MSC/M/45/2015
ADOPTED AT MSC-46

Minutes
of the 45th Meeting of the Member State Committee (MSC-45)
7-11 December 2015

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 45th 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 outcome of the SVHC written procedure, and with addition of an item to the AOB on the planned topical scientific workshop on new approach methodologies in regulatory science and with addition of the information document on 'degradation simulation testing' for discussion following a request from an MSC member. One stakeholder observer asked if topic 'REACH and beyond' is included on the agenda but as the topic was not directly related to MSC the Chairman did not suggest to include it now (final Agenda is attached as Part III of these minutes).

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

One member declared a potential conflict of interest to a specific agenda item. Details of the declared potential conflicts and the mitigating measures are attached to these minutes as Part IV. She 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 member, expert or adviser with any other item on the agenda of MSC-45.

Item 4 - Administrative issues

SECR informed the Committee of the ongoing rearrangements in S-CIRCABC affecting the links previously sent to the MSC.

Item 5 – Minutes of the MSC-44

MSC adopted the revised version of the MSC-44 draft minutes following the written commenting phase with a further minor change as suggested at the meeting. The final minutes will be uploaded on MSC S-CIRCABC and on the ECHA website.

Item 6 – Substance evaluation

6.1 Community Rolling Action Plan (CoRAP) & MSC opinion development

- **Report by the Rapporteur and discussion on the first draft opinion of MSC opinion on the draft Community Rolling Action Plan (CoRAP)**

The Rapporteur introduced the working group (WG) members and explained how they have organised the work in order to come up with the draft MSC opinion. The documents that form the basis for the draft MSC opinion were the draft CoRAP Update 2016-2018, the 2011 selection criteria and the justification documents prepared by the evaluating MSCA for each substance on the draft CoRAP Update. The Rapporteur reflected that for most substances on the draft CoRAP there are sufficient grounds to consider that the substance may constitute a risk for the environment and/or human health, thus the current draft of the MSC opinion supports the draft CoRAP.

However, the recent BoA decision A-005-2014 introduced new elements for the Rapporteur and the WG to consider when looking at the newly introduced substances or the substances from the previous CoRAP 2015-2017 whose justification documents have been updated. All 2016 substances were reviewed by SECR with regards to links between compliance check (CCH) or testing proposal examination (TPE), and possible conflicts/overlaps with substance evaluation (SEv). Discussions between ECHA and eMSCAs on the topic of possible conflicts or overlapping processes took place on several substances with the result that some cases are postponed to await CCH/TPE, for others

SEv will start as planned and it could also be that for few substances SEv and CCH might be performed in parallel. MSC considered that for substances that are postponed SECR should develop an approach to transparently communicate the reason(s) for such a temporary delay.

Furthermore, very recently there were also several substances where dossier updates introduced new information with/without relevance for concerns/inclusion in CoRAP. These updated dossiers are to be reviewed by the eMSCAs for their implications for the justification documents. Among others this includes changes in registration status to isolated intermediates used under strictly controlled conditions only. Additionally several new candidate(s) are (to be) proposed by some Member States after publication of the draft CoRAP 2016-2018 where a review of the justiifcation document by the Rapporteur and Working Group is pending.

MSC was invited to send comments to the Rapporteur on the Annex and draft opinion by 10 January 2016 and to remind their evaluating CA to update the justification documents of the substances they are evaluating latest by same date.

6.2 Decision making process

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

SECR introduced the report on the outcome of the written procedure (WP) for agreement seeking on two substance evaluation cases (see Part V for more detailed identification of the cases). WP was launched on 12 November 2015 and closed on 23 November 2015. By the closing date, unanimous agreement was reached on one DD with no abstentions received. 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, open session)

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

SEV-EE-007/2013 4,4'-methylenediphenyl diisocyanate (EC No. 202-966-0)

Session 1 (open)

Two representatives of the Registrant(s) 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 Estonia (EE-CA) presented the outcome of substance evaluation (SEv) of the above-mentioned substance which was performed by the EE-CA on the basis of the initial grounds for concern relating to Human health/CMR; Sensitiser; Environment/Suspected PBT; Exposure/Wide dispersive use; Consumer use and Aggregated tonnage. MSC was guided through the information on the substance (including PfAs, Registrant(s)' comments, and the eMSCAs responses to them).

Seventeen proposals for amendments (PfAs) were received in total on a) initial information requests regarding toxicokinetics study (EU B.36/OECD TG 417); Extended One Generation Reproduction Toxicity Study (EOGRTS); qualitative risk characterisation for respiratory sensitisation for workers, professionals and consumers; potential of MDI and its metabolites for genotoxicity/mutagenicity, and b) additional information requests on comet assay; simultaneous use with polar solvents; details on the life-cycle from the chemical use to the service-life of manufactured articles, and c) to align the deadline with the type of requests.

The eMSCA took into account the PfAs and the Registrant(s)' comments and considered that the initial request regarding the qualitative risk characterisation for respiratory sensitisation for workers, professionals and consumers was no longer deemed necessary.

Furthermore, the initial request regarding reproductive toxicity endpoint was considered not necessary at this stage of the process and was removed from the decision. However, the possible need to request studies on reproductive toxicity will be reconsidered during the follow-up evaluation process.

Hence, the draft decision presented for discussion at MSC requested for toxicokinetics study (EU B.36/OECD TG 417) and information on the life cycle of the substance with regards to the consumer uses and the simultaneous use of the registered substance with solvents.

Regarding the request for toxicokinetics study (EU B.36/OECD TG 417) using Wistar rats and oral route, one PfA expressed agreement with this request because the outcome from this test could 1) establish whether 4,4'-methylenedianiline (MDA) is formed in the intestine from 4,4'-methylenediphenyl diisocyanate (MDI) and subsequently taken up after oral administration of MDI, 2) establish the bioavailability of MDI after oral application and compare the metabolic profile with the results obtained with inhalation, 3) provide the basis to decide whether reproductive toxicity studies would be needed and the oral route of exposure would be appropriate, 4) provide the basis to design potential further (*in vivo*) mutagenicity studies. This PfA suggested that the eMSCA demonstrates in the decision how the requested information allows clarifying the potential risks related to reproductive toxicity and mutagenicity and in establishing more stringent risk management measures, and proposed a list of elements to be included in the justification for this test in Section III. Another PfA proposed to withdraw the request for toxicokinetics study since 1) the oral route of exposure is not relevant for the registered uses and 2) even if it was considered relevant, there is already enough data available to conclude that MDA would be formed and become bioavailable after oral uptake of MDI. Moreover, if there is concern that MDI needs to be considered a genotoxic carcinogen, it proposed to reassess the genotoxicity database for MDI and consider comet assay (OECD TG 489) or Transgenic Rodent Assay (OECD TG 488) via inhalation or dermal exposure. A third PfA proposed to revise or delete a sentence in Section III to clarify to the Registrant(s) what the outcome of the toxicokinetics study would be used for.

Regarding the potential of MDI and its metabolites for genotoxicity/mutagenicity two PfAs proposed a new information request for an *in vivo* comet assay, rat (OECD 489) albeit diverging on the route of exposure. One PfA proposed oral route whilst the other proposed inhalation. The request for a comet assay was justified in one PfA based on the positive *in vitro* gene mutagenesis assays in mammalian cells and the residual uncertainty relating to whether MDI may cause chromosome mutations *in vivo* in initial site of contact tissues or liver. This PfA proposed the analyses to be done on cells of glandular stomach or jejunum/duodenum, liver and bone marrow. The other PfA considered the positive *in vitro* results to be linked with the solvent used – when DMSO (dimethyl sulfoxide) was used Ames test came out positive whilst when EGDE was used Ames test came out negative. Hence it proposed the eMSCA to reassess the genotoxic database for MDI and consider the need for an *in vivo* comet assay or Transgenic Rodent Assay via inhalation.

New information was proposed to be requested. This was to ask Registrant(s) to provide 1) advice down the supply chain against using MDI simultaneously with aprotic or polar solvents due to the formation of MDA (Carc 1b, MUTA 2); 2) details on the life cycle from the chemical use to the service-life of manufactured articles for each use and/or each type of manufactured article including information on the levels of residues of MDI, MDA and potential other degradation / reaction substances of concern likely to migrate out of the polymer – providing also a total extraction study or a migration study, 3) corresponding exposure scenarios and 4) risk assessment for human health and the environment.

Two general PfAs requested to adequately reflect the Registrant(s)' comments on the initial draft decision and data available in the registration dossier and to align the deadline with the type of requests made in the DD.

The Registrant(s) provided written comments on the PfAs which were reiterated during the discussion by the Registrant(s) representatives. The Registrant(s) is of the opinion that a need for an oral risk assessment for MDI is not indicated by its use and oral toxicity data

cannot be extrapolated for the hazard and risk assessment of inhaled aerosols as the relevant route of exposure for human risk assessment. They considered that the toxicokinetic data for the inhalation route of exposure are sufficient; that it also covers the oral exposure to some extent; that an additional oral study would not create data that would influence the risk management measures; that it can be demonstrated that MDA formation in the lung and following systemic uptake does not occur following relevant inhalation exposure.

With regards to the life cycle requests they argued that there are limited consumer uses and all, except one, consumer use are already subject to an existing use restriction[1]. Most of the consumer uses are a one component use – around 95 to 99% of the uses – with expected exposure from these products once a year. MDA formation from MDI is very unlikely, since if water is present in the One Component can, containing MDI, the container can explode over time. So, no water can be present for safety reasons and if there is no water then no MDA can be formed. Furthermore, the vapour pressure of MDI is very low and that of MDA is even lower, and because of the low vapour pressure exposure via inhalation is very unlikely.

With regards to the use of MDI with polar solvents the Registrant(s)' representatives stated that for MDI, no such solvents are recommended for any type of use due to toxicological concerns. There are only laboratory uses where polar aprotic solvents may be used for MDI applications, whilst polar protic solvents cannot be used as they would chemically react with MDI.

MSC members asked the Registrant(s)' representatives clarifying questions amongst which were whether there is simultaneous use of aprotic solvents in the MDI based products or if there is intended use of MDI based products simultaneously with polar aprotic solvent containing products, and if the oligomeric MDI is a separately registered substance.

