6 FEBRUARY 2014

Responses to Comments Document (RCOM) on ECHA's Draft 5th Recommendation for 4-(1,1,3,3-tetramethylbutyl)phenol, ethoxylated (4-tert-OPnEO)) (EC number:)

This document provides ECHA's responses to the comments received during the public consultation on the draft 5th recommendation for inclusion of substances in Annex XIV of REACH, which took place between 24 June and 23 September 2013. In addition to this Response to Comments table, on ECHA's website there are available zip-file(s) including all attachments to the individual comments (as far as not confidential):
http://echa.europa.eu/addressing-chemicals-of-concern/authorisation/recommendation-for-inclusion-in-the-authorisation-list/previous-recommendations/5th-recommendation (see column "Additional documentation" in substances' table)

PUBLIC VERSION

CONTENT

I - General comments on the recommendation to include the substance in Annex XIV, including the prioritisation of the substance:

#	Date	Submitted by (name, Organisation/MSCA)	Comment	Response
2484 b	2013/09/24	Company, Germany		Intrinsic properties See response to comment 2483 in this section. Please see response to comment 2457 (in this section) regarding substance identity and level of risks / alternatives / socio-economic considerations See also response to comment 2483 regarding Prioritisation of the Substance and (Article 58(2)) exemptions.
2484	2013/09/23 22:37	Alkylphenols & Ethoxylates Research Council Industry or trade association United States	Comments of the European Council for Alkylphenols and Derivatives and the Alkylphenols & Ethoxylates Research Council On the Draft Background Document for 4-(1,1,3,3-tetramethylbutyl)phenol, ethoxylated (4-tert-Octylphenol ethoxylates, 4-tert-OPnEO) Developed in the Context of ECHA's Fifth Recommendation for the Inclusion of Substances in Annex XIV (June 24, 2013) Submitted September 23, 2013 Executive Summary The European Council for Alkylphenols and Derivatives (CEPAD) and the Alkylphenols & Ethoxylates Research Council (APERC) jointly submit these comments in objection to the European Chemicals Agency (ECHA) proposal to include "4-(1,1,3,3-tetramethylbutyl) phenol, ethoxylated - covering well-defined substances and UVCB substances, polymers and homologues", more commonly known as octylphenol ethoxylates (OPEs), under Annex XIV of REACH. The Draft Background Document proposing the prioritization of OPEs for authorization provides rankings assigned by ECHA for the intrinsic	Thank you for your comment. Please see response to comment 2483 in this section.

			properties, volumes in commerce in the EU, and dispersiveness of use of these compounds. As discussed below in these comments the background document overstates the priority assigned to the intrinsic properties and dispersive-ness in the use of OPEs in the EU; therefore these assigned prioritization scores, as well as the total score, are not representative of this compound and overstate the need for its prioritization. In addition, the Draft Background Document for OPEs also does not adequately consider available environmental monitoring data that indicate that 4-tert-Octylphenol (4-tOP), a degradation intermediate of OPEs, which is the compound of actual interest, is not widely detected in EU water and when detected is generally below conservative Annual Average Environmental Quality Standards (AA-EQS) established for this compound under Directive 2000/60/EC (the Water Framework Directive). Furthermore, the Draft Background Document for OPEs does not consider that other existing regulatory instruments are already in place in the EU to control site specific emissions of OPEs and its degradation intermediate, 4-tOP. The ECHA General Approach for Prioritisation of Substances of Very High Concern (SVHCs) for Inclusion in the List of Substances Subject to Authorisation states: "Pursuant to Article 58(3) of the Regulation (EC) No 1907/20061 (REACH), whenever a decision is taken to include substances referred to in Article 57 of REACH in Annex XIV, priority shall normally be given to substances with PBT or vPvB properties, or wide dispersive use, or high volumes. Article 58(3) indeed requires to take the mentioned 3 criteria 'normally' into account, but there is no provision that this needs to be done in all cases or how it should be done, e.g. with respect to evaluating, weighting or scoring of the criteria. Moreover, consideration of further aspects and criteria for priority setting is not excluded. Hence, it can be assumed that Article 58(3) leaves discretion regarding the development and design of a prioritisation approach that in the end provides the Candidate Substances for which the recommendation to include them in Annex XIV is most relevant and appropriate (both in terms of potential risk and regulatory effectiveness) (ECHA, 2010, May 28)." (emphasis added) OPEs do not themselves meet any of the inherent toxicity criteria for prioritization. OPEs are not persistent or bioaccumulative, nor are they carcinogenic (C), mutagenic (M) or reproductive (R) toxicants. OPEs were designated as a candidate chemical primarily on the basis that 4-tOP, one of its degradation intermediates, was previously designated as SVHC. The primary uses of OPEs in the EU are not widely dispersive applications and the monitoring data available for the EU supports this	

			understanding. The following comments provide further explanation to demonstrate that the intrinsic properties, volumes and uses of OPEs, along with available monitoring data in the EU do not support the addition of OPEs to Annex XIV. These comments also explain why authorization is not the most relevant and appropriate regulatory approach for addressing OPEs , both in terms of potential risk and regulatory effectiveness. 1.0 THE PRIORITIZATION SCORE IN THE BACKGROUND DOCUMENT FOR OPES OVERSTATES THE HAZARD FOR THE INTRINSIC PROPERTIES OF OPES. OPEs were identified as a SVHC under Article 57(f) of Regulation (EC) 1907/2006 (REACH) "because (through their degradation) they are substances with endocrine disrupting properties for which there is scientific evidence of probable serious effects to the environment which give rise to an equivalent level of concern to those of other substances listed under Article 57(a) through (e) of REACH" (EHCA, 2013, June 24). For prioritization, the hazard information that is available for a substance is scored (ranging from 0 to 4) and then the volume and dispersive use scores are added to obtain a total score. The total score can be seen as a proxy for potential risk to human health or the environment. Following are the scoring criteria for inherent properties as listed in the ECHA General Approach for Prioritisation of SVHCs for Inclusion in the List of Substances Subject to Authorisation (ECHA, 2010, May 28). Inherent properties Score PBT and vPvB or PBT with T non-threshold C or M 4 PBT or vPvB properties 3 C or M properties (without effect threshold) 1 C, M or R properties (with effect threshold) 0 The ECHA Background Document on OPEs gives a total inherent property score of 0 to 1 for these compounds, indicating that inherent properties of OPE are somewhere between a Carcinogenic (C), Mutagenic (M) or Reproductive Toxicant (R) with a threshold effect and a C or M toxicant without a threshold effect. The only listed inherent property given for OPEs in the ECHA Background Document is that of Art 57(f)"equivalent level of concern having probable serious effects to the environment". As discussed below, OPEs and 4-tOP are not Persistent, Bioaccumulative and Toxic (PBT), nor are they very Persistent or very Bioaccumulative (vPvB). OPEs and 4-tOP are also not C, M or R. Therefore, even based on inherent properties alone OPEs should not even be subject to prioritization As described in companion papers by Staples et al (2008) and Klecka et	

