Mecetronium ethyl sulphate

Biocide for Use as Human hygiene biocidal product (PT 1)

Dossier submitted according to Directive 98/8/EC
and evaluated according to Regulation 528/2012

Document I

Overall Summary and Assessment

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1 STATEMENT OF SUBJECT MATTER AND PURPOSE

The dossier for evaluation of the existing active substance Mecetronium ethyl sulphate (MES) in PT1 was submitted according to Directive 98/8/EC by BODE Chemie GmbH (Applicant) on 31 July 2007. In this specific case the numerous updates of data were submitted by the Applicant over the years. The dossier is evaluated according to Regulation 528/2012.

Based on the data submitted by the Applicant till the CLH report was compiled by the respective CA PL, the RAC opinion was finalized on 14 September 2018 (under Regulation 1272/2008). However, after the RAC opinion, some new data were submitted by the Applicant within the dossier evaluation process according to Regulation 528/2012 (under Regulation 1062/2014).

The evaluation report (draft CAR), compiled based on all the data submitted, was sent for accordance check on 5 March 2020. The first accordance check failed and the reasons were given to the Applicant on 8 April 2020. Taking into account the submitted updates and amendments of the dossier, the updated report (draft CAR) together with a proposed reference specification was sent for accordance check on 26 February 2021. The second accordance check failed and the reasons were given to the Applicant on 30 March 2021.

The ENV WG e-consultation (concerning biotic degradation and ED assessment for non-target organisms) took place between 31 March and 23 April 2021. The outcome of these e-consultation was sent to the Applicant on 13 May 2021.

Following further communication, another set of updates and amendments of the dossier was received from the Applicant. The updated report (draft CAR) was sent for commenting by the Applicant on 1 December 2021. The comments provided by the Applicant were addressed by the eCA and changes in the report (draft CAR) were made. A change to a proposal for a non-approval was due to data gap and in order to avoid major inconsistency. This report (draft) was sent for accordance check on 7 January 2022. The third accordance check passed and the commenting phase started on 1 February 2022. The Applicant refrained from commenting (on 7 March 2022).

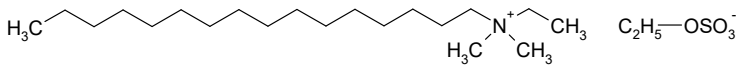
Later during the peer review, the Applicant provided replies to comments by MSCAs and ECHA in RCOM, and submitted: the elaborated read-across justification for a weight of evidence for ED Assessment for human health (on 2 May 2022), multiple position papers (30 March 2022, 17 and 18 May 2022, 15 June 2022), new data (16, 25 and 27 May 2022), notes (22 June 2022, 25 July 2022). The position papers were available for MSCAs and ECHA. The APCP WG II 2022 agreed to allow the new data to be evaluated and included in the CAR, hence a reference specification was set, assessment of (eco)tox batches against it and assessment of relevant impurities, new waivers for physical hazards, B assessment underwent a round of WG Adhoc follow ups (between 20 June 2022 and 1 August 2022).

Based on the outcome of the consultations, organised by the Agency, via the BPC (BPC-44) and its Working Groups (WG-II-2022), the revisions agreed upon were presented and the assessment report and the conclusions were amended accordingly.

2 OVERALL SUMMARY AND CONCLUSIONS

2.1 IDENTITY

Table 2-1 Identity of the Mecetronium ethyl sulphate (Doc III A2.1-2.7)

CAS-No.	3006-10-8
EINECS-No.	221-106-5
Other No. (CIPAC, ELINCS)	
IUPAC Name	Dimethylethylhexadecylammonium ethylsulfate
Common name, synonyma	Mecetronium ethylsulfate, Mecetronium etilsulfat, MES, Ethylhexadecyldimethylammonium ethylsulfate, Cetylethyldimethylammonium ethosulfat Dimethylethylhexadecylammonium-ethylsulfate Ethanesulfonate ethyl-hexadecyl-dimethyl-ammonium
Molecular formula	$C_{20}H_{44}N.C_2H_5O_4S$
Structural formula	
Molecular weight (g/mol)	423.70 g/mol

The active substance Mecetronium ethylsulfate is manufactured as technical concentrate and it contains impurities (see Doc IIIA, Appendix III), including relevant impurities (see Doc IIA and Chapter 1 of Appendix I of Doc I), but no additives. The reference specification of technical concentrate and of dry weight active substance was derived from 5 batch analysis provided by the Applicant in May 2022.
Compliance of batches of active substance used in environmental and human health studies with the new reference specification was investigated as a part of the assessment of Mecetronium ethylsulfate. The data concerning the production of the active substance provided by the Applicant showed that some compounds (impurities originating from the starting material and reaction by-products) are continuously monitored during the manufacture process of the active substance. For the purpose of quality control and process control, concentrations of those compounds are determined with non-specific analytical methods; these methods were used for 5 batch analysis performed in 2019-2020 (see Confidential Appendix III to Doc IIIA, Table 1). However, for 5 batch analysis of active substance performed in 2021-2022 specific analytical methods for individual compounds and impurities were developed and this particular data was used as a basis for the reference specification of the technical active substance and dry weight specification. Nevertheless, impurity profiles of the batches of active substance used for toxicological and ecological tests were determined with the non-specific methods. Because the data concerning content of impurities in (eco)toxicological batches and in 5 batches analysed in 2021-2022 was obtained with different analytical methods, it is not possible to directly compare impurities and their content in (eco)toxicological batches of active substance with the reference specification.
However, according to the statement by the Applicant, the active substance MES is produced [redacted] under GMP conditions and has not been changed. Taking the above

into consideration, although the batches do not comply with the reference specification, the batches used in (eco)toxicity studies can be accepted for the assessment of active substance.

2.2 PHYSICAL AND CHEMICAL PROPERTIES

Pure Mecetronium ethylsulfate (MES) is a white powder with no specific odour. Purity of the active substance is > 85% w/w (dry weight calculation). Its relative density is 1.08 g/cm3 at 20°C and the melting range 87.6 - 111.0°C, while the boiling point could not be measured due to decomposition occurring at 271-286°C.

MES is an ionic substance and its vapour pressure is estimated to be 3.2 10-10 hPa at 20°C. The active substance is very soluble in water (>500g/ 1000g), it is soluble in 1-propanol (333-500 g/L at 20°C), 2-propanol (333-500 g/L at 20°C), n-octanol (168-202 g/L at 20°C) and less soluble in n-heptane (<10 g/L at 20°C). The critical micelle concentration of the technical concentrate was determined as 320.8 mg a.s/L (room temperature, neutral pH).

The active substance is manufactured, handled and presented on the market as aqueous solution and not powder, therefore granulometry data was waived.

MES is not considered a flammable solid, is not self-reactive, self-heating, explosive or oxidising. The active substance does not require classification for physical hazards according to the Regulation (EC) No 1272/2008.

2.3 ANALYTICAL METHODS FOR DETECTION AND IDENTIFICATION

Suitable analytical methods for MES are available (see Doc IIA). These methods show sufficient specificity and accuracy. Sensitivity of analytical methods is insufficient, as LOQ values for soil and for water are higher than indicated in the guidance document (Guidance SANTE/2020/12830, rev.1).

2.4 CLASSIFICATION, PACKAGING AND LABELLING

Table 2-2 Classification and labelling of the active substance in accordance with CLP Regulation (EC) No 1272/2008 according to Risk Assessment Committee (RAC) Opinion (14 September 2018)

Pictogram	GHS05 GHS09
Signal Word	Danger
Class of danger	Skin Corr. 1 Eye Dam. 1 Aquatic Acute 1; M=100 Aquatic Chronic 1; M=1000
Hazard statement	H314 H318 H400 H410 EUH071

Table 2-3 Proposed classification and labelling

Pictogram	GHS05 GHS09
Signal Word	Danger
Class of danger	Skin Corr. 1 Eye Dam. 1 Aquatic Acute 1; M=10 Aquatic Chronic 1; M=10
Hazard statement	H314 H318 H400 H410 EUH071

Note from eCA: The applicant's proposal of classification concerns the revised M factors for Aquatic Acute 1 M = 10 and for Aquatic Chronic 1 M=10 as compared with the RAC opinion (14 Sept 2018). Justification for the revised proposal is a new set of studies provided by the applicant and evaluated by the eCA as reliable. The weight of evidence and expert judgement support the choice of the key studies among all studies submitted due to the feasibility problems caused by the specific active substance properties. Based on CLP Regulation 1272/2008 as amended by Comission Regulation EU 2016/918 and Comission Regulation EU 487/2013 the EC_{50} value from the short-term studies (daphnia and algae, reliability score 1) is between 0.01 and 1 mg/L hence Acute Category 1 with M factor 10, and the NOEC value from long-term studies (fish, reliability score 1) is between 0.0001 and 0.001 mg/L, but also the substance is readily biodegradable, hence Chronic Category 1 with M factor of 10. Therefore, the revised M factors, as proposed by the applicant, are recognized as correct and accepted by the eCA.

For labelling H410 is sufficient instead of both H400 and H410, as well as H314 is sufficient instead of both H314 and H318, according to CLP Regulation 1272/2008 as amended.

2.5 INTENDED USES AND EFFICACY

Mecetronium ethyl sulphate (MES) is a disinfectant with bactericidal and yeasticidal properties. MES containing products are employed as broad-spectrum microbiocides for hygienic and surgical hand disinfection.

The effectiveness of the biocidal active substance MES against the intended target organisms (e.g., gram-negative and gram-positive bacteria and yeasts) has been demonstrated in reliable experimental studies detailed in Doc IIIA5 (active substance). The studies A5.3/01, A5.3/02, A5.3/03 can be used to confirm efficacy biocidal product with MES.

Studies only with active substance show that MES is effective in irreversibly inactivating gram-negative and gram-positive bacteria and yeasts which are representative for the organisms in long time of contact (60 min for all bacteria and 15 min for yeast). Time of contact for the intended field of use like hygienic hand disinfection should be maximal up to 1 min. The submitted efficacy data on biocidal product

(containing 0.2% of MES as well as 30% propan-1-ol and 45% propan-2-ol) proved effectiveness of MES with another active substances in hygienic hand disinfection in contact time less than 1 min.

The submitted efficacy studies with MES (Doc III A5.1) do not concern surgical hand disinfection nor are sufficient to prove virucidal activity. However, the efficacy studies with the representative biocidal product (containing 0.2% of MES as well as 30% propan-1-ol and 45% propan-2-ol) concern also surgical hand disinfection as well as virucidal activity.

At the product authorisation stage, efficacy should be demonstrated according to uses claimed.

2.6 HUMAN HEALTH EFFECTS ASSESSMENT

2.6.1 Toxicokinetics

The relevant exposure path is the dermal route. After dermal exposure (occlusive) to 1 mg 14C-labelled mecetronium ethyl sulphate for 24 h in male and female Long-Evans radioactivity was recovered in urine, faeces, cage washings and tissues during the sampling period of 72 h indicating a minimal absorption of the radiolabelled test substance dissolved in DMSO. Under the condition of this study percutaneous absorption of mecetronium ethyl sulphate is ca. 3%. For the small part of absorbed mecetronium ethyl sulphate a wide distribution of radioactivity in tissue was reported at 72 h post-application. The main parts of radioactivity were located in the gastro-intestinal tract (0.11%) and the carcass (0.7%). Dermal absorption is 4.5% after 24 h occlusive application and 100% for corrosive concentrations.

2.6.2 Human health hazard of the active substance (MES)

Mecetronium ethyl sulphate (MES) was of low toxicity after acute oral or dermal application in rats. The active substance produced in the manufacturing process as 30% aqueous dilution was tested in limit tests at 2000 mg/kg bw with both application routes and did not reach LD_{50}. The LD_{50} was > 600 mg a.s./kg bw. Pathology results indicated that toxicity of the test substance after oral administration is due to local effects in the gastro-intestinal tract (GI tract).

Mecetronium ethyl sulphate is corrosive to skin and eyes and is expected to be irritant/corrosive also for the respiratory tract.

Tests in animals and humans indicate that a concentration of 0.2% is not irritant to skin.

No sensitizing effects of mecetronium ethyl sulphate were observed in a GPMT test.

In a subchronic gavage study (OECD TG 408) rats received 0, 15, 45, 135/90 mg/kg bw (corresponding to a concentration of 0, 0.3, 0.9, 2.7/1.8%) once daily (7 days per week). No effects of toxicological significance were observed at 45 mg/kg bw. At the high dose level of 135/90 mg/kg bw (2.7/1.8% in water) local effects were observed in the stomach. Secondary to the local effects in the stomach clinical signs, reduction in body weight gain and food consumption were reported. Changes in organ weights were not observed and histopathological findings in other organs than the stomach were within the normal range. The NOAEL for local effects is 45 mg/kg bw/day, corresponding to a concentration of 0.9 % MES.