The representatives of the Registrant(s) explained that when MDI is used with polar solvents it is because they are intended to be used in such manner. Water reacts with MDI via the intermediate formation of MDA, which, however, immediately reacts with MDI to form a solid and inert polyurea. They are not aware of intended uses of MDI products simultaneously with polar aprotic solvents. With regards to oligomeric MDI, the representatives of the Registrant(s) explained that this contains 40-50% MDI in the formulation and is used mainly to make insulation products. This is a separately registered substance however for the sake of the evaluation the Registrant(s) did not make any distinction. All the uses of MDI on the market were mapped out and chemical assessment for each use was provided.

Following a request for clarification on the link between the low vapour pressure and the argument by the Registrant(s) that the inhalation is the most valid rout of exposure, the representatives of the Registrant(s) explained that exposure risks are mostly inhalation of aerosol for spray applications and not due to the vapour pressure.

Session 2 (closed)

The first part of the discussion focused on the relevant route of exposure since the toxicokinetic study was requested via oral route whilst a PfA was more in favour of the inhalation route which was re-inforced by the Registrant(s)' comment that inhalation is the most relevant route of exposure. The eMSCA expert explained that a toxicokinetic study via the oral route would be appropriate in order to 1) establish the absorption and systemical bioavailability of MDI after oral application and compare the metabolic profile with the results obtained via inhalation route, 2) establish whether MDA is formed in the gastrointestinal tract from MDI and subsequently taken up after oral administration, 3) provide the basis to decide whether the oral route of exposure would be appropriate for potential reproductive toxicity studies, 4) provide the basis to design potential further (*in vivo*) mutagenicity studies, 5) establish whether oral route of administration is technically

[1] cfr. *Using of gloves that are provided with the product according to DECISION No 1348/2008/EC of the European Parliament and of the Council and Proper labelling according to Commission Regulation EC No 552/2009; REACH Annex XVII instructions will ensure proper use of the gloves by consumers.*

feasible i.e. in case if formed polyurea blocks the GI tract and animals suffer, further testing via oral route would not be viable. Secondly, as the registered substance is widely used by the professionals and consumers, oral exposure cannot be completely ruled out.

MSC considered that the oral route was not sufficiently justified because this route is not relevant for the registered uses. Furthermore, MSC could agree with the comments of the Registrant(s) that inhalation is a more relevant exposure route. Aerosol formation occurs under occupational use conditions leading to inhalatory exposure as shown by concurrent asthma cases. However, when diisocyanates are sprayed the particles in the aerosol have an aerodynamic diameter of >0,1 µm and usually >20 µm, thus one cannot completely exclude limited oral exposure due to redistribution of the larger particle sizes, this, however, would also be covered by appropriate inhalation studies. Since tumours in the lungs were reported on exposure to MDI, MSC agreed that the inhalation route is the most relevant route. In view of this assessment, and as the dossier already has toxicokinetic data on inhalation, MSC unanimously agreed to drop the request for toxicokinetic study via oral route.

MSC unanimously agreed to the evaluation of the eMSCA not to request for EOGRTS at this stage with the possible re-evaluation of this need at the follow-up stage.

MSC acknowledged that the mechanism of carcinogenicity is not sufficiently clear and it is not possible to conclude based on the available data whether tumour formation is attributed to a genotoxic or non-genotoxic mode of action (as claimed by the Registrant(s) based on the local pulmonary irritating effect of MDI, no MDA formation in the lungs and available negative results of the micronucleus test). Hence in order to tackle the concern that MDI may exhibit genotoxic effects at the site of contact, as parent compound or due to the formation of toxicologically relevant metabolites (e.g. MDA - classified as Muta. 2, Carc. 1B), MSC unanimously agreed to request for *in vivo* mammalian alkaline comet assay (OECD TG 489) in Wistar rat, by inhalation route with examination of lungs and liver. In order to address the (potentially limited) indirect oral exposure, MSC unanimously agreed to request for the glandular stomach tissue to be harvested and stored, and analysed if negative results are obtained in liver and lungs.

With regards to the PfA on the use of MDI with polar aprotic solvents, the MSC acknowledged the concern that such solvents accelerate the reaction between MDI and water thus increasing the formation of MDA. However, it is not clear from the available data where use of MDI (and mixtures containing MDI) together with aprotic polar solvents (and mixtures containing such solvents) can be expected and whether the applied measures are protective towards risks arising from the possible formation and subsequent exposure to MDA. Furthermore, there are no clear recommendations on simultaneous use of MDI and aprotic polar solvents provided by the Registrant(s) down into the supply chain. Subsequently, MSC unanimously agreed to ask the Registrant(s) to provide additional specification of the process categories for the intended uses where the use of MDI simultaneously with aprotic polar solvents occurs, and to specify the recommended measures to ensure that MDA is either not formed or exposure to MDA is controlled.

With regards to the PfA on the life cycle, the eMSCA expert explained that following the extensive comments of the Registrant(s) on the PfA, the concern that remained is with the consumer uses especially since there is no information in the registration dossier on exposure to MDA during and after the application phase of consumer products. After considering the proportionality of the PfA and revising the request based on the remaining concern, MSC unanimously agreed to request the Registrant(s) to provide additional information concerning worst case scenarios for consumer uses in relation to generation of and possible exposure to MDA.

Finally, MSC unanimously agreed to revise the deadline from 44 months to 15 months to align this with the timings generally used when requesting for a comet assay.

SEV-HU-019/2013 1,2-dichlorobenzene (EC No. 202-425-9)

Session 1 (open)

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.

The evaluating Member State Competent Authority (eMSCA) from Hungary (HU-CA) presented the outcome of substance evaluation (SEv) of the above-mentioned substance which was performed by the HU-CA on the basis of the initial grounds for concern relating to Human health/suspected CMR, suspected toxicity and mutagenicity, possible exposure/wide dispersive use/high aggregated tonnage, and on the additional concern identified during evaluation regarding the potential reproductive toxicity.

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

Ten PfAs were received in total regarding the requests for a) subchronic inhalation toxicity study extended with sperm quality examinations, b) transgenic rodent somatic and germ cell gene mutation assay (TGR), c) extended one-generation reproductive toxicity study (EOGRTS), and d) one general PfA indicating that i) GLP is a general provision for studies to be performed and does not need to be mentioned in the DD, ii) the deadlines should be set in function of what tests would be required and iii) to fully address the Registrants comments on the uses and exposure scenarios.

Regarding the request for subchronic inhalation toxicity study extended with sperm quality examinations it was proposed to delete under this heading the paragraphs not related to sub-chronic toxicity testing, or to make conjunction of two different endpoints clearer in the DD. Similarly, under DNEL derivation it was proposed to further clarify the request. Also some editorial remarks referring to repeated dose tests were suggested, and a PfA was received to either amend DD to include some information on exposure to provide additional support for the requested study, or to remove the requested test from the decision if it is not possible to show concerns for inhalation exposure.

Regarding TGR (OECD TG 488) three PfAs were received. It was suggested to provide the explanation why performing the TGR is not an option. Also it was justified why instead of requesting a TGR there is a need to request a comet assay and it was proposed to amend the DD requesting to perform a comet assay and the possible combination with a mammalian erythrocyte micronucleus (MN) assay. Another suggestion was to follow a tiered approach requesting sequential testing.

Regarding the request for EOGRTS (OECD TG 443) there were suggested clarifications in the DD on the justification for EOGRTS, on the conditions under which the EOGRTS shall be performed, species and route of administration, and specifications of the EOGRTS and the study design and the addition in DD of a reminder on potential need for additional cohort investigations.

The Registrants provided written comments on the PfAs which were reiterated during the discussion by the Registrant representatives. They described extensively the modifications made in the exposure scenarios to minimize the concern of possible human exposure, including withdrawal of a professional use. They justified that no exposure of staff or the environment is expected in remaining industrial and professional use scenarios due to well controlled conditions, and thus the request on sub-chronic inhalation toxicity study would not be justified. With regard to the request for an EOGRTS they considered that this was not based on real risk and, consequently, they supported the removal of the request.

The eMSCA considered the Registrant(s) dossier update confirming the extensive comments made as late in relation to the substance evaluation process and as such it should not be taken into account. However, it could not ignore the fact that there shall be no wide dispersive use and exposure of professional users. Consequently, concerns identified during evaluation now were partly not substantiated anymore, in particular eMSCA's concern about inhalation toxicity and reproductive toxicity. As final remark the

eMSCA confirmed that they considered it still valid to keep the request related to the mutagenicity concern due to the potential lack of an exposure threshold.

Session 2 (closed)

The discussion focused on the tiered approach requesting sequential mutagenicity testing. Arguments were provided for choosing the oral exposure route instead of inhalation for the combined MN test/comet assay, as well as the choice of tissues for the comet assay and bone marrow for the MN test.

The eMSCA re-confirmed that they took into account the PfAs and the Registrant representatives comments and therefore had amended the DD prior to the meeting dropping the requests for subchronic inhalation toxicity study and EOGRTS.

MSC agreed unanimously to drop the above two specified requests, and MSC also agreed unanimously to request in a tiered approach for: 1) *in vivo* comet assay (OECD TG 489) combined with an *in vivo* MN test (OECD TG 474); the tests shall be conducted on rat and by oral route (gavage). For the comet assay, the following tissues shall be analysed: liver, glandular stomach, duodenum/jejunum and bone marrow. For the micronucleus test, the bone marrow shall be analysed; 2a) In case the MN test is positive a mammalian spermatogonial chromosome aberration test (OECD TG 483), oral route, in rat is requested; 2b) In case the comet assay is positive, a TGR (OECD TG 488) is requested using also oral route, in rat with with 70 days exposure to cover the whole spermatogenesis period.

Different deadlines for submission of the information were agreed. If only the Tier 1 mutagenicity studies are performed a deadline of 18 months applies. In case the performance of the Tier 2a test is necessary the deadline is set at 36 months and in case the performance of the Tier 2b test is needed the deadline is set at 42 months.

SEV-DE-008/2014 p-(1,1-dimethylpropyl)- phenol (EC No. 201-280-9) and

SEV-DE-009/2014 4-tert-butylphenol (EC No. 202-679-0)

Session 1 (open)

The same two representatives of the Registrants participated in the initial discussion for both cases. In absence of specific confidentiality concerns in draft decision (DD), an open session was held.

The evaluating Member State Competent Authority (eMSCA) from Germany (DE-CA) presented the outcome of SEv of the above-mentioned substance which was performed by the DE-CA on the basis of the initial grounds for concern relating to potential endocrine disruptor and Exposure / High (aggregated) tonnage. MSC was guided through the information on the two substances (including PfAs, Registrant(s) comments, and the eMSCAs responses to them). In the course of the evaluation, the eMSCA identified additional concerns for both substances regarding repeated dose toxicity and occupational exposure. Additionally for 4-tert-butylphenol (ptBP), the higher tonnage substance, a developmental concern was identified.