			al (2008) that review the persistence and bioaccumulation potentials for 4-tOP and their ethoxylates, neither of the parent compound nor any of its metabolites meet the various regulatory criteria for PBT or vPvB compounds, including those criteria listed in Annex XIII of REACH. In addition, neither OPEs nor 4-tOP meet the criteria for carcinogen, mutagen or reproductive toxicants category 1 or 2 in accordance with the DSD classification criteria or Cat 1A/1B in accordance with the CLP REGULATION (EC) No 1272/2008. It is important to also note that 4-tOP does not even meet the lesser criteria for Toxic to Reproduction Cat. 3 (DSD) or Cat 2 (GHS), which relates to "suspected human reproductive toxicants". 4-tOP is listed on the list of harmonised classification and labeling of hazardous substances based on its aquatic toxicity. The fact that OPEs do not themselves meet any of the inherent toxicity criteria for prioritization should be basis enough not to prioritize these compounds for authorization. 2.0 THE USE AND EMISSION PROFILE OF OPES DOES NOT SUPPORT PRIORITZATION OF THESE COMPOUNDS UNDER ANNEX XIV, FURTHERMORE THEIR USE IS PROJECTED TO DECLINE. The basis for the recommendation to prioritize OPEs for Authorization is that "these substances are used in high tonnage in products that can be assumed to lead to wide-dispersive emissions to the environment" (ECHA, 2013, June 24). The General Approach to Priority Setting for Authorization states "the extent to which a use is 'wide-dispersive' is roughly a function of the number of sites at which a substance is used and the magnitude of releases caused by those uses over all steps of the life-cycle" (ECHA, 2010, May 28). Therefore, the scoring of the 'wide-dispersive use' criterion is broken up in the two sub-criteria. The first is "Number of Sites", which is basically the number of sites where the substance is used (i.e. the number of point sources or number of sites from which a substance is being released). The second is "Release", which describes the releases in terms of pattern (where relevant) and amount versus anticipated risk. 2.1 The tonnage of OPEs used in the EU is declining The Annex XIV Background Document for OPE acknowledges that since there are no registrants for OPEs under REACH, information on volumes, uses and the supply chain are lacking. Therefore, based on the estimated fraction of 4-tOP used to manufacture its ethoxylates and the estimated average contribution to the molecular weight of its ethoxylates, the volume of ethoxylates produced is assumed in the Background Document to be in the range of 1,000 – 10,000 t/y (ECHA, 2013, June 24). Based on this tonnage estimate the OPE Background document scores OPE as "high" or "7". The UK Risk Assessment on 4-tOP reported that 1,050 t/y OPE were	

			used in 2001 (UK Environment Agency, 2005), based on 400 t/y of 4-tOP conversion to OPE. The UK Risk Assessment also recognized the agreement of the companies that supply OPEs in the EU to not promote OPEs as substitutes for nonylphenol ethoxylates (NPEs) as those surfactants were subject to restrictions on their marketing and use in dispersive uses under EU Directive 2003/53/EC (European Parliament and the Council of the European Union, 2003, June 18). Due to antitrust regulations, APERC and CEPAD cannot share market and volume information directly. Current understanding of volumes for OPEs in the EU based on published reports indicate their tonnage to be in the lower half of the tonnage range estimated in the Annex XIV Background Document for OPEs with a decline in their use projected to be approximately 4.4% between 2009 and 2014 (Janshekar, H., 2010, July). 2.2 The primary uses of OPEs are not widely dispersive applications. OPEs are used predominantly in the formulation of paint and coating products and are used at levels of generally 1% or less in those products. Due to their role in the emulsion polymerization process, OPEs are expected to be bound in the paint polymer and not widely dispersed to the environment. Waste from paint clean up are generally expected to be subject to treatment in wastewater treatment plants (WWTPs). OPEs are not reported as being used in consumer applications with high potential for human exposure or environmental release i.e., household detergents and fabric softeners and personal care products (SRI, 2010). Furthermore, restrictions on the marketing and use of NPEs in dispersive uses under EU Directive 2003/53/EC is not resulting in replacement with OPEs, rather "other surfactants or blends of other surfactants are benefitting from the trend away from OPEs in these applications (Janshekar, H., 2010, July)". Some minor uses of OPEs (i.e., vitro diagnostic applications in the medical device sector) are also not expected to result in widespread dispersive emissions. 3.0 CONCENTRATIONS OF OPES AND 4-tOP IN EUROPEAN SURFACE WATERS DO NOT SUPPORT A NEED FOR AN EU-WIDE AUTHORIZATION PROCESS FOR OPES UNDER REACH. When the UK Environment Agency conducted a risk evaluation on 4-tOP in 2005, information on the presence of 4-tOP and OPEs in the environment was limited; therefore the evaluation relied to a large extent on default assumptions and the Assessment Report acknowledges that its own "exposure assumptions may not be wholly realistic" (UK Environment Agency, 2005). That report also noted that at that time, surface water concentrations of 4-tOP in Europe and	

			elsewhere were typically less than 1 µg/L, with "higher values detected on a few occasions" that may be "a consequence of high local discharges". Since that time more environmental monitoring data are available for 4-tOP and to a lesser extent OPE; these data should be considered in the prioritization process for OPEs, as Article 58 (3) allows for "consideration of further aspects and criteria for priority setting" (ECHA, 2010, May 28). The Water Framework Directive(WFD) established a framework for European Community (EC) water policy and strategies against water pollution, which requires Member States to take action for the progressive reduction of emissions of priority hazardous substances via the aquatic environment, through setting Environmental Quality Standards (EQS) and establishing emission control measures (European Parliament and Council 2000, 23 October Annual Average Environmental Quality Standards (AA-EQS) have been established for 4-tOP (European Parliament and Council, 2008, December 16). Monitoring for this compound has been conducted by the Member States under the WFD and additional monitoring has been published in the peer-reviewed literature. 3.1 Relevant Predicted No Effect Concentrations (PNECs) and Annual Average Environmental Quality Standard (AA-EQS) have been established for 4-tOP, which is the compound of interest. 3.1.1 PNECs for 4-tOP There are reliable toxicity studies for fish, amphibians, and invertebrates for 4-tOP, which cover all parts of the test organisms' life cycles from eggs to reproducing adults and cover life stages likely to be sensitive to an endocrine mode of action. Test procedures included screening tests, short-term reproduction tests, and full life-cycle tests. A consistent and treatment-related set of No Observable Effect Concentration (NOEC)have been reported for 4-tOP and range from approximately 6 to 1,000 µg/L across relevant population-level endpoints related to survival, growth and development, and reproduction (CEPAD-APERC, 2011, October 13, Coady et al, 2013, June 4, UK Environment Agency, 2005). Effects reported for endocrine sensitive endpoints occur at concentrations within the same range of NOECs and Lowest Observable Effect Concentrations (LOECs) that are also consistent with a narcotic mode of action (Coady et al, 2013). The UK Risk Evaluation of 4-tOP calculated an intermittent exposure PNEC for 4-tOP of 0.13 µg/L based on the most sensitive acute toxicity value (EC50 for freshwater shrimp of 13.3 µg/L) and an assessment factor of 10 (UK Environment Agency, 2005). A chronic PNEC for surface water of 0.122 µg/L is calculated in the UK evaluation based on the most sensitive chronic study in fish (NOEC based on growth for rainbow	

			trout) and an assessment factor of 50, which was applied with consideration for potentially more sensitive species (UK Environment Agency, 2005). The REACH Chemical Safety Report (CSR) for 4-tOP utilized a species sensitivity distribution approach along with an assessment factor of five to calculate a freshwater PNEC of 0.632 µg/L for 4-tOP (CSR OP, 2010). 3.1.2 AA-EQS are established for 4-tOP under the WFD Annual Average Environmental Quality Standards (AA-EQS) of 0.10 µg/L (inland waters) and 0.01 µg/L (other waters) have been established for 4-tOP under the WFD (European Parliament and Council (2008, December 16). AA-EQS values are considered protective against both chronic exposures and short-term pollution peaks in continuous discharges (European Parliament and Council (2008, December 16). While the PNEC of 0.632 µg/L calculated in the CSR for 4-tOP can be considered more reliable as it is based on a more robust data set, the AA-EQS developed under the WFD are the most conservative benchmarks for comparison to concentrations in water. 3.1.3 Established PNECs and AA-EQS for 4-tOP are protective of endocrine mediated effects. OPEs were designated as SVHC primarily based on the argument that due to their degradation they are "an environmental source" of 4-tOP, which was previously designated SVHC due to concerns for environmental endocrine effects. Based on the results of targeted in vitro studies, 4-tOP and nonylphenol (NP) have been shown to have a weak binding affinity for the nuclear estrogen receptor, and can, at sufficient concentrations, also cause subsequent estrogen-receptor dependent transactivation (Recchia et al., 2004; Olsen et al., 2005; Preuss et al., 2006; Van den Belt et al., 2004; Van Miller and Staples, 2005; USEPA, 2009). The estrogenic activity of both 4-tOP and NP varies, depending on the assay used, and is generally in the range of one thousand to one million-fold less potent than the endogenous estrogen, 17β-estradiol (E2) (Coady et al., 2010; Van Miller and Staples, 2005; Wenzel et al., 2001). Exposure to alkylphenols, specifically 4-tOP and NP exposure, can increase circulating levels of vitellogenin (VTG) in fish. VTG is a yolk-precursor protein normally expressed in female oviparous species that has been demonstrated to be a highly responsive biomarker for estrogen receptor agonists, especially in males who carry the VTG gene but do not ordinarily express it (Jobling and Sumpter, 1993; Harries et al., 2000; Dussault et al., 2005; Olsen et al., 2005). VTG induction, which is not considered an adverse effect, occurs among various fish species at concentrations of 4-tOP and NP ranging from 1 to 100 µg/L	