In the Salmonella microsome assay and the chromosome aberration assay in CHO cells no mutagenic activity was reported. Contradictory results were reported on gene/chromosome mutations in a former mouse lymphoma assay. Therefore, this test was repeated and in a recent in vitro mammalian cell gene

mutation assay in mouse lymphoma cells according to OECD TG 476 both with and without metabolic activation MES did not show evidence of inducing gene mutations. No induction of unscheduled DNA synthesis was reported in a human cell line. In summary, in vitro results on genotoxicity revealed no evidence for mutagenic or DNA-damaging activity.

In the mouse bone marrow micronucleus test single oral application of 0, 19, 56, 187 mg/kg bw via gavage did not induce a significant increase in the number of micronuclei. However, the recommended MTD was not reached in this study and it is questionable whether an in vivo test is feasible, because the absorption after oral uptake is limited and local but not systemic effects of mecetronium ethyl sulphate are predominating.

No long-term/carcinogenicity studies were performed with MES because long time experiences in humans using biocidal products containing 0.2% MES did not indicate a tumorigenic potential of the substance. The mode of action of MES is determined by its reactivity at the site of first contact and due to the low absorption only very small amounts of the substance can be achieved as systemically available.

In a teratogenicity study in rabbit effects on development were investigated according to OECD TG 415. MES was administered by gavage in dose levels of 0, 4, 12, 30, 40 mg/kg bw/day. Local effects were found in the gastro-intestinal tract at ≥ 30 mg/kg bw/day. Concomitant to the local effects, decreased food intake, decreased body weight gain and mortality were observed, and maternal toxicity was considered to be excessive at ≥ 30 mg/kg bw/day. No treatment-related effects were reported at 12 and 4 mg/kg bw/day and the NOAEL for local maternal effects is 12 mg/kg bw/day corresponding to 0.6% MES. No developmental effects of biological relevance were detected. Abortions at ≥ 30 mg/kg bw/day were secondary due to local effects on the gastro-intestinal tract and excessive maternal toxicity and the NOAEL for fetal development was > 40 mg/kg bw/day. A developmental toxicity study with MES in rats has not been performed because conducting such a study is deemed not necessary due to the absence of developmental or reproductive effects in the existing studies.

Effects on male and female reproductive performance was investigated in a one-generation reproduction toxicity study in rat according to OECD TG 415. Mecetronium ethyl sulphate was administered by gavage in dose levels of 0, 10, 40 and 110 mg/kg bw/day. Local irritant effects in terms of histopathological changes in the stomach were observed in males and females at 40 mg/kg and 110 mg/kg bw/day (corresponding to concentrations of 0.4 % and 1.1% MES in the stomach, respectively). The local effects were associated with clinical symptoms like rales and salivation, decreased body weight gain food consumption and mortality at 110 mg/kg bw/day. A NOAEL for local maternal effects of 10 mg/kg bw/day was determined, corresponding to a concentration of 0.1 % MES. The results of the recovery group revealed that all effects in parent animals in the high dose group corresponding to concentrations of 1.1% were completely reversible after a four-week recovery period. Adverse effects on sexual function, fertility and development were observed in the high dose group at 110 mg/kg bw/day and the number of implantation sites, the number of live pups at first litter check and the pup body weight development were decreased as compared to controls. However, as the maternal mortality was 17%, the maternal toxicity was excessive. Effects on sexual function, fertility and development were not observed in the low- and mid-dose group. The F1 animals showed no test item-related effects.

MES does not belong to a class of compounds for which a neurotoxic potential can be expected. In addition, the available toxicity studies gave no indication of a relevant neurotoxic potential of the compound. There is no need to conduct specific neurotoxicity tests.

Conclusion on Effects Assessment

Overall, local effects in the stomach/GI tract were consistently reported as relevant primary effect in the 90-day repeated toxicity study in rats, in the developmental toxicity study in rabbits and in the 1-generation study in rats as a result of irritant effects at the side of first contact. Consistent with the mode of action of a corrosive substance, local effects represent the major outcome of toxicity related to MES. No specific organ toxicity was evident and the systemic effects such as clinical signs, decrease in body weight are regarded as secondary to the local effects. The NOAEL for local toxicity upon repeated oral administration by gavage was 10 mg/kg bw/day (corresponding to a concentration of 0.1 % MES) based on the 1-generation study in rats. The NOAEL for local toxicity for the dermal route is 0.2 %.

During the WG II 2022 it was agreed that it needs to be verified to which specification the NOAEC value corresponds (whether it is w/w and adjusted if needed). The study reports of the local irritation/corrosion indicate that "the test article is 0.2% or 4% Mecetroniumethilsulfat", as specified by the Applicant (sponsor). According to the Applicant's justification, the concentration of MES in the biocidal product is referred to the unspecific titration method that determines the sum of C12-C18 MES constituents. Furthermore, this analytical method was applied for most studies of the HH part of the dossier. However the titration method was not accepted for establishing the reference specification. For the purpose of the BPR, new analytical data has been generated. A specific and validated analytical method is available for MES using HPLC-ELSD. It is not possible for eCA to relate the concentration of MES determined by the titration method to the actual specification, taking into account that the batches used in (eco)tox studies do not comply with the specification of active substance MES set based on 5 batch data.

2.6.2.1. ED properties

The weight of evidence with elements of read-across to other quaternary ammonium compounds (named as supportive data) was submitted by the Applicant and modified with additional argumentation for a read-across. During the peer review the Applicant submitted 2 published articles on studies with other QACs and a position paper (2 documents), however, no confirmation of rights to use the data was submitted and the provided read-across was not performed in line with RAAF recommendations. The HH WG had asked for a more substantiated read-across justification. If such a more robust read-across explanation could be submitted by the Applicant, the weight of evidence should undergo a peer review by WG (e.g in ad hoc follow up).

With regard to human health, EATS-mediated adversity and EATS-related endocrine activity are not sufficiently investigated when strictly adhering to the ECHA/EFSA ED Guidance. Neither EATS-mediated adversity nor activity was observed for MES in the available *in vivo* studies and the *in silico* predictions.

The HH WG II 2022 agreed that based on the information provided it is not possible to conclude on the ED properties of MES.

2.6.3 Human health hazard of the biocidal product

The representative b.p. is based on propan-1-ol (30% w/w), propan-2-ol (45% w/w) and MES (0.2 % w/w) (given also in Doc IIB sections 1.1 and 2.1) and has low acute toxicity after oral and dermal exposure in laboratory animals. In oral studies in rats lethal effects occurred at high dose levels of ≥ 10700 mg/kg bw. Clinical symptoms were an increase in breathing rate, apathy and reduced reflex suggesting effects on the central nervous system. Pathology revealed local irritation effects on the mucosa of the gastro-intestinal tract. After acute dermal exposure no local or systemic effects were recorded in rabbits exposed to 8500 mg/kg bw even in animals with scarified skin.

The representative b.p. was demonstrated to be not irritating to skin. Data on skin irritant effects in clinical studies after dermal exposure did not reveal any adverse effects in volunteers.

In a clinical study on skin sensitisation, 55 volunteers received during a 3-week induction period a total of 9 occlusive patches each with 0.2 ml undiluted b.p. (each patch was removed after 24 h). Also, for challenge, undiluted b.p. was used as test substance. All subjects demonstrated no skin reaction 24, 48, and 72 h after challenge.

In a clinical study the compatibility of the disinfectant was tested in 15 volunteers in a long-term, double blind, cross-over study. Under the condition of this study, the representative b.p. revealed good skin compatibility. In a Periodic Safety Update Report (PSUR) required for medicinal products the incidence of suspected reactions caused by the b.p. was very low (0.00018%) and can be considered to be “very rare” (< 0.01%).

2.6.4 Risk assessment for Mecetronium ethyl sulphate in the representative b.p.

The representative b.p. is a ready for use solution, which is currently used for hygienic and surgical hand disinfection. The concentration of the active substance in the representative b.p. is 0.2%. Users are exposed to MES via the dermal route. Based on the intended use and the physico-chemical properties of MES exposure by inhalation or the oral route is assumed to be negligible. Due to lack of systemic effects in the absence of local effects, derivation of an AEL would not be appropriate, and thus a systemic exposure assessment was not considered necessary. A local risk assessment has been provided in line with the Guidance for Human Health Risk Assessment (Guidance on the BPR: Volume III Human Health, Part B Risk Assessment).

During WG II 2022 setting of ADI and ARfD was considered consistent with earlier conclusions on similar substances and in line with “ADI and ARfD derivation for biocidal active substances” (WG agreement, 2016). Therefore, it was agreed to use the lowest NOAEL 10 mg/kg bw/day, based on the one-generation study in rat. Since the treatment regimen is by gavage (implying a bolus dose in the absence of food) the local effects are highly dependent on the concentration in situ, therefore, the NOAEL is better defined as a NOAEC and reasonably it represents a worst case. Assuming an AF of 25, the ADI and the ARfD result to be 0.4 mg/kg bw/day.

2.6.4.1 Risk characterisation for professional users

The life cycle steps production of active substance and formulation of biocidal product were evaluated. It is assumed that the processes are performed in conformity with national and European occupational safety and health regulations.

As reasonable worst-case scenario for hygienic hand disinfection, it is assumed that a nurse performs 25 hand disinfections during her shift. The respective scenario for surgical hand disinfection is also given in Recommendation no. 1 of the BPC Adhoc Working Group of Human Exposure. According to ECHA Guidance on BPR: Volume III Parts B+C and the TAB (2018) a qualitative risk characterisation for local effects is triggered when the biocidal product is not classified for local effects and a semi-qualitative approach could be used to support the qualitative assessment. The representative biocidal product is not classified for local effects to skin and available data indicate that mecetronium ethyl sulphate has no skin irritant effects at a concentration of 0.2 % upon single and repeated exposure. In addition, a good skin tolerance of MES after repeated applications was proved in a study with volunteers. Therefore, the human health risk is considered as acceptable for the professional use.

2.6.4.2 Risk characterisation for non-professional users

Hygienic hand disinfection might be performed by non-professional user (i.e. visitors in hospitals, patient at home-dialysis). The frequency is assumed to be much lower than for professionals. The representative biocidal product is not classified for local effects. Available data indicate that mecetronium ethyl sulphate has no skin irritant effects at a concentration of 0.2 % upon single and repeated exposure. In addition, a good skin tolerance of MES after repeated applications was proved in a study with volunteers. Therefore, the human health risk is considered as acceptable for the non-professional use.

2.6.4.3 Human experiences

The active substance was placed on the market in 1965 and has been widely used as disinfectant during the last decades, mainly as medicinal product. The overall time of exposure for professional users is estimated to be months or years. For medicinal products pharmacovigilance documents, so called Periodic Safety Update Report (PSUR) have to be submitted on a regular basis intended to provide an evaluation of the risk-benefit balance of a product at defined time points after its authorization. A Periodic Safety Update Report is given for a period of five years demonstrating the low frequencies of any observed adverse effects during use of the product. No serious drug reactions were reported. The incidence of non-serious drug reactions is very low and can be considered to be “very rare”.

2.6.4.4 Discussion of risk/safety for use

In summary all this given information demonstrates a high skin tolerance to the representative biocidal product and a very low rate of adverse effects for a long time of use in hygienic hand disinfection. Thus, the use of mecetronium ethyl sulphate in the representative b.p. is expected to have no risk to humans.

2.6.4.5 Risk characterisation for indirect exposures

Indirect exposure is not expected for the intended use.

2.7 ENVIRONMENTAL EFFECTS ASSESSMENT

The reference specification of the active substance is set based on the 5 batch data received during the peer review. The test item used in ecotoxicity and fate studies was with the respective Certificate of analysis giving the result of titration method or a radiolabelled test item. In this specific case the batches used in ecotoxicity studies can be accepted for the assessment of active substance, although they do not comply with the reference specification of the active substance MES (see Confidential Appendix

III to Doc IIIA). Therefore, the endpoint values are derived from the study results, which state test substance concentration in the respective study reports.

2.7.1 Fate and distribution in the environment

Biodegradation

Based on available information and experimentally derived data MES is considered as readily biodegradable.

Abiotic degradation

MES dissociates in aqueous solution generating ethyl sulphate and the mecetronium cation. The molecular structure of the mecetronium cation has no hydrolysable functional group. Ethyl sulphate may hydrolyse in aqueous solution forming ethanol and sulphuric acid.

Regarding photolysis MES has one UV absorption maximum < 290 nm. Thus, abiotic degradation by photolysis in water is not expected according to US EPA method OPPTS 835.2210.