The draft decisions for ptBP and p-(1,1-dimethylpropyl) phenol (ptAP) referred to the Member state Competent Authorities requested for a repeated dose 90-day oral toxicity study in a non-albino rat strain rat, by oral gavage; test method: OECD TG 408 (EU B.26) and a higher tier exposure assessment for dermal and inhalation exposure for the usage of the molten substance and the usage of the substance as flakes. Additionally the decision for ptBP requested for a prenatal developmental toxicity study in a non-rodent species (OECD 414) and to conduct a higher tier exposure assessment for dermal exposure for the application of liquid and solid end products containing ptBP as a hardener in paints, adhesives, thinners etc.

PfAs were received on all the requests made in the two decisions.

With regards to the repeated dose 90-day oral toxicity study in a non-albino rat strain, by oral gavage (OECD 408) one PfA asked to specify that the request for measurements of

serum T4, T3 and TSH are mandatory. Another PfA proposed to amend Section III justifying the request for non-albino rats for improved risk management given that industry has indicated issues with using (non-standard) non-albino rat strains and that there is sufficient information to manage the depigmentation risk posed by exposure to this substance.

With regards to the conduct of a higher tier exposure assessment for dermal and inhalation exposure related to the usage of the molten substance and the usage of the substance as flakes, as well as the application as a hardener in different types of products, the same PfA for all three requests was submitted. The PfA agreed that there is a need for the Registrant to provide evidence that performing the tasks described in the CSR for longer than 4 h does not yield an additional risk for the worker caused by the prolonged wearing of gloves. However, the requirement for a justification could go beyond the legal obligations set out in REACH and Directive 89/656/EEC. Hence, the PfA proposed to replace the request in Section II with a recommendation in Section III of the decisions.

With regards to the request for a prenatal developmental toxicity study in a non-rodent species (OECD 414) on ptBP one PfA proposed to include measurements of testosterone levels in the blood of the foetuses at the termination date of the study when conducting the PNDT test. Another PfA proposed to remove any reference to the standard information requirements and justify the request based on the recent BoA decision A-005-2014.

The Registrant(s) provided written comments on the PfAs which were reiterated during the discussion by the Registrant(s)' representatives. The Registrant(s)' representatives mentioned that they discovered a brief summary report from a 90-day study conducted on ptAP in 2013 for the US Food and Drug Administration, on albino rats addressing the main requirements of the request from the DD. This study has already been reviewed and found to be valid by a governmental regulatory body, hence, the Registrants expressed the view that performing a new vertebrate animal study is inconsistent with the principles of animal welfare, and after obtaining a letter of access, information from this study could be added to the dossier to address the information requirement in the DD on repeat-dose toxicity. For ptBP, the Registrant(s)' representatives re-iterated to use read across from the existing study with ptAP as source-substance using an albino rat strain.

Furthermore they re-iterated their disagreement with the use of a (non-standard) non-albino rat strain. They mentioned there are issues with using such non-albino rat strains and that there is sufficient information to manage the depigmentation risk posed by exposure to this substance. In fact to their knowledge of downstream users, vitiligo has not been seen for many years within Europe. They are not aware of any eye depigmentation occurring in their facilities or the facilities of their downstream users. A third party also questioned the benefit of conducting a gavage study on severely irritating/corrosive substances.

Registrant(s)' representatives re-iterated their disagreement with performing a PNDT study on rabbits since there are no indications of developmental effects in rats. In their view conducting a further animal study would not contribute to overall risk assessment and is therefore against the animal welfare policy. The request for the study was initially not contested by the Registrant(s), however the Registrant(s) agreed with the UK-CA's rationale to drop the request as set out in the PfA and therefore determined also to contest the request to conduct the study.

With regards to the higher tier exposure assessment for the usages of both substances, the Registrants indicated a willingness to update the CSR to include a higher tier exposure assessment, and revise the duration of the wearing of gloves as per the PfA received.

During the discussion the representatives of the Registrant(s) were asked if they perform occupational investigations on site like ocular and hearing investigations as vitiligo can lead to hearing loss. The Registrant(s)' representative explained that such monitoring programs do take place and include monitoring of hearing loss, however, they need to go back to check if there are investigations to link hearing loss to ptBP and to elaborate on worker and hygiene information, that will inform the need on further studies on

depigmentation. Such health monitoring programs are missing from the CSR since this was prepared in 2008/9 when there was no practical experience of the regulatory expectations for exposure assessments and the available guidance was not prescriptive on this subject. Regarding the availability of the new 90-day study on albino rats on ptAP the Registrant(s)' representatives stated that they have been given a copy of the summary. The company owning the study would not go any further unless they buy the study. It was further highlighted that the study was conducted in 2012 and every tissue was kept for more additional support.

Regarding the request for a development toxicity study on a second species it was noted by an MSC member that this request does not seems to be concern driven but data gap driven. In fact when looking at the available toxicity data there are only few studies showing bent ribs with no evidence of malformations. He further mentioned that the guidance states that one should consider performing a PNDT on 2nd species when classification is category 2 which does not seem the case for ptBP.

With regards to the conduct of a higher tier exposure assessment it was generally agreed that performing the tasks for longer than 4 h described in the CSR may yield an additional risk for the worker caused by the prolonged wearing of gloves, and that the registrants should address this concern. It was further clarified that the requirement for a justification was not based on German national legislation, but that this was used as an example and did not go beyond the legal obligations set out in REACH and Directive 89/656/EEC. Hence it was agreed to clarify the DD on this point.

Session 2 (closed)

Due to the considerations presented above MSC agreed unanimously to drop the request for prenatal developmental toxicity study in a non-rodent species (for the highest tonnage material ptBP), and to keep the requests for repeated dose 90-day oral toxicity study in a non-albino rat strain with some modifications to the test method to address specific concerns (i.e. depigmentation of the skin but also of the eye and the ear or vitiligo), and for higher tier exposure assessment for dermal and inhalation exposure.

The request for dropping the second species PNDT was agreed on the basis that a data gap should best be filled through a compliance check. Consequently, SECR highlighted the need for DE-CA to provide reasons to ECHA for treating this substance as a priority following the agreed strategy to evaluate substances that matter most.

MSC in principal accepted the read-across between both substances, and since, in the response to the PfAs the Registrant referred to an existing 90-day study on albino rats for ptAP, MSC unanimously agreed to provide the Registrant in both decisions with the option of submitting the existing study instead of the 90-day oral toxicity study in a non-albino rat strain. However, MSC unanimously agreed also that, if this option is chosen, independent of the outcome of the evaluation of the existing 90-day albino study, it is already foreseeable that there is at least a remaining concern on depigmentation which would need to be addressed by a new request for further information after the data requested in the decision has been provided and assessed. The deadline for submission of the information remained 21 months if the Registrant opts to perform the 90-day study on the non-albino strain. However, if the Registrant opts to submit the existing information from the 90-day study, the deadline for submitting the information is 6 months.

SEV-UK-035/2014 2,5-di-tert-pentylhydroquinone (EC No. 201-222-2)

Session 2 (closed)

The written procedure for the draft decision by the eMSCA from UK had been terminated by the Chairman of MSC on request of a MSC member to further discuss and clarify the deadline to submit the required studies. MSC unanimously agreed to give a deadline of 48 months, with the condition that in case the requested biodegradation simulation test (OECD 309) is not needed, the deadline to submit all other studies is 30 months.

d) General topics

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

SECR gave an overview of some recent appeals on evaluation submitted to the Board of Appeal of ECHA (BoA). SECR also presented some learnings from the BoA rulings on the first SEV decisions. This was much appreciated by the MSC.

- **Update on one case referred to the Commission (Closed session)**

A representative from the Commission informed MSC about the progress made and the decision taken by the Reach Committee concerning the SEv case referred to them when MSC did not reach unanimous agreement in February 2014 (SEV-DE-009/2012). MSC was further informed that the decision, after being sent to the registrants, is now also available on ECHA's website.

- **Update of SEV working procedures**

At MSC-44 the MSC Secretariat (MSC-S) had introduced a proposal to update the working procedure of the MSC on the decision making part of the substance evaluation process in particular as regards the decision for a draft decision to be put forward for agreement seeking in written procedure. As a follow-up action from that meeting few members provided support to the suggestions made in writing. Subsequently, MSC-S submitted a formal proposal for this meeting to update the working procedure, including some further minor changes.

To align the MSC SEv working procedure with the existing practice of consultation between the Chairman, the eMSCA and the MSC member of the evaluating Member State to identify the most appropriate and achievable route of agreement seeking, as well as to align with the dossier evaluation process, MSC-S suggested an update to the MSC SEv working procedure. The procedure is kept the same in that the eMSCA indicates its preference for the route of agreement seeking shortly after receipt of the PfAs. The update to the working procedure allocates to the MSC Chair the responsibility for the final decision on the route of agreement seeking, after the end of the Registrant commenting period. This is to take place in close consultation with eMSCA and the MSC member from the evaluating Member State. In the discussion a member suggested that in case this decision would be against the clear preference of the eMSCA the Chair should provide written reasons for his decision, which the Chairman considered as a quite acceptable provision.

MSC adopted the changes as proposed.

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 four dossier evaluation cases (see Part VI for more detailed identification of the cases). WP was launched on 12 November 2015 and closed on 23 November 2015. By the closing date, MSC reached unanimous agreement on all four DDs. No abstentions were received.

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

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

<u>CCH-096/2015 - Tris(2-hydroxyethyl)-1,3,5-triazinetrione (EC No. 212-660-9)</u>

Session 1 (open)

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

SECR explained the PfA that was received to the ECHA's DD on pre-natal developmental toxicity study (PNDT) (OECD TG 414/EU B.31) in rats or rabbits, oral route. The PfA

suggested deleting the "Note for consideration by the Registrant" (hereinafter "Note"), relating to the possibility of adaptation of the request for a test, as it would lead to ambiguity regarding the information required for compliance. It argued that the requested test was indispensable to identify potential adverse effects or exclude them with high reliability. It further noted that the information submitted by the Registrant had not shown fulfilment of REACH standard requirements on PNDT and appeared insufficient to replace the requested test.