			(Coady et al., 2010; USEPA, 2007; Karels et al., 2003; Jobling et al., 1996; Rasmussen et al., 2002; Seki et al., 2003). In addition, reports of histopathological changes among gonadal tissues in fish exposed to either 4-tOP or NP have been reported in the range of 1.6 to 200 µg/L (Miles-Richardson et al., 1999; Gray and Metcalfe, 1997; Jobling et al., 1996; Staples et al., 2004; USEPA, 2007; Rasmussen et al., 2005; Karels et al., 2003; Rasmussen et al., 2002; Gray et al., 1999). While the observation of increased VTG in male fish and the occurrence of altered gonadal histopathology can inform upon one of the potential estrogenic modes of action of NP and 4-tOP, these biochemical and histopathological endpoints are not traditionally used as indicators of adverse effects in ecological risk assessments. For 4-tOP and NP, the threshold for estrogenic activity (measured as induction of the yolk-precursor protein, VTG, and alterations in gonadal histomorphology) in fish is in the range of 1 to 200 µg/L. Therefore the previously described PNECs and AA-EQS are sufficiently protective of even these sensitive estrogenic responses in aquatic species. 3.2 OPEs were determined to be Substances of Very High Concern (SVHC) under REACH primarily based on the argument that due to their degradation they are "an environmental source" of 4-tOP, which was previously designated as SVHC: therefore the focus of environmental monitoring is most appropriately focused on 4-tOP. Biodegradation has been shown to be the dominant mechanism responsible for removal of OPEs, 4-tOP and other alkylphenol (AP) and alkylphenol ethoxylates (APEs) during wastewater treatment and in the environment (Staples, 1999, Staples, 2001, Staples, 2008, Melcer, 2007). While OPEs are highly treatable in WWTPs, with removal rates commonly greater than 90%, low levels of their degradation metabolites have been reported in effluent and surface waters (Melcer, 2007). These intermediates continue to degrade in the environment, including mineralization of the phenolic ring, to carbon dioxide (Ahel, 1994, Staples, 1999, Staples, 2001, Staples, 2008, Naylor, 2006). Considering that 4-tOP is the most toxic of the OPE degradation intermediates, and that degradation to 4-tOP is the primary reason that OPEs were proposed to be SVHC and are now proposed for prioritization for Authorization, the focus of environmental monitoring is most appropriately focused on 4-tOP. 3.3 Results from recent monitoring in the EU indicate that the majority of surface water samples do not contain detectable concentrations of 4-tOP; furthermore when detected, 4-tOP concentrations are generally below the AA-EQS. Results of recent monitoring conducted in the EU are available through governmental monitoring programs and in the published literature. It	

			should also be noted that all environmental monitoring results for 4-tOP represent emissions from all uses of 4-tOP, not just from the use of OPEs. 3.3.1 Results for 4-tOP from Monitoring Reported under the Water Information System of Europe (WISE) As required under the WFD , surface water concentrations of 4-tOP and other substances have been measured in various European waterways. Monitoring data on 4-tOP from Fact Sheets published by the Environment Directorate-General, European Commission (DG ENV) under WISE were reviewed for the following names and CAS numbers for 4-tOP [CAS # 11081-15-5], 4-n-Octylphenol [CAS # 1806-26-4], Octylphenol [CAS # 140-66-9], Octylphenol [CAS # 67554-50-1] , and Octylphenol [No specified CAS number]. Data from nine countries (Belgium, Czech Republic, Spain, France, Ireland, Luxembourg, Poland, Sweden, and United Kingdom) are summarized in the fact sheets, which covered the period from 2000 to 2008. The data were representative of a range of water categories including rivers (2497 samples from 354 stations), lakes (406 samples from 100 stations), coastal waters (22 samples from 18 stations) and estuaries (3 samples from 3 stations) (DG ENV, 2013a, DG-ENV, 2013b, DG-ENV, 2013c, DG-ENV, 2013d, DG-ENV, 2013e). Results for 4-tOP concentrations detected in whole water samples (liquid and suspended particulate matter) as part of this monitoring are summarized in Table 1 below along with a comparison to the AA-EQS for 4-tOP (0.10 µg/L). See attachment for Table 1 Listed in DG-ENV WISE Fact Sheets for 4-tOP (2000-2008) Number of Analyses N = 2795 Range 0 to 1.08 µg/L. Mean ± SD 0.03 ± 0.05 µg/L Median 0.03 µg/L 90th Centile 0.05 µg/L % samples < 0.10 µg/L 96% 0.10 µg/L < % samples < 1.0 µg/L 3.3 % 1.0 µg/L< % samples ≤ 1.08 µg/L 0.7 % The concentrations of 4-tOP reported under the WFD monitoring are taken at discreet moments in time; therefore there were not sufficient data in the Fact Sheets to calculate average values over time in a particular location. Rather than relying on individual sample results, the median and upper 90th percentile concentrations better represent concentrations of 4-t-OP in these waters. 3.3.2 Results for 4-tOP Monitoring Conducted by the Member States under Water Framework Directive Austria	

			Monitoring of 4-tOP concentrations was conducted under the Water Framework Directive by the Austrian Federal Agency for Water Management for the year 2004 (Federal Agency for Water Management, Austria, 2005). Of 403 samples taken from Austrian Waters in 2004, none exceeded the AA-EQS for 4-tOP (0.1 µg/L) and 226 samples (56%) are reported as non-detectable. Switzerland A report on monitoring data from the State of St. Gallen in Switzerland during a 2012 monitoring program where WWTP effluents were measured before dilution in the receiving waters indicates that 4-tOP was found above the detection limit of 0.025 µg/L in only one of 44 WWTP effluents. The one effluent sample where 4-tOP was detected contained 0.14 µg/L 4-tOP. After dilution, this corresponds to a concentration of 0.0001µg/L at this particular waste water treatment plant location (Office of Environment and Energy of the State of St. Gallen, Switzerland, 2013). United Kingdom The Department for Environment, Food and Rural Affairs (DEFRA) in the UK provided data tables with results of monitoring conducted for 4-tOP and OPE in the UK. Only 6 of 4143 samples tested for4-tOP, or 0.1%, are reported at above the method Limit of Detection (LOD), which are listed as 0.1µg/L or 0.05 µg/L depending on the sampling location (UK DEFRA, 2013). Said differently, 99.9% of the UK samples were non-detectable at limits of detection that are less than or equal to the AA-EQS for 4-tOP. Of those samples that were non-detectable, 55% are reported as < 0.05 µg/L. As expected, there are significantly less data reported for OPE. In the UK data tables for OPE, only 15 sample results are reported; however all are reported as non-detectable at LODs of 0.05µg/L (6 samples) , 0.1 µg/L (5 samples) and 0.2 µg/L (4 samples) (UK DEFRA, 2013). 3.4 Monitoring results for 4-tOP reported in the published literature indicate that the majority of surface water samples in the EU contain non-detectable concentrations and those detected are generally below the AA-EQS (0.1 µg/L), which is protective even in chronic exposure situations. Monitoring results for 4-tOP reported in the published, peer-reviewed literature indicate that the majority of surface water samples report non-detectable concentrations of 4-tOP and those detected are generally below the AA-EQS of 0.1 µg/L, which is protective even in chronic exposure situations. Following are summaries of the published monitoring data for 4-tOP in EU waters. Ribeiro et al. (2008) reported monitoring results for 4-tOP in the Mondego River estuary on the west coast of Portugal. Samples were	