The reaction rate of mecetronium ethyl sulphate and the mecetronium cation with OH-radicals in the atmosphere were calculated and the half-life was estimated to be in the range between 9.04 – 9.22 h. As described above due to the UV absorption maximum < 290 nm MES cannot undergo direct photolysis in sunlight. In the gas phase, MES is rapidly degraded in air via reaction with OH radicals. In comparison to this removal mechanism, degradation by nitrate radicals and ozone as well as direct photolysis is negligible. Because of the low volatility and low Henry's law constant of MES, phototransformation in air is of minor importance.

Distribution and Mobility

Experimentally derived soil adsorption data are available for MES. Adsorption coefficient values between 3454 and 47,600 L/kg were experimentally determined. At the environmentally relevant pH (tested at 5.6 up to 7.2) the active substance adsorption is very strong and desorption is poor and there are indications that sorption to soil is dominated by ionic linkage. Because no fundamental differences between soil and sediments with respect to their sorption properties are expected, the value for soil is, as a worst-case approach, also used for sediments and suspended particles.

The distribution in the sewage treatment plant was calculated in a tiered approach. In Tier 1 model calculations of SimpleTreat 4.0 have been considered. In Tier 2 refined distribution values have been calculated based on the results of the STP simulation study.

Bioaccumulation

Non-compartment specific effects relevant to the food-chain (secondary poisoning) was not experimentally assessed for MES. However, considering the log Kow of 2.80, literature review of the bioconcentration data for a range of quaternary ammonium compounds and results of a toxicokinetic study it is assumed that MES does not bioconcentrate in biota.

For surface active substances, for which the octanol/water partition coefficient cannot be measured properly, a high adsorptive capacity (of which solids-water partition coefficient log Kp > 3 may be an indication) can be additional evidence of bioaccumulation potential. However, the log Kow of 2.80 for MES is based on the CMC (critical micelle concentration) value and therefore the cationic surfactant characteristics of the active substance were taken into account. Adsorption onto biological surfaces,

such as gills or skin, may also lead to bioaccumulation and an uptake via the food chain. Possible absorption of surfactants irritants may be enhanced because of damage to cell membranes. Hence, high adsorptive properties may indicate a potential for both bioaccumulation and biomagnification. Both biotic and abiotic degradation may lead to relatively low concentrations of a substance in the aquatic environment and thus to low concentrations in aquatic organisms. However, the uptake rate may still be greater than the rate of the degradation processes, leading to high BCF values even for readily biodegradable substances. Therefore ready biodegradability does not preclude a bioaccumulation potential, but for most readily biodegradable substances concentrations will be low in aquatic organisms (Guidance on the BPR Volume IV, Part B+C, Version 2.0 (2017), Guidance on Information Requirements and Chemical Safety Assessment, Chapter R.7b: Endpoint specific guidance, Version 4.0 (2017) and Guidance on Information Requirements and Chemical Safety Assessment Chapter R.7c: Endpoint specific guidance, Version 3.0 (2017)). What is more, the biodegradation of surfactants means not only transformation and/or mineralisation but also possible deposition in biomass (also mentioned in Regulation (EC) No 648/2004 on detergents).

During the peer review the Applicant submitted four new publications and a position paper (note) as supportive information, which say that permanently charged QAC (of certain chain length) mainly adsorbs to surface tissue and may accumulate mainly in the gills and the systemic uptake may be very slow. The participants of the ENV WG II 2022 Ad hoc follow up agreed that with the information submitted by the Applicant, it can be concluded that MES does not meet the B criteria.

2.7.2. Exposure assessment

The environmental exposure assessment has been conducted based on the fate and distribution properties of the active substance and follows the recommendations of the Emission Scenario Documents for Biocides (Environmental Emission Scenarios for biocides used as human hygiene biocidal products, Product type 1, European Commission DG ENV / RIVM) (ESD PT1), the Guidance on the BPR Volume IV, Part B+C (2017) and of the Technical Agreements for Biocides Environment (ENV), Version 2.0 (TAB 2018). The environmental exposure to MES during the life-cycle steps ‘formulation’ and ‘production’ is provided in a separate document and is not further considered in the risk assessment. Regarding the life-cycle step ‘use’, two intended uses are a use in health care units for hygienic hand disinfection and a surgical hand disinfection, however, based on the data submitted only hygienic hand disinfection with a minimum requirement of innate activity was demonstrated.

Environmental exposure has been calculated for professional use based on annual tonnage applied and based on average consumption. The predicted environmental concentrations (PECs) have been calculated using EUSES 2.2.0 (according to emission scenarios and the Guidance on the BPR Volume IV, Part B+C (2017)) and specific data, where available.

For the average consumption scenario for professionals a picklist value for quaternary ammonium compounds was taken (Table 3.8 in Environmental Emission Scenarios for Biocides used as human hygiene biocidal products, Product type 1, EUBEES 2004), because the nursing staff and surgical staff calculations should only be performed if no pick list values are available. The ENV WG II 2022 agreed that in this case the tonnage based approach represents the worst case of both approaches and should be used for decision making.

2.7.3. Ecotoxicological studies

Ecotoxicological acute and long-term studies with aquatic organisms are available for all trophic levels, i.e. algae, daphnids and fish. The results of the short-term and long-term studies indicate that MES is very toxic to aquatic organisms. Fish was found to be the most sensitive species in long-term testing with a NOEC of 0.56 µg/L corresponding to 0.00056 mg/L.

For the sediment compartment, MES toxicity was tested on midge larvae and a long-term NOEC of 80.1 mg/kg dry sediment was determined from this study.

Inhibition on microbial activity (aquatic) was tested on activated sludge. The EC_{50} was established at a concentration of 22 mg/L.

In the terrestrial compartment, MES toxicity was tested on earthworms, plants and on microbial activity in soil. MES was not harmful towards soil microorganisms. In studies with plants and earthworms the effect values are: the EC_{50} for plants is 114 mg/kg dry soil and the NOEC for earthworms is 18.1 mg/kg soil dw.

PNEC values for all environmental compartment were derived from the results of the ecotoxicological studies according to the recommendations given in the Guidance on the BPR Volume IV, Part B+C (2017) and were compared with the respective PEC values. The results indicate that the active substance MES does not pose an unacceptable risk to the aquatic (including sediment and sewage treatment plant) and soil organisms.

2.7.4. ED properties

The weight of evidence was submitted as the justification of no need for further testing, and modified with additional read-across argumentation (named as supportive data).

With regard to non-target organisms, EATS-mediated adversity and EATS-related endocrine activity are not sufficiently investigated when strictly adhering to the ECHA/EFSA ED Guidance. However, adverse effects observed in the ecotoxicological studies available for MES were associated with general toxicity. The available information provides no indication for potential endocrine disrupting properties of MES, with regard to adverse effects which might be relevant at the population level for non-target organisms.

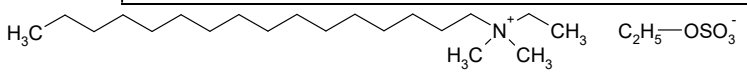
The ENV WG II 2022 agreed that based on the information provided it is not possible to conclude on the ED properties of MES and that extending the weight of evidence approach would not be sufficient to conclude on the ED properties of MES for non-target organisms.

3 APPENDIX I: LIST OF ENDPOINTS

Chapter 1: Identity, Physical and Chemical Properties, Details of Uses, Further Information, and Proposed Classification and Labelling

Active substance (ISO Common Name)	Mecetronium ethyl sulphate
Function (e.g. bactericide)	Human hygiene product
Rapporteur Member State	Poland

Identity (Annex IIA, point II.)

Chemical name (IUPAC)	Dimethylethylhexadecylammonium ethylsulfate
Chemical name (CA)	
CAS No	3006-10-8
EC No	221-106-5
Other substance No.	-
Minimum purity of the active substance as manufactured (g/kg or g/l)	> 85 % w/w (dry weight calculation)
Identity of relevant impurities and additives (substances of concern) in the active substance as manufactured (g/kg)	Dodecylethyldimethylammonium ethyl sulphate (CAS: 3006-13-1) < 0.2% w/w (dry weight calculation) Tetradecylethyldimethylammonium ethyl sulphate (CAS: 19309-23-0) < 1.2% w/w (dry weight calculation) Sodium ethylsulfate (CAS: 546-74-7) < 5% w/w (dry weight calculation) Diethylsulphate (CAS: 64-67-5) < 0.003% w/w (dry weight calculation) Ethanol (CAS: 64-17-5) < 8% w/w (dry weight calculation)
Molecular formula	$C_{20}H_{44}N^{+}\ C_2H_5O_4S^{-}$
Molecular mass	423.70 g/mol
Structural formula	

Physical and chemical properties (Annex IIA, point III., unless otherwise indicated)

Melting point (state purity)	87.6 – 111.0 °C (99.5%)
Boiling point (state purity)	Boiling point could not be measured due to decomposition at 271 °C – 286 °C (99.5%)
Temperature of decomposition	Decomposition starts at 271 °C – 286 °C (99.5%)
Appearance (state purity)	Solid (pure substance)
Relative density (state purity)	1.08 g/cm^3 at 20 °C (99.5%)
Surface tension	38.5 mN/m (99.5%)
Vapour pressure (in Pa, state temperature)	Temperature: 20 °C 3.2 • 10^{-10} hPa (estimated)
Henry's law constant (Pa m^3 mol $^{-1}$)	Temperature: 25 °C 5.9 • 10^{-9} Pa m^3 mol^{-1} (estimated) 3.9 • 10^{-5} Pa m^3 mol^{-1} (estimated)
Solubility in water (g/l or mg/l, state temperature)	Temperature: 20 °C > 500 g /1000 g water Critical micelle concentration: 320.8 mg/l
Solubility in organic solvents (in g/l or mg/l, state temperature) (Annex IIIA, point III.1)	in 1-Propanol at 20°C: 333-500 g/l; at 30°C: >500 g/l in 2-Propanol at 20°C: 333-500 g/l; at 30°C: >500 g/l n-Octanol at 20 °C: 168-202 g/L in n-Heptane at 20°C: <10 g/l; at 30°C: <10g/l
Stability in organic solvents used in biocidal products including relevant breakdown products (IIIA, point III.2)	a.s. is stable in b.p. over 60 months at 25 °C and over 12 months at 40 °C
Partition coefficient (log P_{OW}) (state temperature)	2.80 (Calculation based on the CMC and solubility in n-octanol)
Hydrolytic stability (DT_{50}) (state pH and temperature) (point VII.7.6.2.1)	In water MES dissociates into the mecetronium cation and the ethylsulphate anion. The cation is stable when being boiled for 3 hours at pH values between 4.2 and 8.7
Dissociation constant (not stated in Annex IIA or IIIA; additional data requirement from TNsG)	pKa = 6.5
UV/VIS absorption (max.) (if absorption > 290 nm state ε at wavelength)	<< 290 nm
Photostability (DT_{50}) (aqueous, sunlight, state pH) (point VII.7.6.2.2)	Not required (Doc III A3)
Quantum yield of direct phototransformation in water at Σ > 290 nm (point VII.7.6.2.2)	Not required (Doc III A3)
Flammability	Not flammable (Doc III A3)
Explosive properties	Not explosive (Doc III A3)

Proposed classification and labelling (Annex IIA, point IX.)

with regard to physical/chemical data	no classification
Signal word	Danger
with regard to toxicological data	GHS05 H314 H318 EUH071
with regard to ecotoxicological data	GHS09 H400 (M factor=10) H410 (M factor=10)

Chapter 2: Methods of Analysis

Analytical methods for the active substance

Technical active substance (principle of method) (Annex IIA, point 4.1)	High Performance Thin Layer Chromatography (HPTLC) High Performance liquid chromatography with evaporative light scattering detector (HPLC-ELSD)
Impurities in technical active substance (principle of method) (Annex IIA, point 4.1)	Isocratic HPLC with RI detection High Performance liquid chromatography with evaporative light scattering detector HPLC-ELSD Gas chromatography with flame ionisation detector (CG-FID) Ion chromatography with conductivity detection (IC-CD)

Analytical methods for residues

Soil (principle of method and LOQ) (Annex IIA, point 4.2)	LC-MS/MS. LOQ of the soil extract was 0.04 mg/L
Air (principle of method and LOQ) (Annex IIA, point 4.2)	Not required, MES analysis of air is not relevant due to its very low vapour pressure and Henry's law constant.
Water (principle of method and LOQ) (Annex IIA, point 4.2)	LC-MS-MS. LOQ was 0.2 µg/L.
Body fluids and tissues (principle of method and LOQ) (Annex IIA, point 4.2)	Not required. The a.s. is neither toxic nor highly toxic Due to the intended registration of the b.p. solely for product type 1 only dermal exposure towards MES can be expected. MES has been demonstrated to possess only a very low dermal absorption potential (Doc III A6.2), therefore the development of an analytical method is scientifically not justified.
Food/feed of plant origin (principle of method and LOQ for methods for monitoring purposes) (Annex IIIA, point IV.1)	Not applicable. MES is solely used for product type 1 and not for food/feed disinfection.
Food/feed of animal origin (principle of method and LOQ for methods for monitoring purposes) (Annex IIIA, point IV.1)	Not applicable. MES is solely used for product type 1 and not for food/feed disinfection.

