test material: either a substance longer than 20 µm standard length (as described in the EC guideline for subchronic inhalation toxicity testing of fibres (JRC, 1999)) or a realistic fibre length which is shorter than the 20 µm standard length. In this regards the representatives of the Registrants re-emphasised the

importance to discuss with the eMSCA the results of the characterisation of the fibres before proceeding with the testing.

Regarding the exposure request the PfA submitter that proposed to delete this request explained that they collaborated further with the eMSCA on the text of this request to improve its clarity, define the terminology used and more clearly set out the obligations.

Regarding request 3, the eMSCA expert explained that in their view using the aquatic toxicity information to derive the sediment toxicity information with the equilibrium partitioning method (EPM) is not applicable for poorly water soluble substances for which no effects are observed in aquatic studies. Consequently, the EPM cannot be used to derive the $PNEC_{sediment}$ screen. However, some MSC members argued that the ongoing aquatic tests could give information on whether metal ions are released, hence still seeing merit in waiting for the results of the ongoing tests before deciding on a request for toxicity tests in sediment dwelling organisms.

Session 2 (closed)

MSC agreed with the revisions of the DD suggested by the eMSCA on the new order of the test requests. Regarding the testing material, the DD was revised providing recommendations on the number of fibres and maximum gravimetric concentrations to be applied, as far as technically possible, specifying that the test material shall contain a sufficient number of fibres with the highest range of length that can be generated. MSC also supported the request of the Registrant to have a meeting with the eMSCA after the completion of request 1 (the WHO fibre content characterisation of the substance) to provide contextual clarification that may be useful for determining the appropriate test material when performing request 2 (inhalation 90 day study with integrated comet assay).

Regarding the exposure request (request 3), MSC agreed with the revisions of the DD suggested by the PfA submitter and the eMSCA.

Regarding the environmental request the eMSCA and MSC agreed to remove it from the DD.

The MSC unanimously agreed on the decision as further amended in the meeting.

4. General topics

The SEv Status Report was provided to MSC as an information document prior MSC-64 with the aim of not being presented at the meeting. Few members raised some questions for clarification in writing prior to MSC-64 which were addressed at the meeting.

Item 7 – Dossier evaluation

1. 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 seven dossier evaluation cases (see Section III Final agenda "Appendix to the MSC-64 agenda" for more detailed identification of the cases). WP was launched on 18 April 2019. By the closing date 29 April 2019, MSC reached unanimous agreement on all DDs. One MSC member abstained from voting on four cases and another MSC member who abstained from voting on one case requested to include the note on the abstention in the annex of the written procedure report.

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

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

TPE-017/2019 Bis[O,O-bis(1-methylethyl)phosphorodithioato-S]bis(cyclo-hexanamine)zinc (EC No. 809-986-4)

TPE-018/2019 Methanal, reaction products with 1,3-bis(aminomethyl)benzene and hydroxybenzen (EC No. 701-207-5)

TPE-019/2019 5-Methoxy-2-tetralone (EC No. 457-080-9)

TPE-020/2019 Tetraammine platinum (II) hydrogen Carbonate (EC No. 426-730-3)

TPE-021/2019 Tetraammineplatinum (II) diacetate (EC No. 457-310-8)

TPE-022/2019 Tetraammineplatinum dinitrate (EC No. 243-929-9)

TPE-023/2019 Tetraammineplatinum dichloride (EC No. 237-706-5)

Session 1 (open)

MSC agreed to the Chairman's suggestion to first discuss all seven cases of testing proposal examination (TPE) grouped in three open sessions, after which MSC would further discuss all cases in its closed session. The motivation for this approach was that the same proposal for amendment (PfA) on mutagenicity had been submitted for all seven TPE cases.

TPE-020/2019, TPE-021/2019, TPE-022/2019 and TPE-023/2019

Session 1 (open)

Two representatives of the Registrants participated in the initial discussion concerning all four TPE cases. In absence of specific confidentiality concerns in the DDs, an open session was held.

SECR introduced the proposal for amendment (PfA) on mutagenicity that required discussion in the meeting. The same PfA on the *in vivo* mammalian alkaline comet assay (OECD TG 489) had been submitted for all seven TPE cases. The PfA suggested requesting (a) to prepare slides from single cell/nuclei suspensions from gonadal tissues and store them for up to five years; (b) to analyse slides in case a positive result is obtained from any of the somatic tissues; and (c) to explain that a negative or inconclusive result in whole gonads cannot be used to conclude on the germ cell genotoxicity as the sensitivity of the comet in gonadal cells has not been validated to detect germ cell genotoxicity.

The Registrants had submitted written comments on the PfAs and MSC duly considered them in its discussion.

The representatives of the Registrants of the four TPE cases agreed to carry out the requested comet assay to fulfil the existing data gap. They explained that the PfA had raised issues mainly on storing slides of gonadal tissue for up to five years, because sample quality could be guaranteed only for several weeks, in line with information from some contract research organisations (CRO) they had contacted. Additionally, they noted that such an approach has not been agreed on at international level. They agreed in principle to the aim of using gonadal tissues to avoid potentially unnecessary animal testing, but that the benefits would materialise only when the sample quality was guaranteed.

The MSC took note of the limitations of storage length and tentatively agreed that in comet assay two months would be acceptable for storing gonadal tissues, which could then be inspected in case of a positive result from the somatic cells.