			taken at high and low tides and in shallow and deep water at 8 locations. There were 12 sample results reported for 4-tOP. All results were reported at less than the detection limit of 2.0 ng/L, which is 50 time less than the AA-EQS for 4-tOP. Jonkers et al. (2010) reported on the occurrence and concentrations of 4-tOP in Ria de Aveiro, a shallow coastal lagoon area in Portugal from a monitoring campaign that was conducted in 2006. Results (range, median, average) are provided for lagoons, harbors, sea water, sea water near WWTP outfall, city, rivers and WWTP effluent. With the exception of the rivers Caster and Antuã and WWTP effluent, the average and median concentrations of 4-tOP are reported at less than 1 ng/L. For all analytes, including 4-tOP, the highest concentrations were found in the river samples of Rio Caster and Rio Antuã, which the authors explain as being related to flow rates in those rivers. Nevertheless, all median and average results reported for 4-tOP, including in undiluted WWTP effluent, are below the relevant AA-EQS for inland water (0.1µg/L) and other wateri.e., marine (0.01µg/L). Colin et al (2013) reported the occurrence of 4-tOP and OPE2 in raw water and treated water samples from public water systems in a sampling campaign that was performed from October 2011 to May 2012. Sampling was equally distributed across 100 French departments. In total, 291 raw water samples and 291 treated water samples were analyzed in this study, which the authors state represents approximately 20% of the national water supply. Octylphenol monethoxylate (OPE1) and octylphenol ether carboxylate (OPEC) were not detected in any samples. 4-tOP was not detected in any surface water samples. 4-tOP was detected in only one ground water sample at a LOD of 17 ng/L, which is 6 times less than the AA-EQS for 4-tOP. 4-tOP, OPE and OPEC were not detected at all in any treated drinking water samples. Esteban et al , 2013 analyzed a total of 30 compounds with endocrine activity, including natural and synthetic estrogens in the Jarama and Manzanares rivers, the main rivers in the Madrid Region (central Spain), which is the most densely populated area in Spain and also one of the most densely populated areas in Europe. There were 7 samples taken from the Mananares River and 7 samples taken from the Jarama River. Of the 7 samples taken from the Mananares River concentrations of 4-tOP exceeded the AA-EQS of 0.01µg/L for "other" waters in 5 samples. Of the 7 samples from the Jarama River, 1 sample exceeded this AA-EQS. . While there appears to be high contamination of all pollutants in the Mananares River, the sampling in this study was conducted in a limited time frame. The authors note that while 4-tOP was detected at	

			concentrations exceeding the AA-EQS, there were insufficient data to calculate an average over time. The authors suggest that there is a need for further monitoring of this compound in both of these rivers. The authors further note that the total estrogenicity in these two rivers did not exceed 1 ng/L Estradiol Equivalents Quotient (EEQ), which is the lowest level that may cause estrogenic effects in aquatic organisms, in any of the samples - even considering that 30 estrogenically active compounds were monitored. The authors conclude that "the potential estrogenic risk to aquatic organisms in both rivers is low" (Esteban et al , 2013). Kotowska et al. (2013) monitored for phenols and pharmaceuticals in effluent from WWTPs in 9 cities in Poland. The study found that the removal efficiency for 4-tOP was 96% from wastewater. The range of undiluted effluent concentrations for 4-tOP was reported as non-detected to a maximum of 4.02 µg/L. The authors report that in 3 samples out of 172 samples the concentration of 4-tOP was above 1µg/L. More relevant is that the overall mean effluent concentration for 4-tOP is 0.02 µg/L, which is 5 times less than the AA-EQS of 0.1 µg/L and these concentrations will be diluted further in the receiving surface water. Salgueiro-González et al. (2013) analyzed for alkylphenols in surface water, seawater and drinking water in the Coruna area in the northwest of Spain. Concentrations of 4-tOP in surface water were all less than the detection limit of 0.005 µg/L (n=5), which is 20 times less than the AA-EQS of 0.1 µg/L for inland surface waters. Concentrations of 4-tOP in seawater was 0.019 µg/L for one sample and less than the detection limit of 0.007 µg/L for 7 samples; therefore all but one seawater sample was less than the AA-EQS of 0.01µg/L for "other surface water". Concentrations of 4-tOP in six drinking water samples were all below the level of detection for the method, which was 0.020 µg/L. Stalter et al . (2013) reported monitoring for 26 sites impacted by wastewater effluent in several small rivers or streams and one mid-sized river, all in the Hessian Ried close to Frankfurt, Germany. Average concentrations of 4-tOP in water reported in this German study ranged between 12 and 147 ng/L, with an average result of 38 ng/L 4-tOP. With the exception of one sample (147 ng/L) all of the results in this river were below the AA-EQS for 4-tOP (0.1 µg/L). Rocha et al (2013) report concentrations of 4-tOP and other estrogenically active compounds in the Ria Formosa Lagoon in Portugal, which the authors state is highly impacted by discharge from 28 domestic and industrial WWTPs. The authors also note that these WWTPs have functional problems and, along with direct discharges from recreational boats and non-treated sewage, contribute to the pollution in	

			this area. The authors state that this area is impacted by metallurgic industries, which they note is associated with the use of Alkylphenol Ethoxylates (APEs) and represents 25% of the industrial production in the Ria Formosa area (Rocha et al, 2013). This study found that APEs reached their maximal values in summer, which the authors attribute to "the scarcity of water from several riversides that usually supply the lagoon with fresh water and thus possibly dilute these chemicals in the channels" (Rocha, 2013). Concentrations of 4-tOP ranged from 5.9 to 43 ng/L, with 8 of the 10 samples slightly exceeding the AA-EQS (0.01µg/L) for 4-tOP in "other water" but none exceeding the AA-EQS (0.1µg/L) for inland waters. Rocha et al (2013) report that the hormones estone (E1), 17β-estradiol (E2), 17α-ethynylestradiol (EE2), and a phytoestrogen sitosterol (SITOwere measured in considerable amounts in the Ria Formosa Lagoon. The authors also express concern for the total amounts of phosphorous and organophosphorus pesticides, which are present at up to ten fold higher than maximal concentrations recommended for rivers and streams.. These results indicate that discharge conditions in the Ria Formosa Lagoon can result in concentrations of 4-tOP that slightly exceed the AA-EQS for coastal waters. Considering the general pollution, presence of WWTPs "with functional problems", and heavy industrial discharge in this area, it appears that efforts to improve municipal and industry wastewater treatment would benefit this water body. In addition, considering that other compounds appear to pose more risk to this area, prioritizing 4-tOP for authorization on an EU level does not appear to be the most relevant and appropriate approach for 4-tOP or OPEs, both in terms of potential risk and regulatory effectiveness. 4.0 THE PRIORITIZATION PROCESS FOR OPES SHOULD ALSO CONSIDER THAT 4-tOP IS NOT WIDELY DETECTED IN EU WATERS AND, WHEN DETECTED, IS GENERALLY BELOW THE CONSERVATIVE AA-EQS FOR THIS COMPOUND. The Background Document recommending OPEs for prioritization for Annex XIV of REACH calculates a "relatively high" to "high" priority for inclusion in Annex XIV based scores of 0-1 for inherent properties (IP); 7 for high volume (V) and 9 for wide dispersive uses (WDU). However, as noted in section 2.0 of these comments, most uses of OPE are industrial, not consumer applications; therefore the number of sites and scope of dispersiveness is not as great as estimated in the Background Document prioritization. Also, the available environmental monitoring data for waters in the EU indicate that most samples of surface water tested did not detect 4-tOP at the method LOD and, when detected, most measured concentrations are less than the AA-EQS for	

			this compound. Article 58(3) provides for discretion regarding the development and design of a prioritisation approach that in the end provides the Candidate Substances for which the recommendation to include them in Annex XIV is most relevant and appropriate (both in terms of potential risk and regulatory effectiveness) (ECHA, 2010, May 28). Therefore, the prioritization process for OPEs should consider the available monitoring data and the score for dispersiveness should be subject to modification to reflect a lesser degree of dispersiveness and potential risk. 5.0 THERE ARE OTHER REGULATORY INSTRUMENTS IN PLACE IN THE EU TO CONTROL EMISSIONS OF OPES AND 4-tOP . Recent monitoring studies in the EU show that concentrations of 4-tOP that exceed the AA-EQS are associated with specific locations and points in time, which are otherwise polluted or subject to intense or uncontrolled discharges. The following regulations are already in place in the EU to control emissions and environmental risks from OPEs and/or 4-tOP. The Water Framework Directive (European Parliament and Council, 2000, 23 October Directive 2000/60/EC) established a framework for Community action in the field of water policy, which requires the Members States to measure aquatic concentrations relative to established Environmental Quality Standards (EQS) and to take action in case this value is exceeded. The monitoring data described in section 3.0 above notes specific locations and moments in time where concentrations of 4-tOP slightly exceed its AA-EQS. For the most part, these locations have generalized problems with contamination that are most appropriately addressed under the WFD. A UK voluntary industry agreement for the reduction in risk from NP, NPEs and 4-tOP and OPEs was finalized in 2004 (CSI, 2004, April). This agreement, which has impacted the EU market more generally, was taken to reduce the risks from NP/NPEs and 4-tOP/OPEs with the following objectives: • Rapidly reduce the risk from NP/NPE to the environment by making early progress in replacing NP/E in a number of uses and to minimise discharges into the environment in order to reduce existing risks to the environment; • Prevent the development of new risks from 4-tOP/E by preventing the use of 4-tOP/OPEs as substitutes for NP/E for those uses to be phased out; and • Reduce the risks from 4-tOP/OPE by phasing out any dispersive uses of 4-tOP/OPE in sectors targeted by the M&U Directive for NP/NPE The Integrated Pollution Prevention and Control (IPPC) Directive	