SECR had not modified the DD based on the PfA and the Registrant had not provided comments on the PfA.

Session 2 (closed)

The MSC member from the MSCA that made the PfA referred to a Board of Appeal decision A-019-2013, which in that specific case allowed the Registrant to provide new data for adaptation that he could not have submitted earlier during NONS and not be subject to a statement of non-compliance (SONC), and that it could lead to many consecutive submissions of adaptations. A MSC member noted that a Registrant can provide adaptation arguments any time, but agreed in this case there was so far in-sufficient information for waiving. Another MSC member explored whether the "Note" should be case-specific instead of applying the general approach. Some MSC members supported to keep the "Note" to not deviate from the current consistent approach, and perhaps to include text noting that the Registrant already has tried to use the adaptation possibility.

SECR noted that the initial reasoning behind the text of the "Note" was to provide clarity that in case of a sequential testing strategy the Registrant could use an adaptation on the basis of new results obtained. As the text evolved so it also applied to the use of alternative approaches and other adaptations. SECR further noted that ECHA would need to consider any adaptation submitted whether the "Note" was in the DD or not. However, when a Registrant would adapt the information requirement for an animal test he would need to update the technical dossier with supporting data, although according to current ECHA approach, any update during the agreement-seeking period would not be taken into account until the follow up process (after the issuing of the final decision). SECR informed that this "Note" was not an alternative to the legally binding decision text, and that it previously had allowed a Registrant to decide on the most appropriate order of its testing. Furthermore, if the adaptation and supporting data would not meet the information requirements, the information requirements would be maintained without ECHA passing a new final decision. The Commission's observer noted that the "Note" appeared to have some ambiguity, and could be taken out as the "Note" did not have a legal enforcement status and could help to avoid series of adaptations by the Registrant throughout the decision making and follow up processes.

MSC did not reach unanimous agreement on the DD addressing adaptations to information requirements. The Chairman invited the disagreeing MSC member to provide written justification for the disagreement. SECR will refer the DD to the Commission, which will prepare a decision in accordance with the procedure of Article 133(3) of REACH.

CCH-099/2015 - Reaction mass of 2-tert-butyl-4,6-dimethylphenol and 4-tert-butyl-2,5-dimethylphenol (List No. 911-254-5)

Session 1 (open)

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

SECR explained the four PfAs that were received in total to the ECHA's DD, two of which were discussed in the meeting and are outlined below.

A PfA on simulation testing on ultimate degradation in surface water (EU C.25/ OECD TG 309) suggested (a) including in Section II a requirement to assess simultaneously the biodegradation of each constituent and relevant impurity present in concentrations as low as technically detectable or at 0.1% (w/w), and (b) indicating that the test could be

waived if the chemical safety assessment (CSA) proves that it is not needed, i.e. for neither the assessment of PBT/vPvB nor the risk.

Another PfA on bioaccumulation in aquatic species (OECD TG 305) suggested indicating that the test could be waived if there are indications for a low potential for bioaccumulation and/or to cross biological membranes, unlikely exposure, or if general rules for adaptation of Annex XI were met.

SECR had modified the DD based on the PfAs on simulation testing, only.

The Registrant had provided written comments on the PfA on simulation testing proposing to additionally perform an inherent biodegradability test (OECD TG 302), and – if neither B/vB nor P/vP is ruled out – to perform a simulation test in soil (OECD TG 307).

MSC was satisfied with ECHA's response to the other two PfAs whilst MSC discussed the above-mentioned two PfAs at the meeting.

Session 2 (closed)

One MSC member supported the PfA regarding the interpretation of what to test on information requirement on degradation. The MSC member from the MSCA that made the PfA concluded that there seemed to be an agreement that the study was needed and that it could be left for the Registrant to choose the best approach to testing and the order of testing. SECR noted that in this case it was expected that the degradation products or impurities would not be PBT. SECR suggested to amend the "Note for the consideration of the Registrant" to clarify that the CSA did not contain justification to investigate further the degradation of the substance and its degradation products, and to additionally advice the Registrant to consult the ECHA Guidance on standard information requirements, CSA and adaptation. Several MSC members supported these changes.

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

CCH-106/2015 - 2-ethylhexyl methacrylate (EC No. 211-708-6)

Session 1 (open)

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

SECR explained the two PfAs that were received in total to ECHA's DD, one of which was discussed at the meeting and is outlined below.

A PfA on *in vivo* skin irritation suggested requesting an *in vitro* test for skin irritation (EU B.46) *in lieu* of animal testing, and amending Section III accordingly.

SECR had modified the DD based on the PfA on worker protection. The Registrant had not provided comments on the PfAs.

MSC was satisfied with ECHA's response to the PfA on worker protection whilst MSC discussed only the PfA on *in vivo* skin irritation at the meeting.

The MSC member from the MSCA that made the PfA emphasised that data available on this substance contained important information, including *in vivo* tests, and noted further that the information obtained from *in vitro* skin irritation test alone would be sufficient to conclude on the skin corrosion/irritation endpoint; therefore, the weight of evidence would need to be considered. Several MSC members supported the view of the PfA.

Session 2 (closed)

SECR agreed to amend the DD to acknowledge existing *in vivo* data and to request *in vitro* testing (OECD TG 439) noting, that an adaptation for the *in vivo* test for skin irritation would need to be included in the updated technical dossier based on the generated *in vitro* study and already available *in vivo* data.

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

CCH-107/2015 Triethyl phosphate (EC No. 201-114-5)

Session 1 (open)

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

SECR explained that one PfA to the ECHA's DD was received.

The PfA suggested to include a request for a degradation simulation test on ultimate degradation in surface water (Annex IX, Section 9.2.1.2), (OECD 309), to be performed at 12°C. The PfA provided a justification why the conditions for waiving the studies are not met and why the potential of persistency of the substance and its degradation products needs to be assessed. It was also noted that the Registrant has not regarded hydrolysis as a relevant pathway for degradation in the environment; however, depending on the outcome of the simulation test he may also consider reviewing his PBT/vPvB-assessment.

Due to the available information in the Chemical Safety Report (CSR) the DD was not amended by SECR based on the PfA in advance of the meeting, although it was acknowledged there was a formal data gap. SECR considered that further biodegradation testing will have no impact on the assessment of elimination by Sewage Treatment Plant (STP). An OECD 309 simulation test will only change exposure assessment for PEC regional with limited impact on the Risk Characterisation Ratio (RCR) including indirect exposure of man via environment.
Concerning the PBT assessment, there is definitive information in the registration dossier that the substance is not B. However, there is screening information that the substance is potentially P/vP. There are two higher tier human health testing requests in the draft decision which may affect the T, but currently based on information in the registration dossier the substance does not meet the T criteria. Therefore, SECR considered there would be no change in the PBT/vPvB status.

In his comments on the PfA, the Registrant considered that performing a water simulation study would be unnecessary and scientifically unjustified, as in his view, all existing information indicates that triethyl phosphate has to be evaluated as non-degradable and potentially P/vP in the water phase; therefore the expected result of a water simulation test is already known and would have no impact on the CSR and no relevant additional gain in scientific knowledge would be achieved. The Registrant also provided some further arguments in favour of his view pointing out that having described the substance as (very) persistent, this will not have any impact on the outcome of the Chemical Safety Assessment (CSA) (Classification and Labelling, PBT assessment, Risk characterisation).

Also, the Registrant indicated in his comments on the PfA that based on the PfA, he has revised the technical dossier according to the above described endpoints (PBT assessment, waiver for water simulation testing) and updated the relevant chapter summaries and the CSR.

Session 2 (closed)

During the MSC meeting discussions, a MSC member's expert considered that in his view the PfA was justified as, firstly, consistent information on P/vP is still required as available information would not allow a definite conclusion against the Guidance criteria on persistency; and secondly, the quantitative risk assessment contained indications on exposure general population via the environment and some uses with RCR close to 1. Therefore he asked to accept the PfA.

Another option raised during the discussions was to suggest an amendment of the DD in the "Note for consideration by the Registrant" considering the need for a clear and more specific message. The Chairman clarified that including a "Note for consideration" would not be consistent with the general approach that the DD addresses the information requests or interlinked information requests, only.

Based on the above considerations MSC supported the reasoning for the rejection of the PfA, took note on the MSC member's expert's considerations and agreed with the proposal

of reflecting the considerations in a statement to the minutes as submitted to MSC (attached as Part VII of the minutes).

One MSC member deliberately left the room before the voting took place. MSC agreed unanimously to the DD as submitted to the meeting.

TPE-131/2015 - 3,5-bis(2,4-dimethylcyclohex-3-en-1-yl) polyheterocycle (List No. 700-437-3)

Session 1 (open)

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

SECR explained the two PfAs on *in vivo* mammalian alkaline comet assay (OECD TG 489) combined with *in vivo* mammalian erythrocyte micronucleus test (EU B.12./OECD TG 474) which were received in total to the ECHA's DD. One PfA addressed editorial suggestions, while the other was discussed in the meeting and is outlined below.

A PfA suggested, for the comet assay, three tissues should be analysed: liver, forestomach and duodenum/jejunum. It argued that the stomach is the site of first contact, and proposed analysing also the intestines as the substance may potentially reach them. It further suggested giving preference to the forestomach over the glandular stomach, until it is certain that the substance will always reach the glandular stomach at the same time as the forestomach.

SECR had modified the DD based on the PfA which addressed editorial suggestions.

The Registrant had provided written comments on the PfA arguing that analysing two organs would be sufficient to conclude on the potential of the substance to induce gene mutations *in vivo*: (a) liver, which covers the investigation of the main metabolizing organ, and (b) glandular stomach, as the site of first contact after oral application. He further preferred glandular stomach as it was also chosen as the site of first contact in the pre-validation study of the *in vivo* comet assay and as historical data are available for the glandular stomach. The Registrant did not expect that the substance will reach the duodenum/jejunum, due to hydrolysis of the substance under acidic conditions and expected no further insight gained by investigating the intestines.

MSC was satisfied with ECHA's response to the PfA which addressed editorial suggestions, whilst MSC discussed the above-mentioned PfA at the meeting.

Session 2 (closed)

The MSC member from the MSCA that made the PfA referred to the Registrant's comments on the hydrolysis of the substance and agreed to leave it for the Registrant to analyse the appropriate tissues in this specific case. One MSC member highlighted the information available from the JaCVAM validation report, which indicated high spontaneous damage in stomach. SECR confirmed it preferred to continue its current approach to give the choice of tissues for the Registrant to decide. Some MSC members expressed their wish to further discuss the various aspects of the comet assay in the next MSC meeting.