Chapter 3: Impact on Human Health

Absorption, distribution, metabolism and excretion in mammals (Annex IIA, point 6.2)

Rate and extent of oral absorption:	No data available, 100 % (default)
Rate and extent of dermal absorption:	4.5% percutaneous absorption in the rat, 100 % for corrosive concentrations
Distribution:	Tissue residues (<1%), widely distributed,
Potential for accumulation:	Not expected
Rate and extent of excretion:	1.6% of applied radioactivity within 72 h
Toxicologically significant metabolite	No data available

Acute toxicity (Annex IIA, point 6.1)

Rat LD_{50} oral	> 600 mg/kg bw
Rat LD_{50} dermal	> 600 mg/kg bw
Rat LC_{50} inhalation	No data available
Skin irritation	Corrosive[1]
Eye irritation	Corrosive
Skin sensitization (test method used and result)	negative (Guinea pig maximization test)

Repeated dose toxicity (Annex IIA, point 6.3)

Subchronic

Species/ target / critical effect	Rat (subchronic and 1-generation study, oral)/ local effects in GI tract/stomach, Rabbit (teratogenicity study, oral)/ local effects in GI tract/stomach
Lowest relevant oral NOAEC / LOAEC	Local effects (1-generation study in rat) NOAEC = 0.1% (10 mg/kg bw/day)
Lowest relevant dermal NOAEL / LOAEL	No data available
Lowest relevant inhalation NOAEL / LOAEL	No data available

Long term

Species/ target / critical effect	No data available
Lowest relevant oral NOAEC / LOAEC	No data available
Lowest relevant dermal NOAEL / LOAEL	No data available
Lowest relevant inhalation NOAEL / LOAEL	No data available

Genotoxicity (Annex IIA, point 6.6)	Salmonella microsome assay: negative Chromosome aberration test in CHO cells: negative

[1] Based on RAC opinion of 2018, a preparation containing only 4% MES caused such skin responses and therefore much more severe irreversible effects would be expected for active substance MES.

	Mouse lymphoma assay: negative DNA damage in human cells: negative Mouse bone marrow micronucleus assay: negative

Carcinogenicity (Annex IIA, point 6.7)

Species/type of tumour	No data available but implementation of a long-term study scientifically unjustified.
lowest dose with tumours	No data available

Reproductive toxicity (Annex IIA, point 6.8)

Species/ Reproduction target / critical effect	Rat/1-generation study/ no reproductive effects, excessive maternal toxicity due to local effects in the GI tract/stomach
Lowest relevant maternal NOAEL / LOAEL	NOAEL = 10 mg/kg bw/day
Lowest reproductive NOAEL / LOAEL	NOAEL = 40 mg/kg bw/day
Species/Developmental target / critical effect	Rabbit / developmental toxicity / no developmental effects, excessive maternal toxicity due to local effects in the GI tract/stomach
Lowest relevant maternal NOAEL / LOAEL	NOAEL = 12 mg/kg bw/day
Lowest relevant developmental NOAEL / LOAEL	NOAEL = 40 mg/kg bw/day

Neurotoxicity / Delayed neurotoxicity (Annex IIIA, point VI.1)

Species/ target/critical effect	No data available
Immunotoxicity/ Developmental Immunotoxicity	
Species/ target/critical effect	No data available

Other toxicological studies (Annex IIIA, VI/XI)

.....	No data available

Medical data (Annex IIA, point 6.9)

.....	Good skin compatibility in a clinical study

Summary (Annex IIA, point 6.10)

Summary for systemic effects

	Value	Study	Safety factor
AELlong-term	Not relevant		
AELmedium-term	Not relevant		
AELshort-term	Not relevant		
ADI (if residues in food or feed)	0.4 mg/kg bw/day	Rat/1-generation study	25
AOEL (Operator/Worker Exposure)	n.a.		
Drinking water limit	n.a.		
ARfD (acute reference dose)	0.4 mg/kg bw/day	Rat/1-generation study	25

Summary of Local effects

	Value	Study	Safety factor
AECdermal	0.2 %	Skin irritation studies in animals and humans Only two concentrations were tested, where 4 % was corrosive	

Acceptable exposure scenarios (including method of calculation)

Human exposure during production and formulation of mecetronium ethyl sulphate	The life cycle steps production of active substance and formulation of biocidal product were evaluated
Intended use	Two intended uses are a use in health care units for hygienic hand disinfection and a surgical hand disinfection, however, based on the data submitted only hygienic hand disinfection with a minimum requirement of innate activity was demonstrated.
Mixing & Loading	No mixing & loading, ready-for-use product
Professional user	Inhalation exposure: negligible Dermal exposure: 0.2 %
Non-professional user/ General public	Inhalation exposure: negligible Potential dermal exposure: 0.2%
Indirect exposure as a result of use	Exposure negligible
Exposure via residue in food	Not expected

Chapter 4: Fate and Behaviour in the Environment

Route and rate of degradation in water (Annex IIA, point 7.6, IIIA, point XII.2.1, 2.2)

Hydrolysis of active substance and relevant metabolites (DT_{50}) (state pH and temperature)	Mecetronium cation is not expected to undergo abiotic degradation by hydrolysis relevant for the environmental risk assessment. MES is stable when being boiled for 3 hours at pH values between 4.3 and 8.7.
Photolytic / photo-oxidative degradation of active substance and resulting relevant metabolites	MES is not expected to undergo abiotic degradation by photolysis in water
Readily biodegradable (yes/no)	Yes
Biodegradation in seawater	Not required (Doc IIIA7.1.2 Justification for non-submission)
Non-extractable residues	Not required (Doc IIIA7.1.2 Justification for non-submission)
Distribution in water / sediment systems (active substance)	Not required (Doc IIIA7.1.2 Justification for non-submission)
Distribution in water / sediment systems (metabolites)	Not required (Doc IIIA7.1.2 Justification for non-submission)

Route and rate of degradation in soil (Annex IIIA, point VII.4, XII.1.1, XII.1.4; Annex VI, para. 85)

Mineralization (aerobic)	Not required (Doc IIIA7.1.2 Justification for non-submission)
Laboratory studies (range or median, with number of measurements, with regression coefficient)	DT_{50lab} (20°C, aerobic): not required (Doc IIIA7.1.2 Justification for non-submission)
	DT_{90lab} (20°C, aerobic): not required (Doc IIIA7.1.2 Justification for non-submission)
	DT_{50lab} (10°C, aerobic): not required (Doc IIIA7.1.2 Justification for non-submission)
	DT_{50lab} (20°C, anaerobic): not required (Doc IIIA7.1.2 Justification for non-submission)
	Degradation in the saturated zone: not required (Doc IIIA7.1.2 Justification for non-submission)
Field studies (state location, range or median with number of measurements)	DT_{50f}: not required (Doc IIIA7.1.2 Justification for non-submission)
	DT_{90f}: not required (Doc IIIA7.1.2 Justification for non-submission)
Anaerobic degradation	Not required (Doc IIIA7.1.2 Justification for non-submission)

Soil photolysis	Not required (Doc IIIA7.1.2 Justification for non-submission)
Non-extractable residues	Not required (Doc IIIA7.1.2 Justification for non-submission)
Relevant metabolites - name and/or code, % of applied a.i. (range and maximum)	Not required (Doc IIIA7.1.2 Justification for non-submission)
Soil accumulation and plateau concentration	Not required (Doc IIIA7.1.2 Justification for non-submission)

Adsorption/desorption (Annex IIA, point XII.7.7; Annex IIIA, point XII.1.2)

Ka , Kd Ka_{oc} , Kd_{oc}	Ka 47,600 L/kg not applicable because soil sorption relates to cationic exchange capacity, not organic carbon
pH dependence (yes / no) (if yes type of dependence)	No data

Fate and behaviour in air (Annex IIIA, point VII.3, VII.5)

Direct photolysis in air	9.04 h - 9.22 h half-life (calculated with EPI Suite)
Quantum yield of direct photolysis	n.a.
Photo-oxidative degradation in air	No experimental data available.
Volatilization	Henry's law constant: $3.9 \cdot 10^{-5}$ Pa m^{-3} mol^{-1} (for mecetronium cation), volatilise slowly from aqueous solution

Monitoring data, if available (Annex VI, para. 44)

Soil (indicate location and type of study)	Not available
Surface water (indicate location and type of study)	Not available
Ground water (indicate location and type of study)	Not available
Air (indicate location and type of study)	Not available

Chapter 5: Effects on Non-target Species

Toxicity data for aquatic species (most sensitive species of each group)
(Annex IIA, point 8.2, Annex IIIA, point 10.2)

Species	Time-scale	Endpoint	Toxicity
Fish			
Danio rerio	35 d	Survival	NOEC 0.00056 mg/L (gm)
Invertebrates			
Daphnia magna	48 h	Immobility	EC_{50} 0.016 mg/L (twa)
Daphnia magna	21 d	Reproduction	NOEC 0.00268 mg/L (gm)
Algae			
Desmodesmus subspicatus	72 h	Growth rate	EC_{50} 0.0231 mg/L (gm)
Desmodesmus subspicatus	72 h	Growth rate	NOEC 0.00165 mg/L (gm)
Microorganisms			
activated sludge	3 h	respiration inhibition	EC_{50} 22 mg/L
Sediment dwelling organisms			
Chironomus riparius	28 d	Emergence rate	NOEC = 80.1 mg/kg dw sed (initial measured)

Abbreviation: gm – geometric mean of measured concentrations; twa – time weighted average of measured concentrations.

Effects on earthworms or other soil non-target organisms

Acute toxicity to *Eisenia fetida*. (Annex IIIA, point XIII.3.2)	Mortality: LC_{50} > 1000 mg/kg dry soil (nominal) (OECD 207)
Acute toxicity to *Avena sativa, Phaseolus aureus, Latuca sativa* (Annex IIIA, point XIII.3.2)	Growth: EC/LC_{50} 500, > 1000, 114 mg/kg dry soil (nominal) Seedling emergence: EC/LC_{50} > 1000, > 1000,> 400 mg/kg dry soil (nominal) (OECD 208)
Reproductive toxicity to *Eisenia andrei* (Annex IIIA, point XIII.3.2)	Reproduction: NOEC 18.1 mg/kg dry soil (nominal)

Effects on soil micro-organisms (Annex IIA, point 7.4)

Nitrogen mineralization	NOEC ≥ 1000 mg/kg dry soil (OECD 216)
Carbon mineralization	NOEC ≥ 1000 mg/kg dry soil (OECD 217)

Effects on terrestrial vertebrates

Acute toxicity to mammals (Annex IIIA, point XIII.3.3)	n.a.
Acute toxicity to birds (Annex IIIA, point XIII.1.1)	n.a.
Dietary toxicity to birds (Annex IIIA, point XIII.1.2)	n.a.
Reproductive toxicity to birds (Annex IIIA, point XIII.1.3)	n.a.

Effects on honeybees (Annex IIIA, point XIII.3.1)

Acute oral toxicity	n.a.
Acute contact toxicity	n.a.

Effects on other beneficial arthropods (Annex IIIA, point XIII.3.1)

Acute oral toxicity	n.a.
Acute contact toxicity	n.a.
Acute toxicity to ……..	n.a.

Bioconcentration (Annex IIA, point 7.5)

Bioconcentration factor (BCF)	Calculated BCF_{fish} 47.8 L/kg
Depration time (DT_{50}) (DT_{90})	
Level of metabolites (%) in organisms accounting for > 10 % of residues	

Chapter 6: Other End Points

No tests on other endpoints were conducted.

4 APPENDIX II: INTENDED USES

Effectiveness and field of use as claimed by the Applicant: no industrial use of MES; MES in biocidal products is used by professionals as a broad-spectrum microbicide in numerous areas (e.g. by surgeons and nurses); non-professional use is not envisaged, but hygienic hand disinfections of non-professional e.g. visitors in hospitals, patient at home dialysis can not completely be excluded. Function claimed was bactericide (including *Mycobacterium terrae*) and yeasticide, with the following organisms to be controlled: obligate or facultative pathogenic bacteria, yeasts and viruses (including enveloped and non-enveloped viruses).

For summary of evaluation of intended uses and efficacy please see section 2.5 in Doc I.

5 APPENDIX III: LIST OF STUDIES

The list of references was submitted by the Applicant and forwarded to the accordance check:
Doc_III_A_Appendix_I_Reference_List_by_section_number_rev_Sept_2021,
Doc_III_A_Appendix_II_Reference_List_by_author_rev_Sept_2021,
Doc_III_A_Appendix_IV_List_of_protected_studies_rev_Sept_2021.
Based on those lists, the enumerated submitted studies are given below, as well as the list is amended with the references (including data) as received from the Applicant.