			(96/61/EC) lays down measures designed to prevent or, where that is not practicable, to reduce emissions to air, water and land from the activities mentioned in Annex I to the Directive (European Parliament and Council, 1996, September 24). Annex I of the IPPC Directive lists categories of industrial activities subject to regulation by the Directive. Surfactants and surface active chemicals are specifically covered under Annex I. Since OPEs are surfactants they are specifically covered by the IPPC Directive. Other categories of industrial activities that are subject to the IPPC Directive that are relevant to the major use of OPEs in paint and coatings include the chemical industry, including basic polymers and dyes and pigments. Other industrial activities subject to the IPPC directive that may be relevant to other minor uses of OPE include: energy industries, the production and processing of metals, chemical installations for the production of basic plant health products and biocides, installations using a chemical or biological process for the production of basic pharmaceutical products, waste management installations, and landfills. Industrial activities subject to IPPC where OPE use is not expected due to the voluntary agreement mentioned earlier in these comments include industrial plants that process pulp and paper, plants for the pre-treatment or dyeing of fibers and textiles and tanning facilities. In addition, Annex III to the IPPC Directive is a list including the main polluting substances in water to be taken into account, which includes "Substances and preparations which have been proved to possess carcinogenic or mutagenic properties or properties which may affect reproduction in or via the aquatic environment". As noted in section 1.0, neither OPEs nor 4-tOP are C, M or R toxicants; however, if there is concern about the environmental impact of either the IPPC Directive provides an existing regulatory mechanism for addressing these compounds. 6.0 APERC AND CEPAD RECOMMEND THAT OPES DO NOT WARRANT PRIORITIZATION FOR AUTHORIZATION UNDER ANNEX XIV OF REACH BECAUSE THEY DO NOT THEMSELVES MEET THE PRIORITIZATION CRITERIA FOR INHERENT TOXICITY, ARE NOT USED IN WIDELY DISPERSIVE CONSUMER APPLICATIONS AND ARE NOT DETECTABLE WIDELY IN THE WATERS OF THE EU; FURTHERMORE, LOCATIONS WITH EXCEEDANCES OF AA-EQS CAN BE ADEQUATELY CONTROLLED THROUGH EXISTING REGULATIONS OPE themselves do not meet any of the inherent toxicity criteria for prioritization for authorization, therefore on this basis alone should not be subject to prioritization for authorization. Furthermore, uses of these OPEs are generally not dispersive and the focus on OPEs for prioritization over other SVHC compounds is inappropriate. This is	

			confirmed by recent environmental monitoring in the EU, which should be considered in the priority setting process for OPEs. Monitoring indicates that 4-tOP, the compound of actual interest in this case, does not have widespread occurrence in EU waters. Existing regulatory instruments exist in the EU, which are better suited to address specific locations where concentrations of 4-tOP are detectable and of concern relative to the conservative AA-EQS for 4-tOP. 4-tOP, the degradation intermediate of OPE that is the stated concern for prioritization, is already regulated under the Water Framework Directive 2000/60/EC. In addition, 4-tOP and OPE are regulated under the IPPC Directive (96/61/EC) and are subject to a voluntary agreement among manufacturers not to promote the use of OPEs in dispersive uses that lead to entry in the aquatic environment (CSR, 2004, April). These existing regulations provide grounds for an exemption for OPEs from prioritization under Art. 58(2) of Regulation 1907/2006/EEC. As Rocha et al (2013) found in the Ria Formosa Lagoon, concentrations of 4-tOP that slightly exceed the AA-EQS are generally associated with areas impacted by general pollution, i.e., due to WWTPs "with functional problems", and heavy industrial discharge. It appears that efforts to improve municipal and industry wastewater treatment in categories already regulated under the WFD and IPPC Directive would benefit water bodies such as this more effectively than an authorization process for OPE under REACH. Also, considering that other compounds appear to pose more risk to these areas, prioritizing 4-tOP for authorization under REACH is not the most relevant and appropriate approach , both in terms of potential risk and regulatory effectiveness. The basis for given for prioritizing OPE for authorization is a concern for the environmental estrogenic activity of the degradant 4-tOP. Esteban et al , 2013 found that the total estrogenicity in the two rivers with the highest reported concentrations of 4-tOP – as well as 29 other estrogenically active hormones, phytoestrogens and industrial compounds - did not exceed 1 ng/L Estradiol Equivalents Quotient (EEQ). This is the lowest level that may cause estrogenic effects in aquatic organisms, in any of the samples. The authors conclude that "the potential estrogenic risk to aquatic organisms in both rivers is low." Considering this, prioritizing OPE for authorization does not appear to be necessary to address concerns of environmental estrogenicity from 4-tOP. For these reasons, APERC and CEPAD recommend OPE should not be prioritized for authorization under REACH and inclusion in Annex XIV. REFERENCES - Full reference citations are provided in the attached comments document.	

2483	2013/09/23 22:23	European Council for Alkylphenols and Derivatives Industry or trade association Belgium	Comments of the European Council for Alkylphenols and Derivatives and the Alkylphenols & Ethoxylates Research Council On the Draft Background Document for 4-(1,1,3,3-tetramethylbutyl)phenol, ethoxylated (4-tert-Octylphenol ethoxylates, 4-tert-OPnEO) Developed in the Context of ECHA's Fifth Recommendation for the Inclusion of Substances in Annex XIV (June 24, 2013) Submitted September 23, 2013 Executive Summary The European Council for Alkylphenols and Derivatives (CEPAD) and the Alkylphenols & Ethoxylates Research Council (APERC) jointly submit these comments in objection to the European Chemicals Agency (ECHA) proposal to include "4-(1,1,3,3-tetramethylbutyl) phenol, ethoxylated - covering well-defined substances and UVCB substances, polymers and homologues", more commonly known as octylphenol ethoxylates (OPEs), under Annex XIV of REACH. The Draft Background Document proposing the prioritization of OPEs for authorization provides rankings assigned by ECHA for the intrinsic properties, volumes in commerce in the EU, and dispersiveness of use of these compounds. As discussed below in these comments the background document overstates the priority assigned to the intrinsic properties and dispersive-ness in the use of OPEs in the EU; therefore these assigned prioritization scores, as well as the total score, are not representative of this compound and overstate the need for its prioritization. In addition, the Draft Background Document for OPEs also does not adequately consider available environmental monitoring data that indicate that 4-tert-Octylphenol (4-tOP), a degradation intermediate of OPEs, which is the compound of actual interest, is not widely detected in EU water and when detected is generally below conservative Annual Average Environmental Quality Standards (AA-EQS) established for this compound under Directive 2000/60/EC (the Water Framework Directive). Furthermore, the Draft Background Document for OPEs does not consider that other existing regulatory instruments are already in place in the EU to control site specific emissions of OPEs and its degradation intermediate, 4-tOP. The ECHA General Approach for Prioritisation of Substances of Very High Concern (SVHCs) for Inclusion in the List of Substances Subject to Authorisation states:	Thank you for your comment and for the additional information provided. <u>Inherent properties</u> 4-tert-OPnEO are subject to the Annex XIV prioritisation process as they have been identified as SVHCs and placed on the Candidate List. Due to their degradation to a substance of very high concern (4-(1,1,3,3-tetramethylbutyl)phenol) with endocrine disrupting properties, they cause probable serious effects to the environment which give rise to an equivalent level of concern to those of other substances listed in points (a) to (e) of Article 57 of REACH. They score 0-1 under inherent properties as discussions are ongoing at EU level as to whether endocrine disruptors should be considered as being de facto threshold or non-threshold substances. The question as to whether the endocrine disrupting effects of (the degradation products of) 4-tert-OPnEO are elicited by a mechanism for which it is possible to determine a no-effect threshold is important for the next stage of the authorisation process, namely application for and granting of the authorisations. However ECHA does not assess at this stage of the authorisation process (i.e. recommendation for inclusion in Annex XIV) whether on the basis of the available scientific evidence it can be concluded that a no-effect level for the endocrine disrupting effects of (the degradation products of) 4-tert-OPnEO exists. This is an issue to be addressed in the authorisation applications and be scrutinised by the Risk Assessment Committee when preparing its opinions on