TPE-019/2019

Session 1 (open)

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

SECR introduced the proposal for amendment (PfA) on mutagenicity that required discussion in the meeting. The same PfA on the *in vivo* mammalian alkaline comet assay

(OECD TG 489) had been submitted for all seven TPE cases (see previous group of four TPEs).

The Registrants had submitted written comments on the PfAs and MSC duly considered them in its discussion.

The representative of the Registrant reiterated the disagreement with the PfA, reasoning that the preparation of slides with gonadal tissue was deemed technically and scientifically unjustified, and reminding that the use of the testing outcome for classification was still under discussion. The representative of the Registrant further argued that, in their practical laboratory work, they had not been able to successfully implement the comet assay on gonads; that the analysis of gonadal tissue was not included in the current OECD protocol (OECD TG 489) nor was technical guidance available for e.g. timing and positive control aspects; and that an industrial chemical to be tested was rarely as potent as a control chemical which could lead to difficulties in detecting effects. The representative of the Registrant also informed that they had shared their technical experiences with OECD; welcomed benefiting from other work in implementing gonadal examinations; concluded that currently the outcome of analysing gonadal tissue was not reliable; and foresaw, in absence of a well-established protocol, no further insights to be gained performing gonadal analysis in the comet assay.

The MSC took note of some further remarks from the representative of the Registrant, including that isolating germ cells from gonad sample might be challenging; that there were difficulties for detecting weaker mutagenic substances due to the high background noise, which may prove even more challenging in mixed somatic and germ cells; and that sperm cells at the last stage of maturation contained highly condensated DNA which, when decondensating the DNA for examination, could lead to additional breaks in the DNA, possibly affecting the analysis of the % of tail DNA in the comet assay.

MSC welcomed to hear more on practical experiences from other laboratories, if possible, because a large pool of such information would be helpful in further assessment of the approaches on mutagenicity testing.

TPE-017/2019 and TPE-018/2019

Session 1 (open)

No representatives of the Registrants participated in the initial discussion. In absence of specific confidentiality concerns in the DDs, an open session was held.

SECR introduced the proposal for amendment (PfA) on mutagenicity that required discussion in the meeting. The same PfA on the *in vivo* mammalian alkaline comet assay had been submitted for all seven TPE cases (see previous group of four TPEs).

The Registrants had not provided any written comments on PfA.

The MSC noted that there were no further aspects to be discussed in the open session on these two TPE cases.

TPE-017/2019, TPE-018/2019, TPE-019/2019, TPE-020/2019, TPE-021/2019, TPE-022/2019 and TPE-023/2019

Session 2 (closed)

The MSC took note of the information provided by case owners on possibilities for storing gonadal cells and their practical experiences.

The MSC considered that the scientific understanding and the still limited technical experience would support only to recommend analysis of gonadal cells in the comet assay, in case of positive result from somatic cells. The MSC welcomed to learn more from other laboratory experiences and suggested that future work could cover validating a protocol and guidance on gonadal cells and reducing background noise.

The Chairman suggested that the MSC should first discuss the general approaches on mutagenicity testing, reported in these minutes in section I.4.1, before returning to

agreement seeking on the seven TPE cases. After the general discussion the MSC decided to keep the request unchanged in the DDs of all seven TPE cases, that is, to only recommend the Registrant to consider examining gonadal cells in the comet assay.

The MSC agreed unanimously to the DDs of all seven cases as provided for the meeting.

4. General topics

1. Request of *in vivo* mutagenicity testing on germ cells under compliance check of Annex IX or X dossiers – implementation options (closed session)

ECHA Secretariat (SECR) presented the background document on scientific and regulatory aspects of mutagenicity testing as well as practical implementation options.

The MSC first took note of the current practice in requesting studies on the concerns on mutagenicity. The requests give the Registrant a choice between comet assay (OECD TG 489) and transgenic rodent (TGR; OECD TG 488) assay to follow-up on a concern for gene mutation. The comet assay comprises a request to collect and analyse somatic cells from several tissues and a recommendation to consider examination of gonadal cells in case of positive results on somatic cells. The TGR assay comprises a request to collect and analyse somatic cells from several tissues, a request to collect and store germ cells, and a recommendation to analyse germ cells in case of positive results on somatic cells. Also, the MSC noted that if the concern was on chromosomal aberration, the available tests are comet assay, micronucleus (MN) test on erythrocytes (OECD TG 474), chromosomal aberration test on erythrocytes (OECD TG 475) and chromosomal aberration test on spermatogonia (OECD TG 483).

The MSC then took note of various possibilities to approach mutagenicity testing, including the experience in dossier evaluation on results of ca. thirty comet assays performed following ECHA decisions and assessed under the follow-up process: three of the thirty comet assays provided positive results on somatic cells but no data was provided on gonadal tissue, in spite of the recommendation included in the decision; however, gonadal tissue had been sampled and analysed after one negative result on somatic cells, and provided negative results. SECR informed that it has flagged the three cases with positive somatic cell results for follow up. Furthermore, the MSC noted that, in general, there is a legal requirement (according to Annex IX and X, 8.4., column 2, second paragraph) to have all available data examined after positive genotoxicity results on somatic cells and before potential follow up.