Section No	Author(s)	Year	Title Source Company, Report No. GLP (where relevant) / (Un)published	Data protection claimed (Yes/No)	Owner
A1-2 A3.4 A4.1/03 A7.1.1.1.1	[redacted]	2005	Active substance master file for Mecetronium ethyl sulphate 29 %. Quality overall summary, CVR: 13246149 no author; [redacted] January 05	Y (Exist./First)	BOD
A1-2_01	BODE Chemie	2007	Statement by Applicant concerning the identity of MES 29 % , dated 11.10.2007	Y (Exist./First)	BOD
A1-2_02	BODE Chemie	2007	Statement by Applicant concerning the identity of MES 30 % , dated 29.10.2007	Y (Exist./First)	BOD
A1-2_03	BODE Chemie	2009	Statement by Applicant concerning the placing of MES containing hand disinfectants on the EU-market under different regulations, dated 11.02.2009	Y (Exist./First)	BOD
A1-2_04 A4.1_03	[redacted]	2020	Update Active substance master file for mecetronium etilsulfate 29%. Quality overall summary including long term stability study data and accelerated stability study data CoA and summary 5 batch analysis, no date	Y (Exist./First)	BOD
A2.10/01	BODE Chemie	2006	Product information sheet: Sterillium®	N	BOD
A2.10/02	RKI	2000	RKI (2000) Bundesgesundheitsblatt 43	N	-
A2.10/03	[redacted]	2019a	Estimation of Environmental Concentrations of Mecetronium ethyl sulphate applied as hand and skin disinfectant (product type 1) [redacted], revised version 28.11.2019 unpublished	Y (Exist./First)	BOD
A2.10/03	[redacted]	2019b	Estimation of Environmental Concentrations of Mecetronium ethyl sulphate during formulation of hand and skin disinfectant (product type 1). [redacted], revised version 28.11.2019 unpublished	Y (Exist./First)	BOD
A3.1.1	[redacted]	2002	Determination of the Melting Temperature of Hexadecyl ethyl dimethyl ammonium methyl sulphate according to EC Council Directive 92/69/EEC, A.1. and OECD Guideline No. 102. [redacted], Study No. 01 50 40 822A GLP, unpublished	Y (Exist./First)	BOD

Section No	Author(s)	Year	Title Source Company, Report No. GLP (where relevant) / (Un)published	Data protection claimed (Yes/No)	Owner
A3.1.2 A3.10_01	[redacted]	2002	Determination of the Boiling Temperature of Hexadecyl ethyl dimethyl ammonium methyl sulphate according to EC Council Directive 92/69/EEC, A.2. and OECD Guideline No. 103. [redacted], Study No. 01 50 40 822B GLP, unpublished	Y (Exist./First)	BOD
A3.1.3	[redacted]	2002	Determination of the Density of Hexadecyl ethyl dimethyl ammonium methyl sulphate according to EC Council Directive 92/69/EEC, A.3. and OECD Guideline No. 109. [redacted], Study No. 01 50 40 822C GLP, unpublished	Y (Exist./First)	BOD
A3.2	[redacted]	2007	Estimation of the vapour pressure of mecetronium ethyl sulphate according to OECD guideline 104, [redacted], 28 May 2007	Y	BOD
A3.4.	[redacted] BODE Chemie	2007a	Photometrische Prüfung (BPD Dossier). PH01F, document by Applicant BODE Chemie GmbH & Co. KG, Hamburg 15.03.2007	Y (Exist./First)	BOD
A3.4	BODE Chemie	2008a	600 MHz 1H NMR spectrum of mecetroniumethylsulfate. In: Prenatal developmental toxicity study of mecetronium ethyl sulphate in rabbits by oral administration. [redacted], Report No. 18610/04 (unpublished 1st Draft), no date, no author unpublished	Y (Exist./First)	BOD
A3.4	BODE Chemie	2008b	MS chromatograms. In: Determination of the Adsorption of Dimethylethylhexadecyl-ammonium-ethylsulfate according to the OECD Guideline 106 and the requirements of the EU Test method C.18 (2001/59/EC). [redacted], GLP-Code BOD-005/7-13 Annex VIII Chromatograms (exemplary) no date, no author unpublished	Y (Exist./First)	BOD
A3.5_01 A3.9_01	[redacted]	2002	Determination of the Water Solubility of Dimethylethylhexadecylammonium-ethylsulfate according to OECD Test Guideline 105, flask method [redacted], GLP-Code: BOD-001/7-14 unpublished	Y (Exist./First)	BOD
A3.5_02	[redacted]	2018	Determination of critical micelle concentration (CMC) of Mecetronium ethyl sulfate [redacted], CAL-18-0746, 06.05.2019, unpublished	Y (Exist./First)	BOD

Section No	Author(s)	Year	Title Source Company, Report No. GLP (where relevant) / (Un)published	Data protection claimed (Yes/No)	Owner
A3.6	[redacted]	2007	Final report: MES, Dissociation constant pKa (OECD 112, titration method) [redacted], 24.07.2007, unpublished	Y (Exist./First)	BOD
A3.7	[redacted]	2008	Determination of the solubility of mecetronium ethyl sulphate in organic solvents according to CIPAC methods (CIPAC MT181) [redacted], Test Report: 20080037.01, Study completed on 17.03.2008 GLP, unpublished	Y	BOD
A3.7_01	BODE Chemie	2008	Added to the Final report listed in the previous row (i.e. A3.7 by Huber V (2008)): Statement by Applicant Bode Chemie GmbH, dated 10.05.2010 concerning analytical method MA001, Internal document by Applicant: assay for QACs (Raw Material), Validation record 2ZW0000B.002, not signed, unpublished	Y (Exist./First)	BOD
A3.7_02 A3.9_02	[redacted]	2010c	Mecetroniumethylsulfat Batch No.: 104665. Solubility in organic solvents (n-Octanol), CIPAC MT181 (n-Octanol), [redacted], Study completed on 25.06.2010, Report No. 20100085.03 GLP, unpublished Added: Statement by Applicant of 10.05.2010 concerning analytical method MA001 and Internal document by Applicant: assay for QACs, the same as given in the previous row (i.e. A3.7_01 by BODE Chemie (2008)).	Y (Exist./First)	BOD
A3.8	BODE Chemie	1999	Stability Report: Sterillium (VP 83/227). No. 1ST00040.001, document by Applicant BODE Chemie GmbH & Co. KG, Hamburg, 15.11.1999	Y (Exist./First)	BOD
A3.10_02	BODE Chemie	2004	Validation record: Testing of possible impurities - active substance mecetroniumetilsulfate - stress test, document by Applicant BODE Chemie GmbH & Co. KG, Hamburg, 2ZT00004.002 of 18.10.2004 non GLP, unpublished	Y	BOD
A3.10_03	[redacted]	2011	NMR-spectroscopy-based chemical stability analysis of mecetronium ethylsulfate after high temperature storage. [redacted], 27 January 2011, 8p., Non GLP unpublished	Y	BOD
A3.10_04	[redacted]	2020	Mecetronium etilsulfate. Determination of physico – chemical properties. Thermal Stability (OECD 113). Screening Explosive Substances (UN Class 1). Screening Self – Reactive Substances (UN Class 4, Division 4.1) [redacted], Study No. [redacted]-20-0698.01, date 29.07.2020 GLP, unpublished	Y (Exist./First)	BOD

Section No	Author(s)	Year	Title Source Company, Report No. GLP (where relevant) / (Un)published	Data protection claimed (Yes/No)	Owner
A3.11_01 A3.12	[redacted]	2010a	Mecetroniumethylsulfat Batch No.: 104665. Flammability (Solids) A.10, [redacted], 25.06.2010 GLP, unpublished	Y (Exist./First)	BOD
A3.11_02	[redacted]	2020	Mecetronium etilsulfate. Determination of physico – chemical properties. Auto – ignition Temperature (Liquids and Gases) (EC A.15.) [redacted], Study No. [redacted]-20-0698.02, date 29.07.2020 GLP, unpublished	Y (Exist./First)	BOD
A3.13	[redacted]	2001	Hexadecylethyldimethylammoniumethylsulfat 104666 – Surface Tension [redacted], Report-No.: 20011311.01, 04.12.2001 GLP, unpublished	Y (Exist./First)	BOD
A3.14	[redacted] BODE Chemie	2007	Viscosity of MES. Certificate of analysis, document by Applicant, BODE Chemie GmbH & Co. KG, Hamburg, 18.04.2007 Non GLP, unpublished	Y (Exist./First)	BOD
A3.15	[redacted]	2010b	Mecetroniumethylsulfat Batch No.: 104665. Explosive Properties A.14, [redacted], Report No. 20100085.02, date 25.06.2010 GLP, unpublished	Y (Exist./First)	BOD
A.3.17	BODE Chemie	2007	Statement on Reactivity towards container material. document by Applicant BODE Chemie GmbH & Co. KG, Hamburg, no date unpublished	N	BOD
A3	[redacted] BODE Chemie	2019	pH value of Mecetronium ethyl sulfate document by Applicant BODE Chemie GmbH, Hamburg, 11.04.2019 Non-GLP, unpublished	Y (Exist./First)	BOD
--	BODE Chemie	2022	Position Paper Data and justification for the section physical properties and hazards Mecetronium ethyl sulphate (MES, CAS No. 3006-10-8) APCP, Bode Chemie GmbH, 16 May 2022, 12pages	Y	BOD
A4.1/01	BODE Chemie	2003	Test method: Identity of Mecetroniumetilsulfate in Alcoholic Products. SOP: Nr. DC003.004, document by Applicant BODE Chemie GmbH & Co. KG, 15.07.2003 Non-GLP, unpublished	Y (Exist./First)	BOD
A4.1/01	Hellmann, H	1989	Zur Anwendung des sog. modifizierten Dragendorff-Reagenses bei der Bestimmung von Kationtensiden im aquatischen Milieu Fesenius Z Anal Chem 335: 265-271 published	N	-

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A4.1/02 A4.2c_02	BODE Chemie	2004	Validation record: Determination of the Detection-/ Quantitation Limit (Stress Test Mecetroniumetilsulfate), document by Applicant Bode Chemie GmbH SOP: Nr. 2ZB00004.001, 09.08.2004 Added by Applicant: HPLC-Screening of MES-Solutions – Working instruction by [redacted] date 31.07.2004 , titled [redacted] QUMH AB3-ARW.073 Edition No. 1	Y (Exist./First)	BOD
A4.1_04	[redacted]	2021	Determination of [redacted] Content in MES Solution (Validation Study) [redacted] Date 2021-08-06, Study Code VP 006/2021, Report No. B 006/2021, GLP, unpublished	Y (Exist./First)	BOD
A4.1_05	[redacted]	2021	Determination of [redacted] Content in MES Solution (Validation Study) [redacted] Date 2021-08-06, Study Code VP 042/2021, Report No. B 042/2021, GLP, unpublished	Y (Exist./First)	BOD
A4.1_06	[redacted]	2021	Determination of [redacted] Content in MES Solution (Validation Study) [redacted], Date 2021-08-23, Study Code VP 043/2021, Report No. B 043/2021, GLP, unpublished	Y (Exist./First)	BOD
A4.1_07	[redacted] BODE Chemie	2021	Validation of the [redacted] determination of [redacted] in the raw material MES solution 29 % acc. to method GC037 (Validation Study) internal document by Applicant BODE Chemie GmbH, date 15.06.2021, Study No.: VAL_B_141, Non-GLP, unpublished	Y (Exist./First)	BOD
A1-2	BODE Chemie	2021	Dry weight calculation using QC data for MES and [redacted] (preliminary discussion) Bode Chemie GmbH, 12 November 2021, 6pages	Y	BOD
A1-2	BODE Chemie	2022	Specification and dry weight calculation of Mecetronium ethyl sulphate (MES), Bode Chemie GmbH, 27 May 2022, 10pages	Y	BOD
A4.1_09	[redacted]	2022	Determination of Main Compound Content in MES Solution by means of HPLC-ELSD (Validation Study) [redacted] Date 2022-05-05, Study Code VP 027/2022, Report No. B 027/2022, GLP (unpublished)	Y	BOD
A1-2_10	[redacted]	2022	Determination of Main Compound Content in MES Solution by means of HPLC-ELSD (5 Batch Study) [redacted], Date 2022-05-24, Study Code VP 028/2022, Report No. B 028/2022 GLP (unpublished)	Y	BOD