MSC agreed unanimously to the DD as submitted to the meeting.

TPE-146/2015 - Copper (2+), bis [N-{amino (imino-KN) methyl} urea-KO]-, nitrate (1:2) (List No. 800-038-5)

Session 1 (open)

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

SECR explained the two PfAs that were received in total to the ECHA's DD.

The first PfA on *in vivo* alkaline single-cell gel electrophoresis assay for DNA strand breaks (comet assay) (OECD TG 489) suggested a change to the test title and adding a "Note for consideration by the Registrant" to consider analysis of the collected gonadal cells for gene mutations, in case of a positive result in the somatic cells.

The second PfA suggested replacing the comet assay with a request for a transgenic rodent somatic and germ cell gene mutation assay (TGR) (OECD TG 488), with collection of germ cells, arguing it would be a better test as germ cells can be collected to analyse germ cell mutagenicity, when necessary. However, if a comet assay was performed, three tissues should be analysed: glandular stomach, duodenum/jejunum, and liver. The PfA indicated that forestomach would be preferable as a standard tissue, until it was certain that substance always reaches glandular stomach and forestomach at the same time, but found it acceptable for this substance to use the glandular stomach.

SECR had modified the DD based on the first PfA.

The Registrant had provided written comments on the PfAs. In his comments to the first PfA the Registrant acknowledged the change in the test title and, concerning examination of the gonadal cells in the comet assay, noted that irrespective of positive or negative results in such gonadal cells, an *in vivo* assay on germ cells is required. Therefore, they did not consider gonadal tissue relevant for genotoxicity assessment, and additionally that such examination would not allow a reduction of animal use.

In his comments to the second PfA, the Registrant referred to available study results that indicate low probability of *in vivo* genotoxicity to somatic or germ cells. Another factor why he favoured comet assay over TGR was the limited availability of laboratories with sufficient experience with TGR. As for the tissue selection, in addition to including liver, the Registrant argued that the repeated dose toxicity information shows that stomach (first contact with the substance that induce irritant effects) was more sensitive than intestine, and in contrast to his initial testing proposal now proposed examining only the glandular stomach instead of the forestomach.

One stakeholder observer asked whether comet assay would have a risk for false positives, as high cytotoxicity has been observed previously in the substance. SECR responded that if the test was performed correctly, the results of doses inducing too high cytotoxicity should normally be disregarded during the analysis.

Session 2 (closed)

The MSC member that made the second PfA agreed to request the comet assay instead of TGR and, for this case, also agreed to leave it for the Registrant to choose which of one of the two tissues (glandular stomach or duodenum/jejunum), in addition to liver, to analyse.

MSC agreed unanimously to the DD as submitted to the meeting.

d. General topics

Appeals update (partly closed session)

- See under 6.2d

Overview of Degradation Simulation testing in Compliance Checks - MSCAs PfAs and MSC decisions

- SECR presented an overview of degradation simulation testing, which is standard information requirements as laid down in Annex IX. The studies covered include "Simulation testing on ultimate degradation in water" (OECD TG 309), "Soil Simulation testing" (OECD TG 307) and "Sediment simulation testing" (OECD TG 308). The presentation reviewed the past cases, ECHA's initial requests, PfAs submitted and MSC decisions taken, with an observation that the adaptations provided by the Registrant need to meet the criteria of either the specific or general adaptation rules in order to fulfil the standard information requirements.

Item 8 – SVHC identification

a. Written procedure report on seeking agreement on identification of SVHCs

SECR gave a brief report on the outcome of the written procedure for SVHC agreement seeking on the identification of *Perfluorononan-1-oic acid (PFNA) and its sodium and ammonium salts* proposed to be identified as an SVHC based on Article 57 (c) and (d) due

to its toxic for reproduction and PBT properties. It was noted that MSC agreed unanimously on identification of PFNA and its sodium and ammonium salts as an SVHC in the written procedure launched on 17 November 2015 and closed on 30 November 2015. SECR explained that the final documents will be made available on MSC S-CIRCABC and on the ECHA website and the substance will be included in the Candidate List of SVHCs. The Chairman noted he had declared a potential conflict of interest with this substance and, therefore, that the written procedure had been managed by an alternate Chair.

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

- **Hexamethylene diacrylate (hexane-1,6-diol diacrylate)(EC No. 235-921-9)**

The dossier submitter (DS) representative from the Swedish CA presented to MSC the Annex XV dossier for SVHC identification of hexamethylene diacrylate (HDDA) due to its skin sensitising properties. DS explained that the current SVHC proposal on HDDA had been developed on the basis of the ECHA's general approach paper[2] where 'comparison factors for case-by-case assessment' are suggested to be used for deciding on the level of concerns considering the health effects and other factors. Further, the DS outlined the key elements in the substance-specific argumentation provided for Article 57 (f) identification, as well as the main comments received in the pubic consultation on this SVHC proposal and the way they have been addressed in the draft Support document and in the response-to-comments table (RCOM). DS highlighted the importance of regulating HDDA properly in order to protect workers from occupational exposure to HDDA, in particular in light of the increase in the manufacture and growing uses of HDDA-containing products on the EU market in recent years.

In the following discussion, several members pointed out that there is a need for a more general discussion at policy level on how to regulate skin sensitisers and what the most appropriate risk management option for them would be as a whole. However, members acknowledged that such discussion is not in the remit of MSC which should focus on this particular proposal and consider the arguments provided for SVHC identification on a case-by-case basis.

Further, MSC considered the information provided and the analyses made by DS on each of the different 'comparison factors' listed in the ECHA's general equivalent level of concern (ELoC) approach paper and came to the following conclusions:

As regards the **potency of HDDA to cause adverse effects to human health,** MSC unanimously acknowledged that HDDA is a strong and potent skin sensitiser with already harmonised classification as Skin Sens. 1. Furthermore, MSC supported the DS's conclusion that the available animal and epidemiological data provided in the dossier indicate that HDDA may be classified as Skin Sensitiser 1A if a CLH process under the CLP Regulation to update the entry is initiated.

As regards the **type and severity of the health effects**, different views were exchanged. The majority of MSC members agreed with the DS's conclusions that HDDA can cause severe human health effects in the form of allergic contact dermatitis manifested as eczema, blisters, oozing lesions and disruption of the skin barrier. They agreed that this has been clearly shown in the provided case reports and therefore, on the basis of the inherent properties and the immunological reactions, HDDA can be identified as an SVHC. The majority of MSC acknowledged that ongoing exposure to HDDA may lead to permanent severe skin damage. They also acknowledged that if a greater population of people is exposed to HDDA, more cases with severe effects could be observed and more cases could be reported.

However, several other members argued that although they agree inherent properties of HDDA should be the basis for SVHC identification, the other factors suggested for consideration should be also taken into account in demonstrating ELoC. These members held the opinion that the evidence provided for this substance in the dossier regarding the

[2]Identification of substances as SVHCs due to equivalent level of concern to CMRs (Article 57(f)) – sensitisers as an example: https://echa.europa.eu/documents/10162/13657/svhc_art_57f_sensitisers_en.pdf

type and the severity of the effects is insufficient to draw the conclusion that the substance can be identified as an SVHC. They stated that in all cases quoted symptoms disappeared after exposure stopped. It was noted by the DS that the severe cases sought medical care.

In some members' view it was unclear whether HDDA was the causal agent as exposure was often to a mixture of acrylates. In the nail technician cases it could not even be confirmed that HDDA had been used. Only one study report demonstrated serious effects, diagnosed as toxic epidermal necrolysis (TEN) after a short occupational exposure to printing ink which contained HDDA and other skin sensitising components, even though no permanent lesions were reported. These effects were reversible and the patient recovered completely after hospitalisation and proper medical treatment. In addition, one member noted that it was difficult to establish a causal relationship with only one rare case published. These members noted also that, in their view, the 'prolonged and severe effects' as described in the ECHA ELoC document are not demonstrated, as no scarring or chronic inflammation is reported and after removal from the exposure to HDDA, symptoms disappear. Therefore, they considered that the definition of severe damage provided in ECHA's general ELoC approach paper is not met since there is no evidence of permanent skin damage.

The DS pointed out that the ELoC document states "Ongoing exposure **can** lead to chronic inflammation and scar formation" meaning that no documented permanent effects in humans are required for SVHC identification.

One member noted that TEN is most often seen as a rare drug reaction although, as noted in the case study, may be caused by allergens such as nickel. As the drugs used as treatment in the case belonged to a class of drugs known to cause this reaction and the patient also tested positive to nickel in a patch test, furthermore, the member noted that these possible contributory factors had not been considered/dismissed in the report. The DS stated that the high dose of corticosteroids actually cured the patient and the nickel exposure was low (assumed as no exposure to nickel at the workplace is mentioned in the report and the reported reactions in the patch test were weak and short lasting), and that the patient reacted strongly to HDDA. The authors of the report concluded that HDDA was the most likely cause of the skin reaction. An adviser to an MSC industry observer highlighted that mucosal involvement which is a commonly observed symptom was not reported in the case study. The DS stated that they had contacted a physician with expert knowledge on skin disease who confirmed that the described symptoms in the case report are consistent with TEN.

SECR stressed that the ECHA's general ELoC paper on the identification of substances as SVHCs due to equivalent level of concern to CMRs notes that SVHC identification is based on an assessment of the hazard properties of the substance and comparison of their potential impact on health and other factors with the impacts potentially elicited by CMRs and promotes their use in a holistic assessment. These other factors are meant to be seen as factors capable of causing a concern based on the hazard assessment. A reference was made to a recent judgement of the European Court of Justice[3] where the Court re-confirmed that the SVHC identification is based on a hazard assessment and this is also valid for substances manufactured or used under strictly-controlled conditions, so the additional factors considered during an ELoC assessment simply show the wider impacts related to the intrinsic properties of the substance.