The Chairman received information from a few RAC members on the types of considerations of the Risk Assessment Committee (RAC) when assessing classification proposals for mutagenicity, which suggests that the availability of positive *in vitro* studies and of positive *in vivo* comet assay on gonadal tissue could support considerations for classification as Muta 1B; therefore, the MSC should follow the development of RAC opinions on classification proposals which use information stemming from *inter alia* comet assays. The MSC confirmed that the examination of gonadal cells in comet assay was not yet validated and that, until further notice, it was therefore uncertain how it contributes to a classification assessment.

The MSC noted that after analysis of the data provided by a Registrant in case of a positive somatic cell result, there should be a possibility to request a TGR assay on germ cell mutagenicity or a chromosomal aberration test on spermatogonia in a separate compliance check (CCH). The MSC expressed concern that if the comet assay was negative on gonadal cells the result could not be deemed conclusive in terms of genotoxicity on germ cells due to several uncertainties in the test protocol and the interpretation of the test results. The MSC deemed it important, for now, to keep the obligations in the two alternative tests in balance as much as possible, that is, to have a request on somatic cells and a recommendation on gonadal tissue and germ cells (with the exception that currently in TGR assay the germ cells shall be collected and stored for up to five years).

The MSC took note that for the TGR assay there is an ongoing revision of the OECD TG 488 on sampling timing to be changed from 28+3 days to 28+28 days, as default design

for mouse germ cells; the change is not yet formally adopted by OECD, although it seems scientific consensus has already been reached. Based on this probable change in the TGR recommended protocol, it was proposed that MSC should consider to request, instead of recommend, germ cell analysis in case of a positive somatic cell results in the TGR.

Regarding the requirements in REACH Annexes IX and X, the MSC noted that both at Annex IX and X the comet assay can be followed up with the TGR assay on germ cells when somatic tissue results are positive in the comet assay and if the Registrant had not followed up by examining gonadal tissues.

The MSC re-affirmed that the primary aim of the *in vivo* mutagenicity requests is to confirm that effects observed *in vitro* can occur also in an *in vivo* biological system, although the results could be used in other assessments (for example, classification for Muta 1B). Furthermore, MSC expressed preference for unambiguous requests and decisions to avoid describing complex scenarios. It was suggested that a slightly longer timeline with separate follow up decision could prove a beneficial approach.

The MSC concluded, for now, (a) to continue giving a choice between comet assay and TGR assay (in case gene mutation is the concern); (b) to continue only to recommend gonadal examination in comet assay; (c) to continue to request somatic cell examination and germ cell collection and storing in TGR assay; and (d) to consider the approach applicable to both CCH and TPE cases.

The MSC agreed, in spite of its interim conclusions above, to review in its MSC-65 meeting the regulatory options on requesting further mutagenicity testing on germ cells or gonadal tissues and requested SECR to prepare an analysis on the benefits and disadvantages of different options in order to come to an informed decision which option to follow for future CCH and TPE cases.

2. Brief report and learnings from follow-up stage of dossier evaluation decisions

SECR provided a brief report to MSC on the learnings from follow-up stage of dossier evaluation decisions. It was explained that in the majority of cases (well over 1000 cases now assessed/examined) the registrants comply with ECHA decisions and the information requirement is considered fulfilled. SECR shared examples of cases where the request in the decision had not been met and shared some learnings from those. Members appreciated the opportunity to learn from ECHA's experience and they raised questions with the aim to gain more knowledge and understanding. This discussion touched among others on decisions where a read-across had been rejected, or where characterisation and stability of test material had been an important aspect. An observer also raised issues related to UVCBs where variability of test material should also be accounted for e.g. in the time needed for the testing and proper reporting.

3. Dossier evaluation categories planned for the MSC-66 and MSC-67 MSCA consultations – a brief introduction *(closed session)*

SECR gave a presentation that focused on the categories planned for the upcoming MSCA consultations. MSC was informed on which categories are expected, the approach taken by ECHA with regard to the read across proposed by the registrants, and the support available to the Member State Competent Authorities (MSCA) to facilitate their review of the draft decisions. One MSC member highlighted the need of the MSCAs to be informed of all relevant considerations made by ECHA in the assessment of the categories. The possibility for having some further informal interactions on specific categories was welcomed.

Item 8 – SVHC identification

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

Not relevant for this meeting

2. General topics

Reflections on new combinations of properties that may be considered of Equivalent Level of Concern under Art. 57(f)

SECR provided a presentation for MSC to gain further understanding of case-by-case assessments of Equivalent Level of Concern (ELoC). It specifically addressed possible elements of concern based on certain substance properties, which might not have been considered until now, or combinations of possible elements of concern leading to an overall concern. It emphasised that ELoC is to be considered an equivalence assessment in relation to the overall concerns addressed in paragraphs a to e of Art. 57, and that paragraph f is intended to function as a safety net. There were many interventions, both by members and stakeholders, and the discussion raised issues on i) the method how to assess the level of concern qualitatively and hence derive the ELoC argument, ii) the role of toxicity as a concern element and iii) whether Art 57(f) is to be used as a safety net with case-by-case decision making or if a more general framework with decision making criteria should be developed first. Regarding very persistent and mobile substances some more detailed interventions were made about comparability of those concerns and the concerns for PBTs and vPvBs. Some speakers referred to the importance of RMOA as the first step which then also serves as the confirmatory stage that the planned risk management route is the most appropriate one. In that context for a group of substances use of a consistent approach was suggested.