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A4.1_12	[redacted]	2022	Determination of [redacted] Content [redacted] in MES Solution by means of HPLC-(Validation Study) [redacted], Date 2022-05-25, Study Code VP 029/2022, Report No. B 029/2022 GLP (unpublished)	Y	BOD
A4.1_13	[redacted]	2022	Determination of [redacted] Content [redacted] in MES Solution by means of HPLC-ELSD (5 Batch Study) [redacted] Date 2022-05-25, Study Code VP 030/2022, Report No. B 030/2022 GLP (unpublished)	Y	BOD
A4.1_11	[redacted] BODE Chemie	2021	Validation of the assay of [redacted] in mecetronium etilsulfate 29 % (MES solution, 29 %) according to method MAOII (Ph.Eur.2.5.12) (Validation Study) Internal document by Applicant, BODE Chemie GmbH, Hamburg, date 31.05.2021, Report No: VALB_164 Non-GLP, unpublished	Y	BOD
A1-2_12	BODE Chemie	2022	Determination of [redacted] content in five batches MES solution 29 % 5 Batch Study, Document by Applicant Bode Chemie GmbH, date 23.04.2021, Study No. 50/03/21, 1page Non-GLP, unpublished	Y	BOD
A4.1_10	[redacted]	2022	Determination of Side Compound Content ([redacted]) in MES Solution by means of HPLC-ELSD (Validation Study) [redacted] Date 2022-05-20, Study Code VP 031/2022, Report No. B 031/2022 GLP (unpublished)	Y	BOD
A4.1_11 A1-2_11	[redacted]	2022	Determination of Side Compound Content ([redacted]) in MES Solution by means of HPLC-ELSD 5 Batch Study [redacted] Date 2022-05-24, Study Code VP 032/2022, Report No. B 032/2022 GLP (unpublished)	Y	BOD
A1-2_05	[redacted]	2021	Determination of [redacted] Content in MES Solution (5 Batch Study) [redacted] Date 2021-09-17, Study Code VP 057/2021, Report No. B 057/2021 GLP (unpublished)	Y	BOD
A1-2_06	[redacted]	2021	Determination of [redacted] Content in MES Solution (5 Batch Study) [redacted] Date 2021-09-17, Study Code VP 058/2021, Report No. B 058/2021 GLP (unpublished)	Y	BOD

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A1-2_07	[redacted]	2021	Determination of [redacted] Content in MES Solution (5 Batch Study) [redacted] Date 2021-09-17, Study Code VP 059/2021, Report No. B 059/2021 GLP (unpublished)	Y	BOD
A1-2_08	[redacted] BODE Chemie	2021	Determination of [redacted] content in five batches MES solution 29 % (5 Batch Study) internal document by Applicant BODE Chemie GmbH, date 18.06.2021, , Study No. 50/07/21 non-GLP, unpublished	Y	BOD
A4.1_08	[redacted]	2022	Determination of Diethyl Sulphate Content in MES Solution (Validation Study) [redacted], Date 2022-05-05, Study Code VP 060/2021, Report No. B 060/2021 GLP (unpublished)	Y	BOD
A1-2_09	[redacted]	2022	Determination of Diethyl Sulphate Content in MES Solution 5 Batch Study [redacted], Date 2022-05-20, Study Code VP 061/2021, Report No. B 061/2021 GLP (unpublished)	Y	BOD
A1-2	BODE Chemie	2022	Position Paper Manufacturing process of Mecetronium ethyl sulphate (MES, CAS No. 3006-10-8) and available data on specification and reference source APCP, Bode Chemie GmbH, 17 May 2022, 3pages unpublished	Y	BOD
A4.2a A7.2.3.1	[redacted]	2008	Determination of the Adsorption/Desorption of Dimethylethylhexadecylammonium-ethylsulfate (according to the OECD guideline 106 and the requirements of the EU test method C.18 (2001/59/EC), Final report dated 11.12.2008, Amendment No 1 to the Final Report dated 12.02.2009 [redacted], GLP Code: BOD-005/7-13 GLP unpublished	Y (Exist./First)	BOD
A4.2c_01 A7.4.3.4_01	[redacted]	2008	*Daphnia magna*, Reproduction test (OECD 211) Semi-static exposure, Effect of Dimethylhexadecylammonium-ethysulfate on the reproduction of *Daphnia magna*. [redacted], GLP-Code Report: BOD – 005/4–21, dated 07.05.2008 and Amendment No 1 on deviations from study plan, dated 06.06.2007 GLP, unpublished	Y (Exist./First)	BOD
A4.2c_03	[redacted]	2010	Test item disappearance in aqueous media, Kinetic investigations regarding disappearance of Dimethylethylhexadecylammonium-ethylsulfate, [redacted], Report No. GLP-Code: BOD-005/7-26, 25.08.2010 GLP, unpublished	Y (Exist./First)	BOD

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A5/01	[redacted]	1998	Begutachtung der Remanenzwirkung von Sterillium. [redacted], Report date: 30.06.1998. Non-GLP, unpublished *translation: Report on the persistent effect of STERILLIUM – Lot No. 45616209*	Y (Exist./First)	BOD
A5/02	[redacted]	2003	Prüfbericht – Testung auf Remanenz von VP 83/1U und VP 360/B. [redacted], Report date 13.03.2003. Non-GLP, unpublished *translation: Testing for residual effect of VP 83/1U and VP 360/B*	Y (Exist./First)	BOD
A5.3.1/01	BODE Chemie	2005	Efficacy of mecetronium ethyl sulphate in a quantitative suspension test. document by Applicant Bode Chemie GmbH & Co. KG., Hamburg; Prüfbericht Nr. JPr 101 M70. Report No JPr 101 M70 date 13.01.2005. Non-GLP, unpublished Added: Statement on solvent by Applicant 14.01.2009	Y (Exist./First)	BOD
A5.3.1/02	[redacted]	2002	Bestimmung der fungiziden Basiswirkung nach EN 1275. [redacted]; Prüfbericht Nr. M02-03427/1. Report date 21.06.2002 Non-GLP, unpublished *translation: Determination of fungicidal basis effect* Added: Statement on test item batch identity by Applicant, 10.11.2008	Y (Exist./First)	BOD
A5.3.1/03	BODE Chemie	2009	Efficacy of mecetronium ethyl sulphate in a quantitative suspension test. document by Applicant Bode Chemie GmbH & Co. KG., Hamburg; Report No. 26/06/09 VP 94L/261 of 05.01.2009, Non-GLP, unpublished	Y (Exist./First)	BOD
A6.1.1/01	[redacted]	1992	Acute oral toxicity of "Mecetroniumetilsulfat 30%" in rats. [redacted], Project No.: 10-04-1153/00-92, 26.10.1992 GLP, unpublished	Y (Exist./First)	BOD
A6.1.1/02	[redacted]	1992	Acute oral toxicity of "Mecetroniumetilsulfat 4%" in rats. [redacted], Project No.: 10-04-1155/00-92, 26.10.1992 GLP, unpublished	Y (Exist./First)	BOD
A6.1.2/01	[redacted]	1992	Acute dermal toxicity of "Mecetroniumetilsulfat 30%" in rats. [redacted], Project No.: 10-04-1154/00-92, 26.10.1992 GLP, unpublished	Y (Exist./First)	BOD

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A6.1.2/02	[redacted]	1992	Acute dermal toxicity of "Mecetroniumetilsulfat 4%" in rats. [redacted] Project No.: 10-04-1156/00-92, 26.10.1992 GLP, unpublished	Y (Exist./First)	BOD
A6.1.4/01	[redacted]	1993	Acute dermal irritation/corrosion test of "Mecetroniumetilsulfat 4%" in rabbits. [redacted] Project No.: 10-03-1705/00-92, 25.01.1993 GLP, unpublished	Y (Exist./First)	BOD
A6.1.4/02	[redacted]	1992	Acute dermal irritation/corrosion test of "Mecetroniumetilsulfat 0.2%" in rabbits. [redacted], Project No.: 10-03-1708/00-92, 21.12.1992 GLP, unpublished	Y (Exist./First)	BOD
A6.1.5	[redacted]	1992	Guinea pig maximization test of skin sensitization with "Mecetroniumetilsulfat 30%". [redacted] Project No.: 10-05-1701/00-92, 24.11.1992 GLP, unpublished	Y (Exist./First)	BOD
A6.2_01	[redacted]	1987	14C-mecetroniumetilsulfate: percutaneous absorption in the rats. [redacted], Report No. 5532-549/2, 05.11.1987 Non-GLP, unpublished	Y (Exist./First)	BOD
A6.2_02	Neef C, Oosting, R, Meijer DKF	1984	Structure-pharmacokinetics relationship of quaternary ammonium compounds: Elimination and distribution characteristics. Naunyn-Schmiedeberg's Arch Pharmacol 328:103 – 110 published	N	-
A6.2_02	Arugonda S K IPCS	1999	QUATERNARY AMMONIUM COMPOUNDS; International Programme on Chemical Safety, Poisons Information Monograph G022 (Group PIM), dated 05.10.1998 From: http://www.inchem.org/documents/pims/chemical/pimg022.htm, date 15.10.2009	N	-
A6.3.1	[redacted]	2001	4-Week dose-range finding study for a 90-Day subchronic toxicity study of mecetronium ethylsulfate by repeated oral administration to Sprague-Dawley rats. [redacted], Report No. 14438/01, 21.08.2001 - not signed draft report GLP, unpublished	Y (Exist./First)	BOD
A6.4.1/01	[redacted]	2002	90-Day subchronic toxicity study of mecetronium ethylsulfate by repeated oral administration to Sprague-Dawley rats. [redacted], Report No. 14284/01, 31.05.2002 GLP, unpublished	Y (Exist./First)	BOD

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A6.4.1/02 A6.5 A6.7 A6.8.1/02	Thorup I	2000	Evaluation of health hazards by exposure to quaternary ammonium compounds. Toxicological Evaluation and Limit Values for 2-Ethylhexyl acrylate, Propylene carbonate, Quaternary ammonium compounds, Triglycidyl isocyanurate, and Tripropyleneglycol diacrylate Evaluation of health hazards by exposure to Quaternary ammonium compounds (Cationic surfactants) and estimation of a limit value in air. The Institute of Food Safety and Toxicology, Danish Veterinary and Food Adminstration (published)	N	-
A6.5 A6.12.2- A6.12.8	[redacted]	2006	PSUR Sterillium®, Periodic Safety Update Report, observation period from January 1, 2000 until August 31, 2005; Report by Applicant; [redacted], BODE Chemie GmbH & Co. KG, Hamburg, dated 28.09.2005, 9pages unpublished	Y	BOD
A6.6.	[redacted]	1981	Testing of compound ethyl-hexadecyl-dimethylammonium ethylsulfate (EHDE) for induction of DNA repair synthesis in HeLa cells in vitro. [redacted] 25.07.1981 GLP claimed (no certificate attached), unpublished	Y (Exist./First)	BOD
A6.6.1/01	[redacted]	1992	Final report mutagenicity testing: Salmonella/ microsome test (Ames-test), test article Mecetroniumetilsulfate. [redacted] Project No.: 96-00-1703/00-92, 16.12.1992 GLP, unpublished	Y (Exist./First)	BOD
A6.6.1/02	[redacted]	1981	Salmonella/microsome assay of ethyl-hexadecyl-dimethylammonium ethylsulfate. [redacted] 25.07.1981 GLP claimed (no certificate attached), unpublished	Y (Exist./First)	BOD
A6.6.2	[redacted]	1994	Final report of in vitro chromosome aberration assay with Mecetroniumetilsulfat in CHO cells. [redacted], Study No. 12300103, 27.10.1994 GLP, unpublished	Y (Exist./First)	BOD
A6.6.3_01	[redacted]	1994	Final report of gene mutation assay in mouse lymphoma L5178Y TK+/- cells to trifluorothymidine-resistance with Mecetroniumetilsulfat. [redacted], Study No. 12300113, 15.07.1994 GLP, unpublished	Y (Exist./First)	BOD