			"Pursuant to Article 58(3) of the Regulation (EC) No 1907/20061 (REACH), whenever a decision is taken to include substances referred to in Article 57 of REACH in Annex XIV, priority shall normally be given to substances with PBT or vPvB properties, or wide dispersive use, or high volumes. Article 58(3) indeed requires to take the mentioned 3 criteria 'normally' into account, but there is no provision that this needs to be done in all cases or how it should be done, e.g. with respect to evaluating, weighting or scoring of the criteria. Moreover, consideration of further aspects and criteria for priority setting is not excluded. Hence, it can be assumed that Article 58(3) leaves discretion regarding the development and design of a prioritisation approach that in the end provides the Candidate Substances for which the recommendation to include them in Annex XIV is most relevant and appropriate (both in terms of potential risk and regulatory effectiveness) (ECHA, 2010, May 28)." (emphasis added) OPEs do not themselves meet any of the inherent toxicity criteria for prioritization. OPEs are not persistent or bioaccumulative, nor are they carcinogenic (C), mutagenic (M) or reproductive (R) toxicants. OPEs were designated as a candidate chemical primarily on the basis that 4-tOP, one of its degradation intermediates, was previously designated as SVHC. The primary uses of OPEs in the EU are not widely dispersive applications and the monitoring data available for the EU supports this understanding. The following comments provide further explanation to demonstrate that the intrinsic properties, volumes and uses of OPEs, along with available monitoring data in the EU do not support the addition of OPEs to Annex XIV. These comments also explain why authorization is not the most relevant and appropriate regulatory approach for addressing OPEs , both in terms of potential risk and regulatory effectiveness. 1.0 THE PRIORITIZATION SCORE IN THE BACKGROUND DOCUMENT FOR OPES OVERSTATES THE HAZARD FOR THE INTRINSIC PROPERTIES OF OPES. OPEs were identified as a SVHC under Article 57(f) of Regulation (EC) 1907/2006 (REACH) "because (through their degradation) they are substances with endocrine disrupting properties for which there is scientific evidence of probable serious effects to the environment which give rise to an equivalent level of concern to those of other substances listed under Article 57(a) through (e) of REACH" (EHCA, 2013, June 24). For prioritization, the hazard information that is available for a substance is scored (ranging from 0 to 4) and then the volume and dispersive use scores are added to obtain a total score. The total score can be seen as a proxy for potential risk to human health or the	the authorisation applications. <u>Wide dispersive uses and environmental monitoring data</u> It should be noted that the prioritisation step in the authorisation process comprises a general evaluation of the use pattern and exposure potential a substance may have (in the case of 4-tert-OPnEO for the environment). The inclusion in Annex XIV is per substance and not per use (or installation). Therefore screening of release potential in the prioritisation phase does not assess the exposure levels from single uses (at specific sites), but aims to deduce whether there are uses/situations where potential for exposure cannot be excluded. ECHA acknowledges the confirmation provided regarding the volume of 4-tert-OPnEO in the EU being within the tonnage range specified in ECHA's Background Document. Regarding the wide dispersive applications of 4-tert-OPnEO, the registrations of 4-tert-OP, indicate industrial, professional and consumer end uses of mixtures containing 4-tert-OPnEO, including paints. Environmental release categories indicating potential for environmental release are listed in the registrations for these uses (industrial uses included – please note that in the context of the current prioritisation approach, the term 'wide dispersive use' is not limited to uses by professionals and consumers only). As is documented in the Annex XV report - the registration dossiers and a number of published reports (e.g., COHIBA Project

			environment. Following are the scoring criteria for inherent properties as listed in the ECHA General Approach for Prioritisation of SVHCs for Inclusion in the List of Substances Subject to Authorisation (ECHA, 2010, May 28). Inherent properties Score PBT and vPvB or PBT with T non-threshold C or M 4 PBT or vPvB properties 3 C or M properties (without effect threshold) 1 C, M or R properties (with effect threshold) 0 The ECHA Background Document on OPEs gives a total inherent property score of 0 to 1 for these compounds, indicating that inherent properties of OPE are somewhere between a Carcinogenic (C), Mutagenic (M) or Reproductive Toxicant (R) with a threshold effect and a C or M toxicant without a threshold effect. The only listed inherent property given for OPEs in the ECHA Background Document is that of Art 57(f)"equivalent level of concern having probable serious effects to the environment". As discussed below, OPEs and 4-tOP are not Persistent, Bioaccumulative and Toxic (PBT), nor are they very Persistent or very Bioaccumulative (vPvB). OPEs and 4-tOP are also not C, M or R. Therefore, even based on inherent properties alone OPEs should not even be subject to prioritization As described in companion papers by Staples et al (2008) and Klecka et al (2008) that review the persistence and bioaccumulation potentials for 4-tOP and their ethoxylates, neither of the parent compound nor any of its metabolites meet the various regulatory criteria for PBT or vPvB compounds, including those criteria listed in Annex XIII of REACH. In addition, neither OPEs nor 4-tOP meet the criteria for carcinogen, mutagen or reproductive toxicants category 1 or 2 in accordance with the DSD classification criteria or Cat 1A/1B in accordance with the CLP REGULATION (EC) No 1272/2008. It is important to also note that 4-tOP does not even meet the lesser criteria for Toxic to Reproduction Cat. 3 (DSD) or Cat 2 (GHS), which relates to "suspected human reproductive toxicants". 4-tOP is listed on the list of harmonised classification and labeling of hazardous substances based on its aquatic toxicity. The fact that OPEs do not themselves meet any of the inherent toxicity criteria for prioritization should be basis enough not to prioritize these compounds for authorization. 2.0 THE USE AND EMISSION PROFILE OF OPES DOES NOT SUPPORT PRIORITZATION OF THESE COMPOUNDS UNDER ANNEX XIV, FURTHERMORE THEIR USE IS PROJECTED TO DECLINE. The basis for the recommendation to prioritize OPEs for Authorization is that "these substances are used in high tonnage in products that can be	Consortium, 2012) indicate potentially significant releases of 4-tert-OPnEO from its use in paints. Furthermore, there may be other uses of 4-tert-OPnEO with significant exposure potential (as listed in ECHA's background document) which are not documented in the 4-tert-OP registrations. It is noted that assessment of information that normally requires higher level of assessment (e.g. monitoring data) is beyond the scope of this step of the authorisation process. In addition, it should be noted that compliance with the WFD is a basic requirement, and it does not necessarily have an impact on whether or not the use is wide-dispersive in the context of prioritisation under REACH. On the other hand, under Article 61(5) REACH, if an environmental quality standard established under the WFD is not met, the authorisations granted for the use of a substance may be reviewed. In summary, ECHA has assessed that there are identified uses of 4-tert-OPnEO which have a potential for significant environmental exposure. These substances are used in high tonnage in mixtures that can be assumed to lead to wide-dispersive emissions to the environment. <u>Article 58(2) exemption response</u> As regards your request for exemption please note that uses (or categories of uses) can only be exempted from the authorisation requirement on the basis of Art 58(2) of REACH, unless they are already explicitly exempted in REACH Art 2(5 or 8) or in Art 56 (3-6).