In closing SECR acknowledged that more work is needed on different concern elements how those are combined into an overall concern, and how this is used in the ELoC assessment. For now SECR considered case by case assessment as a way to proceed and gain experiences. SECR thanked for the good and constructive general discussion which also served as a preparatory step for the ELoC discussion on a substance to be referred to MSC for decision making at MSC-65 (June).

Item 9 – ECHA's recommendations of priority substances to be included in Annex XIV and opinion of MSC

1. 9th Draft recommendation for inclusion of substances into Annex XIV

Update from SECR on the progress made, including LAD assignment proposal

SECR provided an update on the work carried out since the previous plenary. It was reiterated that, since the process was reviewed and revised last year, MSC has now for the first time received so called post public consultation assessment documents (provided end of March) in which ECHA provides its initial assessment regarding the impact of the registration updates and comments submitted in the public consultation to the draft recommendation, and which keep evolving. In addition, MSC had received before the meeting the draft responses to the comments as working versions as supporting documents. SECR then introduced the main changes it considers to the recommendation, and highlighted few specific issues per (group of) substance(s) with a conclusion that for the time being all the 18 substances remain as foreseen to be recommended for the inclusion to Annex XIV.

The member from Norway informed that her country has made a notification to the secretariat of the Stockholm convention on Persistent Organic Pollutants (POPs) for proposing Dechlorane Plus as a POP. Later in the year (October) the POPs review committee may consider the Norwegian proposal. She mentioned that the substance is on their national priority list, and hence they have agreed to reduce any exposures to a minimum. SECR thanked for this information but felt it was too short notice to assess if this would have any impact on the inclusion of the substance to the ongoing recommendation.

Other issues raised for discussion as regards prioritisation were grouping of lead stabilisers where industry challenges inclusion of lead oxide sulfate into the group of stabilisers; use

of HHPA and MHHPA as an intermediate; and presumed double-counting of volumes for DOTE and the reaction mass of DOTE/MOTE. Acknowledging that lead oxide sulfate is currently not registered for the use as stabiliser (as stated in the draft background document provided at start of public consultation), SECR explained that the substance was however in the past registered for that use. Therefore, there is the possibility that lead oxide sulfate could be used as stabiliser in PVC and that this possible interchangeability is the reason to keep the substance in the group of stabilisers. In relation to (M)HHPA SECR responded that it does not agree with claims of certain uses as intermediate, and hence the volume and wide dispersive use scores remained unchanged in its assessment. As regards the uncertainties on volumes for DOTE and reaction mass of DOTE/MOTE respectively, SECR noted that the uncertainty on how to interpret registration information had been highlighted already in the document provided for public consultation. SECR reassured that all information made available during the public consultation was used to re-assess the priority of the substances. SECR noted that some registrations are still unclear with regards to the tonnage relevant to each substance and in this case, reasonable worst case assumption had to be made.

Also requests for exemptions under Art. 58(2), including the impact of the upcoming restriction of lead stabilisers in recycled PVC and the use of tetraethyllead in aviation fuel referring to aviation law, were briefly discussed.

Draft opinion of MSC

The Rapporteur presented the draft MSC opinion on the 9th draft ECHA recommendation for inclusion of priority substances in Annex XIV and highlighted few topics and wording options for further reflection. With regards to the question whether a higher priority score for tetraethylead due to professional uses is justified members expressed diverging views. Following on from the previous discussion (above) some members felt that the question whether the conditions for an Art. 58(2) exemption for the use of tetraethyllead in aviation fuel (additive) could be met was unclear and were fine to invite COM to look into this in more detail, in line with what SECR had also expressed. Regarding the question whether the restriction proposal for the use of lead stabilisers in PVC should be used as a basis for disregarding the service life of articles from the prioritisation and for supporting exemption requests under Art. 58(2), as proposed by SECR, those that intervened were hesitant to consider this upcoming restriction since its exact content and stage were not known.

MSC was invited to submit further written comments to the Rapporteur so that she could then further develop the draft opinion for discussion and adoption at MSC-65 in June.

2. Draft recommendation to amend entries of DEHP, BBP, DBP, and DIBP in Annex XIV

Update from SECR on the assessment of potential impact of the comments from public consultation and Draft opinion of MSC

SECR reminded MSC about the basis for its draft recommendation to amend the Annex XIV entries of the four phthalates, and what the foreseen implications of adding the endocrine disrupting properties to Annex XIV entries of REACH are. SECR had assessed all comments received from two public consultations held on this issue (the first consultation was held on behalf of COM) with regard to their impact on the draft amendment and presented those to MSC.

The Rapporteur presented the draft MSC opinion on the 1st draft ECHA recommendation to amend existing entries of 4 phthalates in Annex XIV. He noted that the draft was prepared based on the amendment recommendation and the comments from the public consultations.

The discussion focussed on exemption requests based on Art. 58(2) mainly in the context of ROHS, and whether it provides basis for an exemption, and uses in immediate packaging of medicinal products. An occasional stakeholder observer argued that one should follow the general legal principle that specific legislation (i.e. ROHS) overrides general legislation (REACH). SECR indicated that further draft responses and the so-called

ComRef-documents will be made available in early June. The Rapporteur invited MSC to submit any written comments so that he could finalise the draft opinion for discussion and adoption at MSC-65 (June).