One MSC industry observer and an adviser to another MSC industry observer expressed their concerns with regard to this SVHC proposal (as indicated also in their comments

[3] General Court's judgements on Case T-134/13 and on case T-135/13 on the SVHC identification of the respiratory sensitisers HHPA and MHHPA:
http://curia.europa.eu/juris/document/document.jsf?text=&docid=164047&pageIndex=0&doclang=EN&mode=lst&dir=&occ=first&part=1&cid=506546
http://curia.europa.eu/juris/document/document.jsf?text=&docid=164048&pageIndex=0&doclang=en&mode=lst&dir=&occ=first&part=1&cid=506433

submitted during the public consultation) and noted that HDDA is used by industry only and thus, there is no concern for consumer exposure to HDDA. They noted that case-by-case SVHC assessment is needed for HDDA, as limited number of HDDA-caused skin sensitisation cases have been reported by industry and all of them have been with reversible effects. Further, as HDDA is used under controlled conditions with appropriate PPE in place, it is not considered by them 'of concern' as no exposure or only low exposure to the workers is to be expected.

The DS pointed out that there are several other reported cases where adverse effects have been observed after single or prolonged exposure to HDDA or other acrylates. It was also underlined that in most of the reported cases the workers were exposed despite the personal protective equipment they had worn, and in some cases the symptoms developed also outside the exposed skin areas leading to full body spreading lesions. However, there is no information to indicate whether the PPE was ineffective, or not used correctly. Furthermore, although the worker's symptoms disappeared, they are not able to continue working in the same job, as if they do so, the symptoms will re-occur (as also shown in another reported case) as these workers are permanently sensitised to HDDA. Finally, DS stated it is also proven that a person sensitised to HDDA shows adverse reaction after exposure to other acrylates due to cross-reactivity.

As regards the **irreversibility of health effects**, MSC unanimously acknowledged that the effects caused by HDDA in the induction stage of sensitisation are irreversible. In line with the Court's judgements for HHPA and MHHPA, SECR reminded the members that the (ir)reversibility of the effects should not be seen as and not used as a criterion for SVHC identification on its own, but should be considered jointly with the other ELoC factors.

The majority of the MSC members agreed with the DS's conclusions that while the contact allergy to HDDA is of irreversible nature, the allergic skin reactions are reversible if the patient completely avoids exposure to HDDA and cross reacting substances. Furthermore, they agreed that prolonged or repeated exposures can lead to persistent dermatitis and scarring.

Several members, however, had the view that in the reported cases the effects observed after prolonged or repeated exposure were not of an irreversible nature and considered the DS's conclusion theoretical and insufficient to justify the inclusion of HDDA to the Candidate list. It was underlined that the irreversibility should be assessed in the context of the severity of the effects caused by HDDA and that it is not possible to extrapolate the judgement of the Court of Justice concerning a respiratory sensitiser (HHPA) that cause a permanent lung damage to the cases of contact dermatitis presented in the report. They also noted that no evidence was provided for permanent skin lesions. Therefore they also disagreed with the DS's interpretation of the applicability and relevance of the Court's judgements for the respiratory sensitisers HHPA and MHHPA to the skin sensitiser HDDA as regards the irreversibility and severity of effects, due to differences in adverse effects observed in the skin and in the respiratory system.

DS explained that although the adverse effects at the elicitation stage should be seen as reversible, it is proven that the allergic contact dermatitis persists as long as the exposure to HDDA continues. Although for HDDA no proof has been found for scarring or persistent effects, such cannot be excluded after prolonged exposure. In addition the DS pointed out that in the TEN case, although the patient fully recovered after hospitalisation and proper medical treatment, it remains unclear what would happen if no such treatment was provided. The DS considered the judgement of the Court of Justice concerning ECHA's/MSC's conclusion on the irreversibility of the sensitising effects caused by the respiratory sensitisers HHPA and MHHPA relevant for the skin sensitisation property of HDDA. Although no cases showing permanent damage were documented for either HHPA, or HDDA, it is expected that prolonged exposure to these substances can lead to permanent damage of the lung (HHPA) and skin (HDDA).

An MSC NGO observer noted that the issue of potential cross-reactions of a HDDA-sensitised person to other acrylates should also be taken into account in these considerations.

SECR noted it is important to compare this case with the HHPA case and what the General Court accepted and not accepted as argument in their judgements. In this regard the same argument had been brought to the Court on the reversibility of effects in elicitation stage if a person is exposed at a workplace, however, irreversibility was not the only point to be considered in the ELoC assessment, but it is relevant together with the other factors. It was further noted that in the case of HHPA there were examples where irreversible effects were shown. Furthermore, the SECR noted that the Court's conclusion on the ECHA's decision to identify HHPA as an SVHC cannot be directly applied to HDDA since the Court have not assessed HDDA and its circumstances.

Concerning the assessment of irreversibility of the human health effects under ELoC assessment (ref. MSC Support Document for identification of HDDA as SVHC, p. 9), it is noted that irreversibility is not stated as a classification criterion for e.g. reproductive toxicity.

As regards **the delay of the health effects**, most of the MSC members supported the DS's conclusion that skin sensitisation is generally recognised as a delayed effect and the HDDA case reports indicate that the time from first exposure to HDDA until allergic response can vary from days to years. A member noted that no long period for the appearance of the adverse effects is observed in the HDDA cases; however, according to this member, the main reason for including this factor in the ELoC paper seemed to be that if the hazard is unknown, appropriate risk reduction measures may not be in place but, as the hazards of this substance are known, HDDA has been classified as skin sensitiser and, skin/eye irritant, the risks should be managed with PPE (gloves).

Another member pointed out that this factor is irrelevant on its own, as in SVHC identification of CMRs, exposure is not considered; thus, SVHC identification of HDDA should be based on the inherent properties of the substance.

A remark was made on the difficulty to demonstrate actual exposure to HDDA for workers, as they are most often exposed to a mixture of substances. A member noted that this could also be the reason for the limited number of cases attributed to HDDA in the literature.

SECR highlighted that the general ELoC paper aims to compare potential Article 57 (f) substances with CMRs as a starting point, using the same factors considered for CMRs, while also considering other factors at the same time.

As regards the **DNEL derivation** for HDDA, MSC supported the DS's conclusion that although the skin sensitisation is regarded as a threshold effect, it is difficult to determine such a safe level of exposure. Further, the members agreed that it is not possible to derive a DNEL for HDDA based on the currently available dataset, as provided in the registration dossiers.

Regarding the **effects on quality of life**, a member provided the view that the information on this point has not been made case-specific for HDDA in the SVHC proposal and it is not very clear how HDDA sensitisation affects the quality of life of the concerned individual after the removal of the exposure and disappearance of the symptoms.

The DS acknowledged it is difficult to provide substance-specific evidence with regard to the impaired quality of life, however also provided the view that HDDA does impact on the quality of life of an exposed and sensitised individual, even when the actual exposure is removed, as the affected person is permanently sensitised, and thus should avoid all exposures to HDDA and other cross reacting acrylates; therefore, the person cannot work (anymore) in the same/similar job or activity where such exposures potentially occur.

An adviser of an MSC industry observer pointed out that as regards the nail manicurist example, it cannot be unequivocally proven that HDDA is causing the adverse effects which could be also due to other acrylates. Referring to a recent survey run by industry she also noted that although it is known that all dermal contacts with HDDA should be avoided, 21 cases have been reported where HDDA could be one of the problem-causing

agents. However, as PPE seems to be efficient enough even if a person is sensitised, only few of the affected individuals changed their job positions.

As regards the **societal concerns**, two members provided the view that the information on HDDA-related cost burden for the society included in the SVHC proposal is not very clear and not substance-specific. DS responded that although it is not possible to make reliable estimations of the societal costs related to allergic contact dermatitis to HDDA, the collected data indicate that the overall occupational exposure to HDDA in the EU is of societal concern.

SECR clarified that the societal concern criterion aims rather to assess the effects to society, not so much to individuals, and that according to the proposed general approach the different aspects should be jointly considered.

Finally, the MSC Chair asked the members to assess **all factors altogether** and to indicate potential missing information or any points for further considerations as regards the SVHC identification of this substance. Two members explained that they found it difficult to compare the HDDA effects to those of the CMR substances (i.e. when comparing the concerns from the dermatitis with those of the cancer-causing agents) with regard to the severity and irreversibility of the adverse effects. In these members' view, as the observed effects caused by HDDA vary from mild to severe, the critical point should be whether HDDA causes prolonged and very adverse effects constituting the same level of concern as CMRs. Although contact dermatitis merit consideration, all symptoms disappeared after cessation of exposure and no permanent lesions were reported. Another member expressed a similar view explaining that he does not see issues with the information provided in the HDDA support document, but could not support the conclusions made in the ELoC assessment for the reasons specified under the specific factors above. Two other members supported these considerations and expressed some further doubts on whether the authorisation process is the most appropriate route to regulate HDDA.

SECR stated that at the SVHC identification stage, the hazard properties of a substance proposed as an SVHC should be considered and not the most appropriate company level risk management measures (RMMs) or regulatory risk management options (RMOs), as these should be considered at the stage preceding the preparation of an SVHC proposal in line with the SVHC Roadmap 2020. It was also mentioned that the potential SVHC identification of HDDA would not affect other aspects of defining the safe conditions of use or other regulatory actions that could be undertaken.

In line with the suggestions made to the MSC draft agreement document and draft support document, the documents were modified during the meeting. The Chairman concluded that MSC would not reach consensus on the final conclusion, and therefore that a minority position was expected when bringing these documents to a vote. On Chair’s request, the members with minority views summarised their arguments to ensure that all technically relevant aspects had been appropriately addressed in the draft agreement document and support document. When these draft documents were brought to a vote, including the mandate to MSC-S and the dossier submitter to align the support document’s summary chapter with the draft agreement document after the meeting, MSC **did not reach** unanimous agreement on the proposal for identification of HDDA as an SVHC.

A majority of the members agreed the available information for HDDA was sufficient to conclude that there is scientific evidence of probable serious effects giving rise to an equivalent level of concern in relation to human health (i.e. to substances listed in points (a) to (e) in Article 57 of the REACH Regulation). One member submitted a statement to the minutes (Part VIII) on his positive vote.

Three members abstained from the vote.

A minority of nine members expressed the view that they do not rule out potential identification of skin sensitisers on the basis of ELoC, but since this should be done on a case-by-case basis, they do not consider the specific proposal for HDDA strong enough to justify an SVHC identification under Article 57 (f), because the adverse skin reactions

attributed to HDDA exposure are reversible and not as severe in nature at the elicitation stage to qualify as ELoC to those of the CMR substances (Cat 1A or 1B). Consequently these members did not agree on the identification of HDDA under Article 57(f) as giving rise to an equivalent level of concern in relation to human health (i.e. to substances listed in points (a) to (e) in Article 57 of the REACH Regulation).