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A6.6.3_02	[redacted]	2008	In Vitro Mammalian Cell Gene Mutation Test in Mouse Lymphoma L5178Y/TK$^{+/-}$ Cells with MES (Final Report), [redacted], Study No: 17G08019, 18.11.2008, GLP, unpublished	Y (Exist./First)	BOD
A6.6.4	[redacted]	1994	Final report in vivo micronucleus test of mecetronium etilsulfat in mice. [redacted] Study No. 12300123, 16.06.1994 GLP, unpublished	Y (Exist./First)	BOD
A6.8.1/01	[redacted]	2008	Prenatal developmental toxicity study of mecetronium ethyl sulphate (MES) in rabbits by oral administration. [redacted] Report No. 18610/04 (final report); 10.06.2008 GLP (unpublished) Within the report Appendix: Verification of the test item concentration in samples from [redacted]-Study Number 18610/04, by [redacted] dated 23.10.2006, [redacted]	Y (Exist./First)	BOD
A6.8.1/02	Pang S, Willis l	1997	Final report on the safety assessment of cetrimonium chloride, cetrimonium bromide and steartrimonium chloride. International Journal of Toxicology 16; 195-220 published	N	-
A6.8.2	[redacted]	2008	Mecetronium ethyl sulphate (MES) 29% (aqueous solution) One-Generation Reproduction Tocixity Study in the Rat. [redacted] Study no. B10056 (final report); 19.08.2008, GLP (unpublished)	Y (Exist./First)	BOD
A6.12/01	[redacted]	1992	Sterillium +/- Mecetronium etilsulfat, PV 360, PV 83, Dermatologische Befundung des Hautzustandes im Verlauf der Anwendung vom 27.8.92 bis 26.11.92. Research communication of [redacted] on Test no. 1938, conducted by [redacted] unpublished *translation: STERILLIUM +/- mecetronium etilsulfate PV 360, PV 83, Dermatological evaluation of skin condition during a usage period from 27.8.92 to 26.11.92.*	Y (Exist./First)	BOD
A6.12/01	[redacted]	1994	Die Hautverträglichkeit von Mecetronium etilsulfat in einem Händesinfektionsmittel - Eine klinische Studie. Report Nr. 2092, no date of report, study dates: 27.8.92 – 24.9.92, 29.10.92 – 27.11.92. unpublished *translation: Skin-compatibility of mecetronium etilsulfate in a hand disinfectant - A clinical study.*	Y (Exist./First)	BOD
A6.12.2-A6.12.8	[redacted]	2007	Statement on medical surveillance at workplace, 27.03.2007, Bode Chemie GmbH &Co. KG	Y	

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A7.1.1.1.1	Harris JC	1990	Rate of hydrolysis. In: Handbook of chemical property estimation methods (Eds: Lyman WJ, Reehl WF, Rosenblatt DH), American Chemical Society, Washington DC, 7-1 – 7-48. published	N	-
A7.1.1.2.1	Painter HA, Reynolds P, Comber S	2003	Application of the headspace CO_2 method (ISO 14 593) to the assessment of the ultimate biodegradability of surfactants: results of a calibration exercise. Chemosphere, 50, 29-38 published	N	-
A7.1.1.2.1	van Ginkel CG, Gancet C, Hirschen M, Galobardes M, Lemaire Ph, Rosenblom J,	2008	Improving ready biodegradability testing of fatty amine derivatives. Chemosphere, 73, 506-510 published	N	-
A7.1.1.2.1	Boggs S, Livermore D, Seitz M.G	1985	Humic substances in natural waters and their complexation with trace metals and radionuclides: A review Argonne National Laboratory, Illinois, USA published	N	-
A7.1.1.2.1	Klavins M, Rodinov V, Druvietis I	2003	Aquatic chemistry and humic acid substances in bog lakes in Latvia Boreal Environment Research 8, 113 – 123 published	N	-
A7.1.1.2.1	Frimmel F.H	2005	Aquatic humic substances In: Biopolymers Biology, Chemistry, Biotechnology, Applications, ISBN: 9783527302901, Wiley-VCH Verlag GmbH & Co. KGaA, Chapter 10 Aquatic Humic Substances, Section 4 Chemical structure, pages 302-310 published	N	-
A7.1.1.2.1/01	[redacted]	1995	Bestimmung der biologischen Abbaubarkeit von MES Lösung 30%-ig in Wasser im Closed-Bottle-Test. [redacted] Report No. Lab 95/72/9788/9.400, date 14.07.1995 Non-GLP, unpublished *translation: Determination of the biodegradability of MES solution 30% in water in the closed bottle test*	Y (Exist./First)	BOD
A7.1.1.2.1/02	[redacted]	1999	Biologische Abbaubarkeit gemäß OECD 301 A, Prüfung der leichten biologischen Abbaubarkeit von Produkten: MES-Lösung 29 %". [redacted] Report No. 99TE007585, date 09.03.1999 Non-GLP, unpublished *translation: Testing of ready degradability of products*	Y (Exist./First)	BOD

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A7.1.1.2.1/03	[redacted]	2008	Manometric Respirometry Test – Ready Biodegradability of Mecetronium ethyl sulphate by Activated Sludge; [redacted], Study Report GLP-code of Test Facility: BOD-005/3-15, 13.10.2008, GLP, unpublished	Y (Exist./First)	BOD
A7.1.1.2.1/04	[redacted]	2011a	Biodegradability in the CO_2-headspace test according to OECD 310 (03/2006). [redacted] Report No. 2379.1, dated 08.06.2011 Non-GLP, unpublished	Y (Exist./First)	BOD
A7.1.1.2.1/05	[redacted]	2011b	Non-GLP screening study: CO_2-Headspace Test, Ready Biodegradability of Dimethylethylhexadecylammonium-ethylsulfate by Activated Sludge. [redacted], Report: 2011-10 BOD-01, date 11.10.2011 Non-GLP, unpublished	Y (Exist./First)	BOD
A7.1.1.2.1/06	[redacted]	2011c	Non-GLP screening study: CO_2-Headspace Test, Ready Biodegradability of Dimethylethylhexadecylammonium-ethylsulfate by Activated Sludge. [redacted], Report: 2011-10 BOD-02, date 11.10.2011 Non-GLP, unpublished	Y (Exist./First)	BOD
A7.1.1.2.1/07	[redacted]	2013	Mecetroniumethylsulfate (MES) Ready Biodegradability Modified Sturm Test [redacted], Study ID 120926FK/AST15296, date 02.10.2013, Amendment No 1 to report dated 21.10.2013. GLP, unpublished	Y (Exist./First)	BOD
A7.1.1.2.1/08	[redacted]	2019	Mecetronium ethyl sulphate (MES) Ready Biodegradability Modified Sturm Test [redacted], Study ID: 181128BM/AST18487, dated 09.09.2019 GLP, unpublished	Y (Exist./First)	BOD
A7.1.2 A7.2.1	Boethling RS.	1984	Environmental fate and toxicicty in wastewater treatment of quaternary ammonium compounds. Water Res 18:1061-1076. published	N	-
A7.1.2 A7.2.1	Games LM, King JE, Larson RJ	1982	Fate and distribution of a quaternary ammonium surfactant, octadecyltrimethylammonium chloride (OATC), in wastewater treatment. Environ Sci Technol 16: 483-488. published	N	-
A7.1.2 A7.2.1	Garcia MT, Ribosa I, Guindulain T, Sánchez-Leal J, Vives-Rego J	2001	Fate and effect of monoalkyl quaternary ammonium surfactants in the aquatic environment. Environ Pollut 111:169-175. published	N	-
A7.1.2 A7.2.1	Nishiyama N, Toshima Y, Ikeda Y	1995	Biodegradation of alkyltrimethylammonium salts in activated sludge. Chemosphere 30:593-603. published	N	-

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A7.1.2 A7.2.1	Ying GG	2006	Fate, behavior and effects of surfactants and their degradation products in the environment. Environ Int 32:417-431. published	N	-
A7.1.2.1.1	[redacted]	2019	Simulation Test - Aerobic Sewage Treatment Biodegradability of Dimethylethylhexadecylammonium ethylsulfate in Activated Sludge Units [redacted] BOD-005/5-12, dated 14.11.2019 GLP, unpublished	Y (Exist./First)	BOD
A7.1.3	[redacted]	2002	Estimation of the adsorption behaviour of Dimethylethylhexadecylammonium-ethylsulfate. Study report. [redacted] GLP-Code: BOD-001/7-13, 02.12.2002. GLP, unpublished	Y (Exist./First)	BOD
A7.1.4	[redacted]	2008	Adsorption of dimethylethylhexadecyl-ammonium-ethylsufate on activated sludge (according to the ISO-guideline 18749 “water quality – adsorption of substances on activated sludge – batch test using specific analytical methods”), Study report, [redacted] GLP Code: BOD-005/7-93, 11.12.2008 GLP unpublished	Y (Exist./First)	BOD
A3.2.1 A7.3.1	EPI-Suite	2005	EPIWIN 3.12 estimations for MES and . Mecetronium cation (HenryWINv3.10, .log KOW v1.67, AOPWIN v1.91) no date, no author GLP not applicable, published	N	Not applicable
A7.4.1.1	[redacted]	1992	Fischtest, akute Toxizität [redacted], Report No. Lab 803/4652/2.000, date 07.12.1992 Non-GLP, unpublished *translation: Fish test, acute toxicity*	Y (Exist./First)	BOD
A7.4.1.2_01	[redacted]	2000	Study on the acute toxicity towards Daphnia of Mecetronium etilsulfate (Powder) according to the OECD-test guideline 202, Part I ("Daphnia sp., Acute Immobilisation Test"). [redacted] Report No. IF-99/21392-00, date 25.09.2000 GLP, unpublished	Y (Exist./First)	BOD
A7.4.1.2_02	[redacted]	2010	*Daphnia magna*, Acute Immobilisation Test (OECD 202) - Static exposure - Effect of Dimethylethylhexadecylammonium-ethylsulfate on the immobilisation of *Daphnia magna*. [redacted], Report No. BOD-005/4-20/G, date 17.08.2010 GLP, unpublished	Y (Exist./First)	BOD

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A7.4.1.3_01	[redacted]	2000	Study on the 'toxicity towards algae' of Mecetronium etilsulfate (Powder). [redacted], Report No [redacted]-99/2139-00, date 25.09.2000 GLP, unpublished	Y (Exist./First)	BOD
A7.4.1.3_02	[redacted]	2019	Freshwater Alga, Growth Inhibition Test (OECD 201), Dimethylethylhexadecylammonium-ethylsulfate: Effects on *Desmodesmus subspicatus*, [redacted] BOD-005/4-10/B, dated 21.11.2019 GLP, unpublished	Y (Exist./First)	BOD
A7.4.1.4	[redacted]	2002	Study on the acute toxicity towards bacteria of Hexadecylethyldimethylammoniumethylsulfate according to OECD-guideline no. 209 in the version of 04-04-1984. [redacted], Report No. [redacted]-101/35263-00, date 17.05.2002 GLP, unpublished	Y (Exist./First)	BOD
A7.4.2 A7.4.3.3 A7.5.5	Arnot JA, Gobas FAPC	2006	A review of bioconcentration factor (BCF) and bioaccumulation factor (BAF) assessments for organic chemicals in aquatic organisms. Environ. Rev. 14: 257-297 published	N	-
A7.4.2 A7.4.3.3 A7.5.5	Banerjee S, Sugat RH, O'Grady DP	1984	A simple method for determining bioconcentration parameters of hydrophobic compounds. Environ. Sci. Technol. 18: 79-81 published	N	-
A7.4.2 A7.4.3.3 A7.5.5	de Wolf W, Lieder PH	1998	A novel method to determine uptake and elimination kinetics of volatile chemicals in fish. Chemosphere 36: 1713-1724 published	N	-
A6.2_02 A7.4.2 A7.4.3.3 A7.5.5	Hughes RD, Millburn P, Williams T	1973	Molecular weight as a factor in the excretion of monoquaternary ammonium cations in the bile of the rat, rabbit and gunea pig. Biochem. J. 136: 967-978 published	N	-
A7.4.2 A7.4.3.3 A7.5.5	Koss G, Marquardt H, Schäfer S	2004	Lehrbuch der Toxikologie (2nd edition). Wissenschaftliche Verlagsgesellschaft. Stuttgart. *translation: Toxicology textbook, section 24.4.2. n-Hexane, 3pages*	N	-
A7.4.2 A7.4.3.3 A7.5.5	Meylan WM, Howard PH, Boethling RS, Aronson D, Printup H, Gouchie S	1999	Improved method for estimating bioconcentration/bioaccumulation factor from octanol/water partition coefficient. Environ. Toxicol. Chem. 18: 664-672 published	N	-
A7.4.2 A7.4.3.3 A7.5.5	Tolls J, Kloepper-Sams P, Sijm DTHM	1994	Surfactant bioconcentration - a critical review. Chemosphere 29: 693-717 published	N	-