			assumed to lead to wide-dispersive emissions to the environment" (ECHA, 2013, June 24). The General Approach to Priority Setting for Authorization states "the extent to which a use is 'wide-dispersive' is roughly a function of the number of sites at which a substance is used and the magnitude of releases caused by those uses over all steps of the life-cycle" (ECHA, 2010, May 28). Therefore, the scoring of the 'wide-dispersive use' criterion is broken up in the two sub-criteria. The first is "Number of Sites", which is basically the number of sites where the substance is used (i.e. the number of point sources or number of sites from which a substance is being released). The second is "Release", which describes the releases in terms of pattern (where relevant) and amount versus anticipated risk. 2.1 The tonnage of OPEs used in the EU is declining The Annex XIV Background Document for OPE acknowledges that since there are no registrants for OPEs under REACH, information on volumes, uses and the supply chain are lacking. Therefore, based on the estimated fraction of 4-tOP used to manufacture its ethoxylates and the estimated average contribution to the molecular weight of its ethoxylates, the volume of ethoxylates produced is assumed in the Background Document to be in the range of 1,000 – 10,000 t/y (ECHA, 2013, June 24). Based on this tonnage estimate the OPE Background document scores OPE as "high" or "7". The UK Risk Assessment on 4-tOP reported that 1,050 t/y OPE were used in 2001 (UK Environment Agency, 2005), based on 400 t/y of 4-tOP conversion to OPE. The UK Risk Assessment also recognized the agreement of the companies that supply OPEs in the EU to not promote OPEs as substitutes for nonylphenol ethoxylates (NPEs) as those surfactants were subject to restrictions on their marketing and use in dispersive uses under EU Directive 2003/53/EC (European Parliament and the Council of the European Union, 2003, June 18). Due to antitrust regulations, APERC and CEPAD cannot share market and volume information directly. Current understanding of volumes for OPEs in the EU based on published reports indicate their tonnage to be in the lower half of the tonnage range estimated in the Annex XIV Background Document for OPEs with a decline in their use projected to be approximately 4.4% between 2009 and 2014 (Janshekar, H., 2010, July). 2.2 The primary uses of OPEs are not widely dispersive applications.	Please note that according to Article 58(2) of REACH it is possible to exempt from the authorisation requirement uses or categories of uses "*provided that, on the basis of the existing specific Community legislation imposing minimum requirements relating to the protection of human health or the environment for the use of the substance, the risk is properly controlled*". ECHA considers the following elements when deciding whether to include an exemption of a use of a substance in its recommendation: - There is existing EU legislation addressing the use (or categories of use) that is proposed to be exempted. Special attention has to be paid to the definition of use in the legislation in question, compared to the REACH definitions in accordance with Art. 3(24). Furthermore, the reasons for and effect of any exemptions from the requirements set out in the legislation have to be assessed; - This EU legislation properly controls the risks to human health and/or the environment from the use of the substance arising from the intrinsic properties of the substance that are specified in Annex XIV; generally, the legislation in question should specifically refer to the substance to be included in Annex XIV either by naming the substance or by referring to the group the substance belongs to, e.g. by referring to the classification criteria or the Annex XIII criteria;

			OPEs are used predominantly in the formulation of paint and coating products and are used at levels of generally 1% or less in those products. Due to their role in the emulsion polymerization process, OPEs are expected to be bound in the paint polymer and not widely dispersed to the environment. Waste from paint clean up are generally expected to be subject to treatment in wastewater treatment plants (WWTPs). OPEs are not reported as being used in consumer applications with high potential for human exposure or environmental release i.e., household detergents and fabric softeners and personal care products (SRI, 2010). Furthermore, restrictions on the marketing and use of NPEs in dispersive uses under EU Directive 2003/53/EC is not resulting in replacement with OPEs, rather "other surfactants or blends of other surfactants are benefitting from the trend away from OPEs in these applications (Janshekar, H., 2010, July)". Some minor uses of OPEs (i.e., vitro diagnostic applications in the medical device sector) are also not expected to result in widespread dispersive emissions. 3.0 CONCENTRATIONS OF OPES AND 4-tOP IN EUROPEAN SURFACE WATERS DO NOT SUPPORT A NEED FOR AN EU-WIDE AUTHORIZATION PROCESS FOR OPES UNDER REACH. When the UK Environment Agency conducted a risk evaluation on 4-tOP in 2005, information on the presence of 4-tOP and OPEs in the environment was limited; therefore the evaluation relied to a large extent on default assumptions and the Assessment Report acknowledges that its own "exposure assumptions may not be wholly realistic" (UK Environment Agency, 2005). That report also noted that at that time, surface water concentrations of 4-tOP in Europe and elsewhere were typically less than 1 µg/L, with "higher values detected on a few occasions" that may be "a consequence of high local discharges". Since that time more environmental monitoring data are available for 4-tOP and to a lesser extent OPE; these data should be considered in the prioritization process for OPEs, as Article 58 (3) allows for "consideration of further aspects and criteria for priority setting" (ECHA, 2010, May 28). The Water Framework Directive(WFD) established a framework for European Community (EC) water policy and strategies against water pollution, which requires Member States to take action for the	- This EU legislation imposes minimum requirements[1] for the control of risks of the use. Legislation setting only the aim of imposing measures or not clearly specifying the actual type and effectiveness of measures to be implemented is not regarded as sufficient to meet the requirements under Article 58(2). Furthermore, it can be implied from the REACH Regulation that attention should be paid as to whether and how the risks related to the lifecycle stages resulting from the uses in question (i.e. service-life of articles and waste stage(s) as relevant) are covered by the legislation. On the basis of the criteria above, it is considered that: (i) Only existing EU legislation is relevant in the context to be assessed (no national legislation). (ii) Minimum requirements for controlling risks to human health and/or the environment need to be imposed in a way that they cover the life cycle stages that are exerting the risks resulting from the uses in question. (iii)There need to be binding and enforceable minimum requirements in place for the substance(s) used. The relevant EU legislation referred to by the commenting party is assessed below. In relation to the Water Framework Directive 2000/60/EC (WFD) (and its

[1] Legislation imposing minimum requirements means that:
- The Member States may establish more stringent but not less stringent requirements when implementing the specific EU legislation in question.
- The piece of legislation has to define the measures to be implemented by the actors and to be enforced by authorities in a way that ensures the same minimum level of control of risks throughout the EU and that this level can be regarded as appropriate.

			progressive reduction of emissions of priority hazardous substances via the aquatic environment, through setting Environmental Quality Standards (EQS) and establishing emission control measures (European Parliament and Council 2000, 23 October Annual Average Environmental Quality Standards (AA-EQS) have been established for 4-tOP (European Parliament and Council, 2008, December 16). Monitoring for this compound has been conducted by the Member States under the WFD and additional monitoring has been published in the peer-reviewed literature. 3.1 Relevant Predicted No Effect Concentrations (PNECs) and Annual Average Environmental Quality Standard (AA-EQS) have been established for 4-tOP, which is the compound of interest. 3.1.1 PNECs for 4-tOP There are reliable toxicity studies for fish, amphibians, and invertebrates for 4-tOP, which cover all parts of the test organisms' life cycles from eggs to reproducing adults and cover life stages likely to be sensitive to an endocrine mode of action. Test procedures included screening tests, short-term reproduction tests, and full life-cycle tests. A consistent and treatment-related set of No Observable Effect Concentration (NOEC)have been reported for 4-tOP and range from approximately 6 to 1,000 µg/L across relevant population-level endpoints related to survival, growth and development, and reproduction (CEPAD-APERC, 2011, October 13, Coady et al, 2013, June 4, UK Environment Agency, 2005). Effects reported for endocrine sensitive endpoints occur at concentrations within the same range of NOECs and Lowest Observable Effect Concentrations (LOECs) that are also consistent with a narcotic mode of action (Coady et al, 2013). The UK Risk Evaluation of 4-tOP calculated an intermittent exposure PNEC for 4-tOP of 0.13 µg/L based on the most sensitive acute toxicity value (EC50 for freshwater shrimp of 13.3 µg/L) and an assessment factor of 10 (UK Environment Agency, 2005). A chronic PNEC for surface water of 0.122 µg/L is calculated in the UK evaluation based on the most sensitive chronic study in fish (NOEC based on growth for rainbow trout) and an assessment factor of 50, which was applied with consideration for potentially more sensitive species (UK Environment Agency, 2005). The REACH Chemical Safety Report (CSR) for 4-tOP utilized a species sensitivity distribution approach along with an assessment factor of five to calculate a freshwater PNEC of 0.632 µg/L for 4-tOP (CSR OP, 2010). 3.1.2 AA-EQS are established for 4-tOP under the WFD Annual Average Environmental Quality Standards (AA-EQS) of 0.10 µg/L (inland waters) and 0.01 µg/L (other waters) have been	daughter Directive 2008/105/EC), while these Directives set environmental quality standards for certain substances in the aquatic environment, and a framework for control of emissions, discharges and losses of these substances into the aquatic environment, they do not establish specific emission limits for substances or define risk management measures required. These aspects would be covered in specific permits issued by national authorities. It is further noted that pursuant to Article 62(5)(b)(ii) REACH an applicant may justify in his authorisation application that discharges of a substance from a point source governed by the requirement for prior regulation referred to in Article 11(3)(g) of Directive 2000/60/EC and legislation adopted under Article 16 of that Directive do not need to be considered when deciding on an authorisation. This implies that a case specific consideration is needed to judge whether risks arising from such discharges are properly controlled. For these reasons the WFD does not appear to be a sufficient justification for exemption under Article 58(2) REACH. In relation to Directive 2010/75/EU (IED), (which will replace a number of existing Directives including the IPPC Directive (2008/1/EC) from 7 January 2014), Annex II is an indicative list of the main polluting substances and includes large groups of substances. The directive does not specify how to identify polluting substances for which a permit for an installation needs to include an emission limit value. For these reasons the substances for which the minimum requirements set out in the directive apply are not specified in a way that would allow the use of the IED