The minority view submitted after the meeting in writing will be annexed to the MSC opinion.

The Chairman thanked the dossier submitter for the challenging proposal submitted to the SVHC identification process and MSC for its thoughtful deliberations on it. He noted that the MSC opinion, the minority position and the other supporting documentation will be referred to the Commission for further decision making and made publicly available on ECHA website and MSC S-CIRCABC by mid-January 2016.

Item 9 – Any other business

SECR informed MSC about the next Topical Scientific Workshop on New Approach Methodologies in Regulatory Science to be organised in ECHA 19-20 April 2016. MSC Members, their alternates, experts and advisors were invited to register by end of the year in order to participate.

Item 10– Adoption of main conclusions and action points

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

II. List of attendees

Members/Alternate members
ALMEIDA, Inês (PT)
ANDRIJEWSKI, Michal (PL)
BUSUTTIL, Ingrid (MT)
COCKSHOTT, Amanda (UK)
COSGRAVE, Majella (IE)
DEIM, Szilvia (HU)
DIMCHEVA, Tsvetanka (BG)
DUNAUSKIENE, Lina (LT)
FINDENEGG, Helene (DE)
GAIDUKOVS, Sergejs (LV)
HERMES, Joe (LU)
HUMAR-JURIC, Tatjana (SI)
KREKOVIC, Dubravka Marija (HR)
KULHANKOVA, Pavlina(CZ)
LONDESBOROUGH, Susan (FI)
LØFSTEDT, Magnus (DK)
MALKIEWICZ, Katarzyna (SE)
MARTÍN, Esther (ES)
MIHALCEA UDREA, Mariana (RO)
PISTOLESE, Pietro (IT)
REIERSON, Linda (NO)
RUSNAK, Peter (SK)
TERENDIJ, Carline (FR)
VANDERSTEEN, Kelly (BE)
VESKIMÄE, Enda (EE)
WIJMENGA, Jan (NL)
Representatives of the Commission
KOBE, Andrej (DG ENV)
RIEPMA, Wim (DG GROW)
Observers
ANNYS, Erwin (Cefic)
DE KNECHT, Joop (OECD)
DROHMANN, Dieter (ORO)
HYNES, Jarlath (HSI)
KERÄNEN, Hannu (CONCAWE)
LEROY, Didier (CEPE)
REID, Kirsty (Eurogroup for Animals)
VAN VLIET, Lisette (HEAL)
WAETERSCHOOT, Hugo (Eurometaux)
WELZ, Stefanie (Cefic)

ECHA staff
AJAO, Charmaine
BELL, David
BERCARU, Ofelia
BERNASCONI, Giovanni
BONNOMET, Vincent
BORNATOWICZ, Norbert
BROERE, William
CALEY, Jane
CARLON, Claudio
DELOFF-BIALEK, Anna
DE WOLF, Watze
DEYDIER, Laurence
DREVE, Simina
FABJAN, Evelin
FEEHAN, Margaret
HAUTAMÄKI, Anne
HELLSTEN, Kati
JOHANSSON, Matti
KARHU, Elina
KASARUHO, Anisa
KORJUS, Pia
LOUEKARI, Kimmo
LE CURIEUX, Frank
MÜLLER, Birgit
NAUR, Liina
NYGREN, Jonas
O'FARRELL, Norah
PELLIZZATO, Francesca
PHILLIPS, Andrew
ROSSI, Laura
RYAN, Paul
RÖCKE, Timo
RÖNTY, Kaisu
SCHOENING, Gabriele
SUMREIN, Abdel
TAI, Kaihsu
VAHTERISTO, Liisa
VASILEVA, Katya

Proxies

- BUSUTTIL, Ingrid also acting as proxy of PALEOMILITOU, Maria (CY)
- LONDESBOROUGH, Susan (FI) also acting as proxy of LUNDBERGH, Ivar (SE) on 7-8 December
- MARTÍN, Esther (ES) also acting as proxy of KOUTSODIMOU, Aglaia (EL)
- MARTÍN, Esther (ES) also acting as proxy of DRUGEON, Sylvie (FR) in the morning of 7 December
- VANDERSTEEN, Kelly (BE) also acting as proxy of WIJMENGA, Jan (NL) in the morning of 7 December and on 11 December
- WIJMENGA, Jan (NL) also acting as proxy of TYLE, Henrik (DK) in the afternoon of 7 December and on 8 December

Experts and advisers to MSC members
ATTIAS, Leonello (IT) (expert to PISTOLESE, Pietro)
AAVIK, Jaanika (EE) (adviser to VESKIMÄE, Enda)
BOUWMAN, Tialda (NL) (expert to WIJMENGA, Jan)
BUDASOVA, Jana (EE) (expert to VESKIMÄE, Enda)
GRACZYK, Anna (PL) (expert to ANDRIJEWSKI, Michal)
GRINCEVICIUTE, Otilija (LT) (expert to DUNAUSKIENE, Lina)
HEESCHE-WAGNER, Kerstin (DE) (expert to FINDENEGG, Leni)
INDANS, Ian (UK) (expert to COCKSHOTT, Amanda)
KOZMIKOVA, Jana (CZ) (expert to KULHANKOVA, Pavlina)
NYGREEN, Beryl C. (NO) (expert to REIERSON, Linda)
NYITRAI, Viktor (HU) (expert to DEIM, Szilvia)
RISSANEN, Eeva (FI) (adviser to LONDESBOROUGH, Susan)
WARHOLM, Margareta (SE) (expert to LUNDBERGH, Ivar)
WODLI, Jordane (FR) (adviser to DRUGEON, Sylvie)

MSCA Experts for SEV cases
HERZBERG, Frank (DE)
MOLDOV, Raili (EE)
SURJÁN, András (HU)

MSCA Experts for SVHC cases
KLINT, Helén (SE)

By WEBEX-phone connection:
During the agenda item 6 for SEV-DE-008/2014 and SEV-DE-009/2014: from DE Christian UNKELBACH, Susanne BREDENDIEK-KÄMPER, Carolin DUMKE and Martin TISCHER
For SEV-EE-007-2013: Matthias HERZLER (DE) Katarzyna MALKIEWICZ (SE) and Elsa MENDONÇA (PT)
For SEV-HU-019/2013: from HU Kriszina GRÁNER, István SEBESTYÉN, Borbala ÁDER and Károly NÁGY; Christian UNKELBACH (DE) and Katarzyna MALKIEWICZ (SE)
During the agenda item 7 for CCH-107/2015 and CCH-099-2015: Daniel SÄTTLER (DE), for CCH-106/2015 Karin KILIAN (DG ENV), for CCH-017/2015 Elsa MENDONÇA (PT)
During the agenda item 8: Katarzyna MALKIEWICZ (SE), Johanna BARHELEMY (FR), Nathalie PRINTEMPS (FR), Elodie PASQUIER (FR) and Matthias HERZLER (DE)
During the agenda items 6, 7 and 8 and 9 from DG GROW: Valentina BERTATO, Enrique GARCÍA-JOHN and Giuseppina LUVARA
During the whole meeting: Henrik TYLE (DK)

Case owners:
Representatives of the Registrants were attending under the agenda item 6.2b for SEV-EE-007/2013, SEV-HU-019/2013, SEV-DE-008/2014 and SEV-DE-009/2014.

Apologies:
DRUGEON, Sylvie (FR)
KOUTSODIMOU, Aglaia (EL)
LUNDBERGH, Ivar (SE)
PALEOMILITOU, Maria (CY)
TYLE, Henrik (DK)
WAGENER, Alex (LU)

III. Final Agenda

ECHA/MSC-45/2015/A/45

Agenda
45th meeting of the Member State Committee

7-11 December 2015
ECHA Conference Centre
Annankatu 18, in Helsinki, Finland
7 December: starts at 9 am
11 December: ends at 1 pm

Item 1 – Welcome and Apologies

Item 2 – Adoption of the Agenda

MSC/A/045/2015
For adoption

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

Item 4 – Administrative issues

For information

Item 5 – Minutes of the MSC-44

- Draft minutes of MSC-44

MSC/M/44/2014
For adoption

Item 6 – Substance evaluation
Closed session for 6.2c, partly closed for 6.2d

6.1 Community Rolling Action Plan (CoRAP) & MSC opinion development

- Report by the Rapporteur and discussion on the first draft opinion of MSC opinion on the draft Community Rolling Action Plan (CoRAP)

6.2 Decision making process

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

ECHA/MSC-45/2015/001
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)*:

ECHA/MSC-45/2015/002

For discussion followed by agreement seeking under 6.2c:

MSC code	Substance name	EC number	Documents
SEV-EE-007/2013	4,4'-methylenediphenyl diisocyanate	202-966-0	ECHA/MSC-45/2015 /003-004
SEV-HU-019/2013	1,2-dichlorobenzene	202-425-9	ECHA/MSC-45/2015 /005-006
SEV-DE-008/2014	p-(1,1-dimethylpropyl)-phenol	201-280-9	ECHA/MSC-45/2015 /007-008
SEV-DE-009/2014	4-tert-butylphenol	202-679-0	ECHA/MSC-45/2015 /009-010

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

SEV-UK-035/2014	2,5-di-tert-pentylhydroquinone	201-222-2

For agreement

d) General topics

- Appeals update[4]
- Update on one case referred to the Commission *(Closed session)*

For information

- Update of SEV working procedures

ECHA/MSC-45/2015/027
For adoption

Item 7 – Dossier evaluation

Closed session for 7c, partly closed for 7d
Indicative start time for 7b is Day 3

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

ECHA/MSC-45/2015/012
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)*

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

For discussion followed by agreement seeking under 7c:

Compliance checks

MSC code	Substance name	EC/List No.	Document
CCH-096/2015	Tris(2-hydroxyethyl)-1,3,5-triazinetrione	212-660-9	ECHA/MSC-45/2015/014-015
CCH-099/2015	Reaction mass of 2-tert-butyl-4,6-dimethyl-phenol and 4-tert-butyl-2,5-dimethylphenol	911-254-5	ECHA/MSC-45/2015/016-017
CCH-106/2015	2-ethylhexyl methacrylate	211-708-6	ECHA/MSC-45/2015/018-019
CCH-107/2015	Triethyl phosphate	201-114-5	ECHA/MSC-45/2015/020-021