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A7.4.2 A7.4.3.3 A7.5.5	Versteeg, DJ, Shorter S	1992	Effect of organic carbon on the uptake and toxicity of quaternary ammonium compounds to the fathead minnow, *Pimephales promelas*. Environ. Toxicol. Chem. 11: 571-580 published	N	-
A7.4.2 A7.4.3.3 A7.5.5	WHO [World Health Organisation]	1991	Environmental Health Criteria 122: n-Hexane. From: http://www.inchem.org/documents /ehc/ehc/ehc122.htm, date 16.05.2007	N	-
A7.4.3.2	[redacted]	2012	Zebrafish (*Danio rerio*), Early Life Stage Toxicity Test, flow through conditions, Test item: Dimethylethylhexadecylammonium-ethylsulfate (MES) [redacted] BOD-005/4-18/A, dated 10.09.2012 GLP, unpublished	Y (Exist./First)	BOD
A7.4.3.4_02	[redacted]	2018	*Daphnia magna*, Reproduction test (OECD 211) Semi-static exposure, Effect of Dimethylhexadecylammonium-ethysulfate on the reproduction of *Daphnia magna*. [redacted] GLP-Code: BOD–005/4–21/G/1, dated 26.02.2018 GLP, unpublished	Y (Exist./First)	BOD
A7.4.3.4_03	May M, Drost W, Germer S, Juffernholz T, Hahn S	2016	Evaluation of acute-to-chronic ratios of fish and Daphnia to predict acceptable no-effect levels. Environ Sci Eur. 28:16 published	N	-
A7.4.3.5.1_01	[redacted]	2007	Non-GLP screening study. Sediment – water chironomid toxicity test using spiked sediment. Effect of Dimethylethylhaxadecylammonium-ethylsulfate on the development of *Chironomus riparius*. [redacted] date 15.05.2007, report not signed. Non-GLP, unpublished	Y (Exist./First)	BOD
A7.4.3.5.1_02	[redacted]	2008	Study Report: Sediment – water chironomid toxicity test using spiked sediment, Effect of Dimethylethylhexadecylammonium-ethylsufate on the development of *Chironomus riparius*, [redacted] GLP-Code of testing Facility: BOD-005/4-29, 29.04.2008, GLP, unpublished	Y (Exist./First)	BOD
A7.5.1.1/01 A7.5.1.1/02	[redacted]	2007	Soil Microorganisms: Effects of Dimethylhexadecylammonium-ethylsulfate on Nitrogen and Carbon Transformation, [redacted] Report GLP-Code: BOD-005/3-35, dated 25.01.2007, Study Report Amendment No 1 dated 15.02.2007 GLP, unpublished	Y (Exist./First)	BOD

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A7.5.1.2	[redacted]	2006 (as says the front page of the report)	Earthworm Acute Toxicity Test. Acute Toxicity of Dimethylethylhexadecylammonium-ethylsulphate on *Eisenia fetida*, [redacted] Report GLP-Code: BOD-005/3-08, signed by study director 08.01.2007, Amendment No 1 on deviations from study plan dated 24.11.2006 GLP, unpublished	Y (Exist./First)	BOD
A7.5.1.3	[redacted]	2006 (as says the front page of the report)	Terrestrial plants, growth test. Effect of Dimethylethylhexadecylammonium-ethylsulphate on the seedling emergence and growth of *Avena sativa*, *Phaseolus aureus*, and *Latuca sativa*, [redacted] GLP-Code: BOD-005/4-40, signed by study director 08.01.2007 GLP, unpublished	Y (Exist./First)	BOD
--	BODE Chemie	2007	Statement saying that ecotoxicological studies are still ongoing, by Applicant Bode Chemie GmbH, 29.10.2007		BOD
A7.5.2.1	[redacted]	2019	Earthworm Reproduction Test, chronic effects of Dimethylethylhexadecylammonium-ethylsulfate on *Eisenia andrei* [redacted], Study number: BOD-005/4-80/V, dated 11.02.2019 GLP, unpublished	Y (Exist./First)	BOD
Sections in the Doc IIA; 3.14, 4.2.9 Sections in the Doc I (AR): 2.6.2.1, 2.7.4	[redacted]	2020	Assessment of potential endocrine disrupting properties of Mecetronium ethylsulphate (MES, CAS No. 3006 10 8), Project number 111503, [redacted], Report completion date 13 February 2020, 22pages unpublished Appendices: MES_CAS 3006-10-8_LiteratureSearch.pdf Lit Search ED_MES_Title list 20191205.xls ED QSAR_MES_final_2020-02-14.pdf EDEG_Appendix-E_MES_HH_2020-02-07.xlsm EDEG_Appendix-E_MES_ENV_2020-01-14.xlsm	Y	BOD
Sections in the Doc IIA; 3.14, 4.2.9 Sections in the Doc I (AR): 2.6.2.1, 2.7.4	BODE Chemie	2021	Weight of Evidence on potential endocrine disrupting properties for the environment of Mecetronium ethylsulphate (MES, CAS No. 3006-10-8), Bode Chemie GmbH, Report completion date 28 September 2021, 12pages unpublished *Weight of Evidence on potential endocrine disrupting properties for the environment of Mecetronium ethylsulphate (MES, CAS No. 3006-10-8) Bode Chemie GmbH, Report completion date 28 September 2020, 12pages*	Y	BOD

Section No	Author(s)	Year	Title Source Company, Report No. GLP (where relevant) / (Un)published	Data protection claimed (Yes/No)	Owner
Sections in the Doc IIA; 3.14, 4.2.9 Sections in the Doc I (AR): 2.6.2.1, 2.7.4	BODE Chemie	2021	Weight of Evidence on potential endocrine disrupting properties for human health of Mecetronium ethylsulphate (MES, CAS No. 3006-10-8), Bode Chemie GmbH, Report completion date 28 September 2021, 12pages unpublished *Weight of Evidence on potential endocrine disrupting properties for human health of Mecetronium ethylsulphate (MES, CAS No. 3006-10-8), Bode Chemie GmbH, Report completion date 28 September 2020, 12pages*	Y	BOD
Sections in the Doc IIA; 3.14, 4.2.9 Sections in the Doc I (AR): 2.6.2.1, 2.7.4	BODE Chemie	2021	Weight of Evidence on potential endocrine disrupting properties for human health of Mecetronium ethylsulphate (MES, CAS No. 3006-10-8), Bode Chemie GmbH, Report completion date 10 November 2021, 16pages unpublished	Y	BOD
Sections in the Doc IIA; 3.14, 4.2.9 Sections in the Doc I (AR): 2.6.2.1, 2.7.4	BODE Chemie	2022	Weight of Evidence on potential endocrine disrupting properties for human health of Mecetronium ethylsulphate (MES, CAS No. 3006-10-8), Bode Chemie GmbH, Report completion date 29 April 2022, 18pages unpublished	Y	BOD
Sections in the Doc IIA; 3.14, 4.2.9 Sections in the Doc I (AR): 2.6.2.1, 2.7.4	[redacted]	2022	Position Paper on sufficiency of the available dataset to conclude on endocrine disrupting properties for human health of the active substance Mecetronium ethylsulphate (MES, CAS No. 3006-10-8), [redacted], Report completion date 09 May 2022, 5pages unpublished	Y	BOD

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	BODE Chemie	2022	Applicants note to the ENV ad hoc follow up concerning the B part of the PBT/vPvB assessment, June 22, 2022 unpublished		BOD
	Timmer N, Droge STJ	2017	Sorption of Cationic Surfactants to Artificial Cell Membranes: Comparing Phospholipid Bilayers with Monolayer Coatings and Molecular Simulations, Environ. Sci. Technol. 2017, 51, 2890−2898 published		

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	Mueller C, Trapp S, Polesel F, Kuehr S, Schlechtriem Ch	2020	Biomagnification of ionizable organic compounds in rainbow trout *Oncorhynchus mykiss*, Environ Sci Eur (2020) 32:159 published		
	Kierkegaard A, Sundbom M, Yuan B, Armitage JM, Arnot JA, Droge STJ, McLachlan MS	2021	Bioconcentration of Several Series of Cationic Surfactants in Rainbow Trout, Environ. Sci. Technol. 2021, 55, 8888−8897 published		
	Kierkegaard A, Chen Ch, Armitage JM, Arnot JA, Droge S, McLachlan MS	2020	Tissue Distribution of Several Series of Cationic Surfactants in Rainbow Trout (*Oncorhynchus mykiss*) Following Exposure via Water, Environ. Sci. Technol. 2020, 54, 4190−4199 published		

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	BODE Chemie	2022	Position Paper MES, Fate and distribution in the environment and effects on environmental organisms, BODE Chemie GmbH, 30.03.2022, 7pages Amended with 8 EUSES reports dated 28-03-2022 and 29-03-2022.		BOD
	BODE Chemie	2022	Position Paper Professional use scenario, consumption approach, nursing staff Mecetronium ethylsulphate (MES, CAS No. 3006-10-8) Environment, Bode Chemie GmbH, 16 May 2022, 2pages		BOD
	BODE Chemie	2022	Note to Relevance_of_impurities_AS-EVA_MES_PT1_rev, Bode Chemie GmbH, 29 July 2022, 7pages unpublished		BOD
	BODE Chemie	2022	Note to Relevance_of_impurities_AS-EVA_MES_PT1_rev and the draft BPC opinion on MES with regard to the assessment of relevant impurities, Bode Chemie GmbH, 12 September 2022, 9pages unpublished		BOD
	BODE Chemie	2022	Position Paper on the proposal for a non-approval for Mecetronium ethylsulfate (MES, CAS No. 3006-10-8) due to insufficient APCP data General, Bode Chemie GmbH, 16 May 2022, 13pages unpublished		BOD

Section No	Author(s)	Year	Title Source Company, Report No. GLP (where relevant) / (Un)published	Data protection claimed (Yes/No)	Owner
	Keith A. Hostetler, Louan C. Fisher, Benjamin L. Burruss	2021	Reproductive toxicity assessment of alkyl dimethyl benzyl ammonium chloride and didecyl dimethyl ammonium chloride in CD® rats, Birth Defects Research. 2021;113:1368–1389 published *eCA note: The article contains a disclaimer on conflict of interest, which says authors are consultants to the ADBAC and DDAC Issues Steering Committees, the studies' sponsor; among them also employed at and participated in the collection and tabulation of the data for these studies conducted by Bushy Run Research, which received funding from the ADBAC and DDAC Issues Steering Committees to conduct these studies.* *The data are not publicly available due to privacy or ethical restrictions.*		
	Keith A. Hostetler, Louan C. Fisher, Benjamin L. Burruss	2021	Prenatal developmental toxicity of alkyl dimethyl benzyl ammonium chloride and didecyl dimethyl ammonium chloride in CD rats and New Zealand White rabbits, Birth Defects Research. 2021;113:925–944 published *eCA note: The article contains a disclaimer on conflict of interest, which says authors are consultants to the ADBAC and DDAC Issues Steering Committees, the studies' sponsor; among them also employed at and participated in the collection and tabulation of the data for these studies conducted by Bushy Run Research Center, which received funding from the ADBAC and DDAC Issues Steering Committees to conduct these studies.* *The data are not publicly available due to privacy or ethical restrictions.*		
	BODE Chemie	2022	Position Paper Identity of the active substance Mecetronium ethylsulphate (MES, CAS No. 3006-10-8) Human health, Bode Chemie GmbH, 16 May 2022, 2pages unpublished		BOD
	BODE Chemie	2022	Statement Limit of Detection (LOD) of Diethylsulphate in Mecetronium Ethylsulphate, 12.09.2022. unpublished *Statement by the Applicant referring to the report by GLP Laboratory*		BOD
			Position paper addressing RCOM APCP comment 5 and 6 and related comments, not dated, no author, received from BODE Chemie, 3pages unpublished		
			Justification of hazard endpoints not adequately covered by the current documentation, not dated, no author, received from BODE Chemie, 6pages unpublished		

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A2.10/04	Royal Haskoning	2004	Supplement to the methodology for risk evaluation of biocides. Environmental Emission Scenarios for biocides used as human hygiene biocidal products (Product type 1), January 2004	N	
A7.1.1.1.2	U.S. EPA	1998	Fate, Transport and Transformation Test Guidelines OPPTS 835.2210 “Direct Photolysis Rate in Water by Sunlight”. EPA 712-C-98-060, January 1998	N	
A7.1.2 A7.2.1	EC	2000	Technical Notes for Guidance in support of the Directive 98/8/EC concerning the Placing of Biocidal Products on the Market - Guidance on Data Requirements for Active Substances and Biocidal Products. European Commission Final Draft 2000	N	
A7.4.2 A7.4.3.3 A7.5.5	EC [European Commission]	2003	Technical Guidance Document in support of Commission Directive 93/67/EEC on Risk Assessment for new notified substances, Commission Regulation (EC) No 1488/94 on Risk Assessment for existing substances and Directive 98/8/EC of the European Parliament and of the Council concerning the placing of biocidal products on the market (2nd edition). Part II.	N	
A7.4.2 A7.4.3.3 A7.5.5	ECETOC [European Centre for Ecotoxicology and Toxicology of Chemicals]	2005	Alternative Testing Approaches in Environmental Safety Assessment. Technical Report 97.	N	
A7.4.3.1	EC	2000	(2000) Technical Notes for Guidance in support of the Directive 98/8/EC concerning the Placing of Biocidal Products on the Market – Guidance on Data Requirements for Active Substances and Biocidal Products. Final Draft 2000	N	

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A7.4.2 A7.4.3.3 A7.5.5	EC [European Commission]	2002	European Union Risk Assessment Report dimethyldioctadecylammonium chloride (DODMAC)		
A6.2_02	Hendersen ND	1992	A review of the environmental impact and toxic effects of DDAC Prepared for: Environmental Protection division BC environment, Ministry of Environment, Lands and Parks, Victoria, British Columbia		