Item 10 – Any other business

1. Update on appeals and court cases of relevance to MSC (partly closed session)

SECR gave an overview of the status of recent appeals on evaluation submitted to the Board of Appeal of ECHA and cases submitted to the European Court of Justice. MSC took note of the information received. MSC shortly discussed the acrylamide Court case and its impact of ECHA's interpretation on intermediates, while awaiting a more definitive interpretation by the Commission. SECR indicated that priority scores would not change significantly.

2. Interact information session and introduction of its features to the users

SECR explained the scope of the first release of the IT tool Interact and its collaboration module. The Committee was informed of the established access rights and how the tokens will be distributed and used.

3. Suggestions from members

a. EOGRTS Workshop update

The Chairman of the Organising Committee of the EORGTS workshop, which is to take place on 8-9 October 2019 at ECHA premises, informed MSC that the workshop will focus on the association of sex steroid hormonal activity with developmental neurotoxicity (DNT) and developmental immunotoxicity (DIT). Second aim of the Workshop is to discuss the quality of evidence that can be used to trigger the DNT/DIT cohorts. The Chairman of the EORGTS Workshop invited MSC and the Commission to attend with as many experts as possible noting the importance for MSC and the need to reach a conclusion. He informed MSC that the invitations and programme of the Workshop will be circulated by the end of May 2019.

b. DNT/DIT reporting

SECR presented the status of two reports on the extended one-generation reproductive toxicity study (EOGRTS) and its cohorts, which ECHA commissioned in 2018. The reports have been finalised and are used for ECHA's internal assessments of the possible role of sex steroid hormones as triggers. The reports will not be made publically available as some elements could be further augmented with additional perspectives to provide a more complete overview. SECR has made the reports available to the Member State experts of the past Advisory Group on EOGRTS and it intends to make the reports available for the forthcoming Dutch workshop on the topic. The MSC welcomed the intended targeted distribution of the reports. The MSC members or their experts attending the forthcoming Dutch workshop on EOGRTS were encouraged to review the reports and consider where their coverage should be broadened.

c. Sterile controls

The Chairman informed on the status and next steps foreseen in the work on sterile controls as related to requests on simulation tests (OECD TG 307/308/309) under dossier and substance evaluation. The MSC welcomed the status update and foresaw to receive further details on this topic in a forthcoming MSC meeting.

Item 12 - Adoption of main conclusions and action points

Table with conclusions and action points from MSC-64 was adopted at the meeting.

II. List of attendees

Members/Alternate members
AAVIK, Jaanika (EE)
ALMEIDA, Inês (PT)
ANDRIJEWSKI, Michal (PL)
ATTIAS, Leonello (IT)
COCKSHOTT, Amanda (UK)
CONWAY, Louise (IE)
COPOIU, Oana (RO)
DE KNECHT, Joop (NL)
DIMITROVA, Rada (BG)
DUNAUSKIENE, Lina (LT)
FERNANDEZ SANCHEZ, Raquel (ES)
FINDENEGG, Helene (DE)
HERMES, Joe (LU)
HJORTH, Rune (DK)
HORSKA, Alexandra (SK)
HUMAR-JURIC, Tatjana (SI)
JANTONE, Anta (LV)
KREKOVIĆ, Dubravka (HR)
KULHANKOVA, Pavlína (CZ)
LE, Elisa (FR)
LUNDBERGH, Ivar (SE)
REIERSON, Linda (NO)
RISSANEN, Eeva (FI)
STESSEL, Helmut (AT)
VANDERSTEEN, Kelly (BE)
Representatives of the Commission:
KOBE, Andrej (DG ENV)
Observers
DROHMANN, Dieter (ORO)
FERNANDES DE BARROS, Mariana (Cefic)
GRANGE, Emma (ECEAE)
KERÄNEN, Hannu (CONCAWE)
TILLIEUX, Geoffroy (EuPC)
WAETERSCHOOT, Hugo (Eurometaux)

ECHA staff
AHRENS, Birgit
AJAO, Charmaine
ANASTASI, Audrey Anne
BALDUYCK, Bo
BELL, David
BERCARU, Ofelia
BICHLMAIER, Ingo
BROERE, William
CARLON, Claudio
CARTLIDGE, George
DEYDIER, Laurence
DE WOLF, Watze
HALLING, Katrin
HAUTAMÄKI, Anne
HERBATSCHEK, Nicolas
JOHANSSON, Matti
KARJALAINEN, Anne-Mari
KORJUS, Pia
KREUZER, Paul
LE CURIEUX, Frank
LOIKKANEN, Jarkko
MUSSET, Christel
NAUR, Liina
PELTOLA-THIES, Johanna
RALLO, Claudia
RÖNTY, Kaisu
SOSNOWSKI, Piotr
VAHTERISTO, Liisa
VALENTINI, Marco
VÄÄNÄNEN, Virpi
WALKER, Lee

Proxies

- ANDRIJEWSKI, Michal (PL) also acting as proxy of VANDERSTEEN, Kelly (BE) during the afternoon of 16 May
- ATTIAS, Leonello (IT) also acting as proxy of ELLUL, Nathanael (MT)
- ATTIAS, Leonello (IT) also acting as proxy of KOUTSODIMOU, Aglaia (EL)
- DE KNECHT, Joop (NL) also acting as proxy of DUNAUSKIENE, Lina (LT) during short periods
- DIMITROVA, Rada (BG) also acting as proxy of PALEOMILITOU, Maria (CY)
- HUMAR-JURIC, Tatjana (SI) also acting as proxy of KRECOVIC, Dubravka (HR) on 14 May
- STESSEL, Helmut (AT) also acting as proxy of KULHANKOVA, Pavlina (CZ) during the afternoon of 16 May