Testing proposal examinations

MSC code	Substance name	EC/List No.	Document
TPE-131/2015	3,5-bis(2,4-dimethylcyclohex-3-en-1-yl)polyheterocycle	700-437-3	ECHA/MSC-45/2015/028-029
TPE-146/2015	Copper (2+), bis [N-{amino (imino-KN) methyl} urea-KO]-, nitrate (1:2)	800-038-5	ECHA/MSC-45/2015/030-031

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**

For agreement

d) General topics

1) Appeals update[1]

For information

2) Overview of Degradation Simulation testing in Compliance Checks - MSCAs PfAs and MSC decisions (presentation slides)

For discussion

Item 8 – SVHC identification

a) Written procedure report on seeking agreement on identification of SVHC

ECHA/MSC-45/2015/022
For information

b) Seeking agreement on Annex XV proposals for identification of SVHC

Substance name	EC number	Documents
Hexamethylene diacrylate (hexane-1,6-diol diacrylate)	235-921-9	ECHA/MSC-45/2015/023-025

For discussion and agreement

Item 9 – Any other business

- Topical scientific workshop on new approach methodologies in regulatory scienceSuggestions from members

For information

Item 10 – Adoption of main conclusions and action points

- Table with conclusions and action points from MSC-45

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

- *Substance evaluation status report (presentation slides)*
- *Dossier evaluation status report (presentation slides)*
- *ECHA's draft recommendation of priority substances to be included in Annex XIV - Brief update concerning the 7th draft recommendation (ECHA/MSC/I/2015/035)*
- *Update from other ECHA bodies and activities (ECHA/MSC/I/2015/034)*

Outside plenary activities (tentatively during lunch hour of Day 3)**:**
- *Presentation by ECHA entitled: Opportunities for 'Omics' under REACH*

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 7 b: CCH-106/2015	Helene Findenegg	Annual declaration as published on the ECHA website. No participation in the Committee's deliberation and voting.

V. 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
SEV-BE-004/2014	N,N'-dithiodi-o-phenylenedibenzamide

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

Draft decisions unanimously agreed by MSC in WP:

Compliance checks (CCH)

MSC ID number	Substance name used in draft decision	EC number
CCH-102/2015	n-(2-hydroxyethyl)-n,n-dimethyl alkyl-c12-14-(even numbered)-1-aminium chloride	931-275-3
CCH-103/2015	Sodium xylenesulphonate	215-090-9
CCH-105/2015	Tetrahydrothiophene	203-728-9

Testing proposal examinations (TPE)

MSC ID number	Substance name used in draft decision	EC number
TPE-145/2015	2,6,10,15,19,23-hexamethyltetracosane	203-825-6

VII – Statement to the minutes on CCH 107/2015 from the MSC member from Germany

The DE MSC member and her alternate did not take part in the vote on CCH 107/2015 during MSC 45 as DE does not agree with the decision not to include a request for a degradation simulation test into the decision. As DE supports the requests included in the decision the MSC member did not oppose the decision.

During MSCA-Consultation for MSC 45 the DE CA provided a PfA requesting to add a simulation test on ultimate degradation in surface water because we see the need for further information to decide on persistency of the substance and the identity and properties of its degradation products.

In our opinion there is enough evidence from the perspective of quantitative chemical safety assessment that waiving of the simulation test according Annex IX, number 9.2 does not apply and further information about persistency shall be requested.

We do not agree to ECHA's argumentation that the information from the available biodegradation tests on screening level together with QSAR prediction provides a sufficient database to definitely conclude on persistency.

Based on these considerations we still consider that the study is necessary.

VIII. Declaration in relation to the vote by the Danish member of the Member State Committee on inclusion of HDDA (EC No. 235-921-9) in the Candidate list

A SVHC proposal for HDDA submitted by Sweden was discussed at the MSC 45 meeting (7th to 11th of December 2015). In the proposal Sweden argued to include HDDA on the Candidate list due to its skin sensitizing properties.

In its deliberations the MSC discuss the technical and scientific aspects of matters within the competences of the MSC. On this background, The Danish member of the MSC voted yes to the Swedish proposal based purely on a scientific/technical case-by-case assessment of the information presented in this specific case cf. the Annex XV dossier. However, as the Danish vote is based on the assessment of the specific case presented, the vote on the case cannot be taken as precedence for that other skin sensitizers should be regarded as substances of equivalent level of concern.

The Danish CA finds that since skin sensitizers neither has been included amongst the types of substances that by default are covered by REACH Authorization, nor mentioned in Article 57(f) as example of possible substances of equivalent level of concern to other Substances of Very High Concern, a policy discussion is warranted on a general level to address the preferred risk management options for skin sensitizers.

The Danish CA appreciates that the case has been referred to the Commission which allows for a policy discussion in the REACH Committee on the matter.

In that regard, the "yes" vote in MSC based on technical/scientific considerations on the specific case does not preclude the position of Denmark in regard to neither the specific case nor to the general policy of inclusion of skin senzitisers in the candidate list after having scrutinized the general implications of this specific case.

IX. Main Conclusions and Action Points

Main conclusions and action points
MSC-45, 7-11 December 2015
(adopted at MSC-45)

CONCLUSIONS / DECISIONS / MINORITY OPINIONS	ACTIONS REQUESTED
Item 5 – Minutes of the MSC-44	
MSC adopted the draft minutes with a minor change made in the meeting.	**MSC-S** to upload final version of the minutes on MSC CIRCABC by 16 December 2015 and on ECHA website without undue delay.
Item 6 – Substance evaluation ***6.1 Community Rolling Action Plan (CoRAP) & MSC opinion development*** Report by the Rapporteur and discussion on the first draft opinion of MSC opinion on the draft Community Rolling Action Plan (CoRAP)	
MSC took note of the update.	**MSC members** to send comments to Rapporteur on the draft CoRAP opinion by 10 January 2016.
Item 6.2 - 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 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-EE-007/2013 4,4'-methylenediphenyl diisocyanate (EC No. 202-966-0) SEV-HU-019/2013 1,2-dichlorobenzene (EC No. 202-425-9) SEV-DE-008/2014 p-(1,1-dimethylpropyl)-phenol (EC No. 201-280-9) SEV-DE-009/2014 4-tert-butylphenol (EC No. 202-679-0) SEV-UK-035/2014 2,5-di-tert-pentylhydroquinone (EC No. 201-222-2) MSC mandated ECHA and eMSCAs to perform and	**MSC-S** to upload on MSC CIRCABC the final ECHA decisions of the agreed cases. eMSCA's and ECHA to perform and implement editorial checks

CONCLUSIONS / DECISIONS / MINORITY OPINIONS	ACTIONS REQUESTED
implement final editorial checks on the decisions	
Item 6 - Substance evaluation **6.2 Decision making process** **d) General topics** • Update of MSC Working Procedures	
MSC adopted the update to the MSC Working procedures for substance evaluation.	**MSC-S** to upload the adopted working procedure document to MSC CIRCABC and on ECHA website. **MSC and MSC-S** to apply the slightly revised working procedure from the next decision making round onwards.
Item 7 – Dossier evaluation **a. Written procedure report on seeking agreement on draft decisions on dossier evaluation**	
MSC took note of the report.	**MSC-S** to upload on MSC CIRCABC the final ECHA decisions agreed in written procedure, as indicated in document ECHA/MSC-45/2015/012.
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): CCH-099/2015 Reaction mass of 2-tert-butyl-4,6-dimethyl-phenol and 4-tert-butyl-2,5-dimethylphenol (List No. 911-254-5) CCH-106/2015 2-ethylhexyl methacrylate (EC No. 211-708-6) CCH-107/2015 Triethyl phosphate (EC No. 201-114-5) TPE-131/2015 5-bis(2,4-dimethylcyclohex-3-en-1-yl)polyheterocycle (List No. 700-437-3) TPE-146/2015 Copper (2+), bis [N-{amino (imino-KN) methyl} urea-KO]-, nitrate (1:2) (List No. 800-038-5) MSC could not reach unanimous agreement on the following draft decision, as submitted to the meeting: CCH-096/2015 Tris(2-hydroxyethyl)-1,3,5- triazinetrione (EC No. 212-660-9)	**MSC-S** to upload on MSC CIRCABC the final ECHA decisions of the agreed cases. **MSC-S** to provide COM for further decision making with documents (DD, RCOM, outcome of the vote, justifications for "no" votes;

CONCLUSIONS / DECISIONS / MINORITY OPINIONS	ACTIONS REQUESTED
	meeting minutes) of the case on which MSC did not reach agreement.
Item 8 – SVHC identification **a) Written procedure report on seeking agreement on identification of SVHC**	
MSC took note of the report.	**MSC-S** to upload on MSC CIRCABC the final MSC documents on the substance identified as an SVHC in written procedure, as indicated in the room document ECHA/MSC-45/2015/022. **SECR** to add the newly identified SVHC (in written procedure) to the Candidate List within its next update.
Item 8 – SVHC identification **b) Seeking agreement on Annex XV proposals for identification of SVHC**	
After thorough consideration on the Annex XV proposal for identification of SVHC on • Hexamethylene diacrylate (hexane-1,6-diol diacrylate) (HDDA) (EC No. 235-921-9) under Article 57(f) as giving rise to an equivalent level of concern due skin sensitising properties, MSC unanimously acknowledged that for HDDA, there is scientific evidence suggesting that HDDA is a strong skin sensitiser, that the induction phase of the skin sensitisation caused by HDDA is irreversible and that cross-reactivity between HDDA and other acrylates cannot be excluded. The majority of MSC acknowledged that an ongoing exposure to HDDA may lead to permanent skin damage Unanimous agreement of MSC on HDDA identification as an SVHC under Article 57(f) was not reached. A majority of the members supported this substance's SVHC identification, whereas a minority of nine members held a different view.	**MSC members who voted against** the SVHC identification of HDDA to provide their minority view in writing to the MSC-S in draft by 11 December, and its final version by 14 December 2015. **MSC-S** to finalise the MSC opinion documentation on HDDA without undue delay **MSC-S** to refer the MSC opinion on HDDA, the minority position and the other supporting documentation to the Commission for further decision making by 15 January 2016. **MSC-S** to upload MSC opinion on HDDA, the minority position and the other supporting documentation on MSC S-CIRCABC and on the ECHA website by 15 January 2016
Item 10– Adoption of main conclusions and action points	
MSC adopted the main conclusions and action points of MSC-45 at the meeting.	**MSC-S** to submit draft minutes of MSC-45 for commenting by 15 January 2016. **MSC-S** to upload the main conclusions and action points on MSC CIRCABC by 11 December 2015.