Experts and advisers to MSC members

AVERBECK, Frauke (DE) (adviser to FINDENEGG, Helene)
BAUMBUSH, Angelica (NO) (adviser to REIERSON, Linda)
BOISEN, Anne (DK) (adviser to HJORTH, Rune)
BOLWIG, Asger (DK) (expert to HJORTH, Rune)
CIESLA, Jacek (PL) (expert to ANDRIJEWSKI, Michal)
COSGRAVE, Majella (IE) (expert to CONWAY, Louise)
DOBRAK-VAN BERLO, Agnieszka (BE) (expert to VANDERSTEEN, Kelly)

EINOLA, Juha (FI) (adviser to RISSANEN, Eeva)
FILIPOVA, Hristina (BG) (expert to DIMITROVA, Rada)
JÖHNCKE, Ulrich (DE) (adviser to FINDENEGG; Helene)
KUROVA, Martina (SK) (expert to HORSKA, Alexandra)
LANDVIK, Nina (NO) (expert to REIERSON, Linda)
LOZACH, Jerome (FR) (expert to LE, Elisa)
MALKIEWICZ, Katarzyna (SE) (expert to LUNDBERGH, Ivar)
RAITALA, Suvi (FI) (adviser to RISSANEN, Eeva)
ROSENTHAL, Esther (DE) (adviser to FINDENEGG, Helene)
SOMMER, Yasmin (DE) (expert to FINDENEGG, Helene)
SPURIENE, Otilija (LT) (expert to DUNAUSKIENE, Lina)
TARNOCZAI, Timea (HU) (expert to DEIM, Szilvia)

MSCA experts for SEv cases:
PASQUIER, Elodie (FR)
SCHWIRN, Katrin (DE)

Registered to the WEBEX-phone connection:
BARICIC, Peter (DG GROW)
BOEL, Els (BE)
CORRELL MYHRE, Ingunn (NO)
DAHLBERG PERSSON, Marie (NO)
DOYLE, Ian (UK)
GALERT, Wiebke (DE)
GUDBRANDSEN, Marius (NO)
GÜNDEL, Ulrike (DE)
HAUZENBERGER, Ingrid (AT)
HEGGELUND, Audun (NO)
HERZBERG, Frank (DE)
HOFFMANN, Frauke (DE)
HORNEK-GAUSTERER, Romana (AT)
HÖLZL, Christine (AT)
KOPANGEN, Marit (NO)
KUITTINEN, Marko (FI)
MARTIN, Esther (ES)
MÜHLEGGER, Simone (AT)
PEPPIN, Lindsay (UK)
SCHUTTE, Katrin (DG ENV)
STOCKER, Eva (AT)
STRECK, Georg (DG GROW)
TIETJEN, Lars (DE)
VÖLKER, Doris (DE)
WEBER, Philippe (FR)

Case owners:
Representatives of the Registrants were attending under the Agenda Item 6.2 for SEV-DE-006/2017 and SEV-FR-004/2017 and under the Agenda Item 7.2 for TPE-019/2019, TPE-020/2019, TPE-021/2019, TPE-022/2019 and TPE-023/2019.

Apologies:
DEIM, Szilvia (HU)
ELLUL, Nathanael (MT)
FRANZ, Michel (FR)
KOUTSODIMOU, Aglaia (EL)
MARTIN, Esther (ES)
MIHALCEA UDREA, Mariana (RO)
PALEOMILITOU, Maria (CY)
WAGENER, Alex (LU)

III. Final Agenda

MSC/A/064/2019

Agenda

64th meeting of the Member State Committee

14-16 May 2019
ECHA Conference Centre
Annankatu 18, in Helsinki, Finland

14 May: starts at 9 am
16 May: ends at 4 pm

Item 1 – Welcome and Apologies

Item 2 – Adoption of the Agenda

MSC/A/064/2019
For adoption

Item 3 – Declaration of specific interests to items on the Agenda

Item 4 – Administrative issues

- Refresher and update on ECHA's conflict of interest policy
- Outlook for MSC-65

For information

Item 5 – Minutes of the MSC-63

- Final minutes of MSC-63

MSC/M/63/2018
For information

Item 6 – Substance evaluation

Tentative timing: Start at Day 1, Closed session for 6.3

1. **Written procedure report on seeking agreement on draft decisions on substance evaluation[1]**

   ECHA/MSC-64/2019/006
   For information

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

   ECHA/MSC-64/2019/001

[1] List of agreed cases can be found as an appendix at the end of this draft agenda

MSC code	Substance name	EC/List No./ Documents
SEV-DE-006/2017	Zinc oxide	215-222-5 / ECHA/MSC-64/2019/002-3
SEV-FR-004/2017	Potassium titanium oxide ($K_2Ti_6O_{13}$)	432-240-0 / ECHA/MSC-64/2019/004-5

For discussion

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

Cases as listed above under 6.2

For agreement

Item 7 – Dossier evaluation

Closed session for 7.3 and partly for 7.4

1. Written procedure report on seeking agreement on draft decisions on dossier evaluation[1]

ECHA/MSC-64/2019/007

For information

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

ECHA/MSC-64/2019/008

For discussion followed by agreement seeking under 7.3:

Testing proposal examinations

MSC code	Substance name	EC/List No./ Document No.
TPE-017/2019	Bis[O,O-bis(1-methylethyl)phosphorodithioato-S]bis(cyclohexanamine)zinc	809-986-4 ECHA/MSC-64/2019/009-10
TPE-018/2019	Methanal, reaction products with 1,3-bis-(aminomethyl)benzene and hydroxybenzen	701-207-5 ECHA/MSC-64/2019/11-12
TPE-019/2019	5-Methoxy-2-tetralone	457-080-9 ECHA/MSC-64/2019/13-14
TPE-020/2019	Tetraammine platinum (II) hydrogen carbonate	426-730-3 ECHA/MSC-64/2019/15-16
TPE-021/2019	Tetraammineplatinum (II) diacetate	457-310-8 ECHA/MSC-64/2019/17-18
TPE-022/2019	Tetraammineplatinum dinitrate	243-929-9 ECHA/MSC-64/2019/19-20
TPE-023/2019	Tetraammineplatinum dichloride	237-706-5 ECHA/MSC-64/2019/21-22

For discussion

3. 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 7.2

For agreement

4. General topics

4. Request of *in vivo* mutagenicity testing on germ cells under compliance check of Annex IX or X dossiers – implementation options *(Closed session)*

ECHA/MSC-64/2019/023

For discussion and agreement

5. Brief report and learnings from follow-up stage of dossier evaluation decisions

For information

6. Dossier evaluation categories planned for the MSC-66 and MSC-67 MSCA consultations – a brief introduction *(Closed session)*

For information

Item 8 – SVHC identification

Tentative timing: Day 3

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

Not relevant for this meeting

2. General topics

- Reflections on new combinations of properties that may be considered of Equivalent Level of Concern under Art. 57(f)

For information and discussion

Item 9 – ECHA's recommendations of priority substances to be included in Annex XIV and opinion of MSC

1) 9th Draft recommendation for inclusion of substances into Annex XIV

- Update from SECR on the progress made, including LAD assignment proposal[2]

For information and discussion

- Draft opinion of MSC

ECHA/MSC-64/2019/025

For discussion

2) Draft recommendation to amend entries of DEHP, BBP, DBP, and DIBP in Annex XIV

- Update from SECR on the assessment of potential impact of the comments from public consultation[2]

For information

- Draft opinion of MSC

[2] Post public consultation assessment documents and draft responses (as working versions) are available in MSC S-Circabc under 04. Recommendation / 9th (2018-2019) / Draft recommendation and substance specific information. For item 9.2 draft responses (as working versions) for exemption requests to be available under 04. Recommendation / Recommendation to amend entries (2019)

For discussion

Item 10 – Any other business

1. Update on appeals and court cases of relevance to MSC

(Partly closed session)

For information

2. Interact information session and introduction of its features to the users

For information

3. Suggestions from members

For information

(a) EOGRTS Workshop

For information

(b) DNT/DIT reports

For information

(c) Follow-up from AOB at MSC-63 (Sterile controls)

For information

Item 11 – Adoption of main conclusions and action points

- Table with conclusions and action points from MSC-64

For adoption

Information documents

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

- Status report on on-going substance evaluation work (presentation slides)
- Status report on on-going dossier evaluation work (presentation slides)

APPENDIX to the MSC-64 agenda:

List of evaluation cases agreed by MSC in written procedure in advance of the MSC-64 meeting:

Substance evaluation

MSC code	Substance name	EC/List No.
SEV-NL-023/2016	O,O,O-triphenyl phosphorothioate	209-909-9

Dossier evaluation

Compliance checks

MSC code	Substance name	EC/List No.
CCH-001/2019	Octene, hydroformylation products, low-boiling	273-110-1
CCH-005/2019	2-Ethylhexyl diphenyl phosphate	214-987-2
CCH-006/2019	Reaction products of 3,4,5,6-tetrabromobenzene-1,2-dicarboxylate with 2,2'-oxy-diethanol and 2-epoxypropane	616-436-5

Testing proposal examinations

MSC code	Substance name	EC/List No.
TPE-007/2019	Dodecamethylcyclohexasiloxane	208-762-8
TPE-016/2019	4,4'-methylenebis[2,6-diethylaniline]	237-185-4
TPE-034/2019	Slags, ferromanganese-manufg.	273-728-1
TPE-046/2019	Renewable hydrocarbons (diesel type fraction)	618-882-6

IV. Main Conclusions and Action Points

Main conclusions and action points
MSC-64, 14-16 May 2019
(adopted at MSC-64)

CONCLUSIONS / DECISIONS / MINORITY OPINIONS	ACTIONS REQUESTED
Item 6 – Substance evaluation 1. **Written procedure report on seeking agreement on draft decisions on substance evaluation**	
MSC took note of the report.	**MSC** to consider the decisions uploaded on MSC S-CIRCABC for the written procedure as agreed ones.
Item 6 – Substance evaluation **3. Seeking agreement on draft decisions when amendments were proposed by MSCA's/ECHA *(Session 2, closed)***	
MSC reached unanimous agreement on the following ECHA draft decisions (as modified in the meeting): SEV-DE-006/2017 Zinc oxide (EC No. 215-222-5) SEV-FR-004/2017 Potassium titanium oxide ($K_2Ti_6O_{13}$) 8EC No. 432-240-0)	**MSC-S** to upload on MSC S-CIRCABC the agreed decisions in the respective case folders.
Item 7 – Dossier evaluation **1. Written procedure report on seeking agreement on draft decisions on dossier evaluation**	
MSC took note of the report.	**MSC** to consider the decisions uploaded on MSC S-CIRCABC for the written procedure as agreed ones.
Item 7 – Dossier evaluation **3. Seeking agreement on draft decisions on compliance checks and testing proposal examinations when amendments were proposed by MS-CA's *(Session 2, closed)***	
MSC reached unanimous agreement on the following ECHA draft decisions (as provided for the meeting): **<u>Testing proposal examinations</u>** TPE-017/2019 Bis[O,O-bis(1-methylethyl)phosphorodithioato-S]bis(cyclohexanamine)zinc (EC No. 809-986-4) TPE-018/2019 Methanal, reaction products with 1,3-bis-(aminomethyl)benzene and hydroxybenzen (EC No. 701-207-5) TPE-019/2019 5-Methoxy-2-tetralone (EC No. 457-080-9) TPE-020/2019 Tetraammine platinum (II) hydrogen carbonate (EC No. 426-730-3)	**MSC-S** to upload on MSC S-CIRCABC the agreed decisions in the respective case folders.

CONCLUSIONS / DECISIONS / MINORITY OPINIONS	ACTIONS REQUESTED
TPE-021/2019 Tetraammineplatinum (II) diacetate (EC No. 457-310-8) TPE-022/2019 Tetraammineplatinum dinitrate (EC No. 243-929-9) TPE-023/2019 Tetraammineplatinum dichloride (EC No. 237-706-5)	
Item 7.4 – Dossier evaluation - General topics 1. Request of *in vivo* mutagenicity testing on germ cells under compliance check of Annex IX or X dossiers – implementation options (Closed session)	
MSC took note of the background document and the presentation on practical implementation options. MSC agreed to keep the current approach in requests of the comet assay. MSC agreed to review in MSC-65 meeting regulatory options on requesting further mutagenicity testing (germ cell or gonadal tissues) e.g. in one decision or follow up.	**MSC** requested **SECR** to prepare an MSC-65 meeting document and presentation on benefits and disadvantages on the identified options for requesting further mutagenicity testing (germ cell or gonadal tissues). **MSC** requested **the Chairman** to include this topic as an agenda point (closed session) for MSC-65.
Item 7.4 – Dossier evaluation - General topics 2. Brief report and learnings from follow-up stage of dossier evaluation decisions 3. Dossier evaluation categories planned for the MSC-66 and MSC-67 MSCA consultations – a brief introduction (Closed session)	
2. MSC took note of the report.	**MSC** to consider the learnings from dossier evaluation follow-up in its decision making process.
3. MSC took note of the planned MSCA consultations.	**MSC members** to share with their MS experts the plans for consultations on categories.
Item 8.2 – SVHC identification - General topics • Reflections on new combinations of properties that may be considered of Equivalent Level of Concern under Art. 57(f)	
MSC took note on specific properties that may be considered of Equivalent Level of Concern (ELoC).	**MSC members** to consider the reflections presented and discussed when reviewing SVHC proposals as ELoC.
Item 9 – ECHA's recommendations of priority substances to be included in Annex XIV and opinion of MSC 3) 9th Draft recommendation for inclusion of substances into Annex XIV • Update from SECR on the progress made, including LAD assignment proposal • Draft opinion of MSC	
MSC took note on the progress made and the proposed LADs. MSC discussed the draft opinion and some topics that were flagged by the Rapporteur for MSC's attention.	**MSC** to submit further comments to the Rapporteur in writing by 27 May 2019 (using FMB). **Rapporteur** to submit the draft opinion for final discussion and adoption to MSC-S by 11 June 2019.
Item 9 – ECHA's recommendations of priority substances to be included in Annex XIV and opinion of MSC 4) Draft recommendation to amend entries of DEHP, BBP, DBP, and DIBP in Annex XIV	

CONCLUSIONS / DECISIONS / MINORITY OPINIONS	ACTIONS REQUESTED
• Update from SECR on the assessment of potential impact of the comments from public consultation • Draft opinion of MSC	
MSC took note of the assessment done by SECR and discussed the draft opinion.	MSC to submit further comments to the Rapporteur in writing by 27 May 2019 (using FMB).
Item 10 – Any other business	
1. Workshop on EOGRTS MSC took note of the update on the NL workshop on EOGRTS.	**Chairman of the Organising Committee** to send out invitation for the workshop to MSC members and Commission observers (and MSC FMB).
2. DNT/DIT reporting MSC took note of information on two reports on EOGRTS and cohorts, commissioned by ECHA in 2018.	**MSC members or their experts** attending the NL workshop on EOGRTS to review the reports and consider where their coverage should be broadened.
3. Sterile controls MSC took note of the information on the next steps in work on sterile controls.	**FI member** to inform **MSC** further on this topic in one of the upcoming meetings.
Item 11 – Adoption of main conclusions and action points	
MSC adopted the main conclusions and action points of MSC-64 at the meeting.	**MSC-S** to upload the main conclusions and action points on MSC S-CIRCABC by 17 May 2019.