			established for 4-tOP under the WFD (European Parliament and Council (2008, December 16). AA-EQS values are considered protective against both chronic exposures and short-term pollution peaks in continuous discharges (European Parliament and Council (2008, December 16). While the PNEC of 0.632 µg/L calculated in the CSR for 4-tOP can be considered more reliable as it is based on a more robust data set, the AA-EQS developed under the WFD are the most conservative benchmarks for comparison to concentrations in water. 3.1.3 Established PNECs and AA-EQS for 4-tOP are protective of endocrine mediated effects. OPEs were designated as SVHC primarily based on the argument that due to their degradation they are "an environmental source" of 4-tOP, which was previously designated SVHC due to concerns for environmental endocrine effects. Based on the results of targeted in vitro studies, 4-tOP and nonylphenol (NP) have been shown to have a weak binding affinity for the nuclear estrogen receptor, and can, at sufficient concentrations, also cause subsequent estrogen-receptor dependent transactivation (Recchia et al., 2004; Olsen et al., 2005; Preuss et al., 2006; Van den Belt et al., 2004; Van Miller and Staples, 2005; USEPA, 2009). The estrogenic activity of both 4-tOP and NP varies, depending on the assay used, and is generally in the range of one thousand to one million-fold less potent than the endogenous estrogen, 17□-estradiol (E2) (Coady et al., 2010; Van Miller and Staples, 2005; Wenzel et al., 2001). Exposure to alkylphenols, specifically 4-tOP and NP exposure, can increase circulating levels of vitellogenin (VTG) in fish. VTG is a yolk-precursor protein normally expressed in female oviparous species that has been demonstrated to be a highly responsive biomarker for estrogen receptor agonists, especially in males who carry the VTG gene but do not ordinarily express it (Jobling and Sumpter, 1993; Harries et al., 2000; Dussault et al., 2005; Olsen et al., 2005). VTG induction, which is not considered an adverse effect, occurs among various fish species at concentrations of 4-tOP and NP ranging from 1 to 100 µg/L (Coady et al., 2010; USEPA, 2007; Karels et al., 2003; Jobling et al., 1996; Rasmussen et al., 2002; Seki et al., 2003). In addition, reports of histopathological changes among gonadal tissues in fish exposed to either 4-tOP or NP have been reported in the range of 1.6 to 200 µg/L (Miles-Richardson et al., 1999; Gray and Metcalfe, 1997; Jobling et al., 1996; Staples et al., 2004; USEPA, 2007; Rasmussen et al., 2005; Karels et al., 2003; Rasmussen et al., 2002; Gray et al., 1999). While the observation of increased VTG in male fish and the occurrence of altered gonadal histopathology can inform upon one of the potential estrogenic modes of action of NP and 4-tOP, these biochemical and	Directive as a reason for exemption under Article 58(2) REACH. It is further noted that pursuant to Article 62(5)(b)(i) REACH an applicant may justify in the authorisation application that emissions from an installation for which an IPPC-permit has been granted do not need to be considered when deciding on an authorisation. This implies that a case specific consideration is needed to judge whether risks arising from IED installations are properly controlled. It is acknowledged that there is a UK voluntary industry commitment to reduce risk from 4-tert-octylphenol ethoxylates and other substances. It is noted that risk management measures and operational conditions identified, recommended and implemented need to be documented in the CSR part of the authorisation application and the level of control achieved will be assessed by RAC when forming its opinion on the application. While the voluntary commitment does not justify an exemption under Art 58(2) REACH, any monitoring and reporting systems established under such commitment can be used to strengthen the documentation of the control of the risks in the CSR.

			histopathological endpoints are not traditionally used as indicators of adverse effects in ecological risk assessments. For 4-tOP and NP, the threshold for estrogenic activity (measured as induction of the yolk-precursor protein, VTG, and alterations in gonadal histomorphology) in fish is in the range of 1 to 200 µg/L. Therefore the previously described PNECs and AA-EQS are sufficiently protective of even these sensitive estrogenic responses in aquatic species. 3.2 OPEs were determined to be Substances of Very High Concern (SVHC) under REACH primarily based on the argument that due to their degradation they are "an environmental source" of 4-tOP, which was previously designated as SVHC: therefore the focus of environmental monitoring is most appropriately focused on 4-tOP. Biodegradation has been shown to be the dominant mechanism responsible for removal of OPEs, 4-tOP and other alkylphenol (AP) and alkylphenol ethoxylates (APEs) during wastewater treatment and in the environment (Staples, 1999, Staples, 2001, Staples, 2008, Melcer, 2007). While OPEs are highly treatable in WWTPs, with removal rates commonly greater than 90%, low levels of their degradation metabolites have been reported in effluent and surface waters (Melcer, 2007). These intermediates continue to degrade in the environment, including mineralization of the phenolic ring, to carbon dioxide (Ahel, 1994, Staples, 1999, Staples, 2001, Staples, 2008, Naylor, 2006). Considering that 4-tOP is the most toxic of the OPE degradation intermediates, and that degradation to 4-tOP is the primary reason that OPEs were proposed to be SVHC and are now proposed for prioritization for Authorization, the focus of environmental monitoring is most appropriately focused on 4-tOP. 3.3 Results from recent monitoring in the EU indicate that the majority of surface water samples do not contain detectable concentrations of 4-tOP; furthermore when detected, 4-tOP concentrations are generally below the AA-EQS. Results of recent monitoring conducted in the EU are available through governmental monitoring programs and in the published literature. It should also be noted that all environmental monitoring results for 4-tOP represent emissions from all uses of 4-tOP, not just from the use of OPEs. 3.3.1 Results for 4-tOP from Monitoring Reported under the Water Information System of Europe (WISE) As required under the WFD , surface water concentrations of 4-tOP and other substances have been measured in various European waterways. Monitoring data on 4-tOP from Fact Sheets published by the Environment Directorate-General, European Commission (DG ENV) under WISE were reviewed for the following names and CAS numbers	

			for 4-tOP [CAS # 11081-15-5], 4-n-Octylphenol [CAS # 1806-26-4], Octylphenol [CAS # 140-66-9], Octylphenol [CAS # 67554-50-1] , and Octylphenol [No specified CAS number]. Data from nine countries (Belgium, Czech Republic, Spain, France, Ireland, Luxembourg, Poland, Sweden, and United Kingdom) are summarized in the fact sheets, which covered the period from 2000 to 2008. The data were representative of a range of water categories including rivers (2497 samples from 354 stations), lakes (406 samples from 100 stations), coastal waters (22 samples from 18 stations) and estuaries (3 samples from 3 stations) (DG ENV, 2013a, DG-ENV, 2013b, DG-ENV, 2013c, DG-ENV, 2013d, DG-ENV, 2013e). Results for 4-tOP concentrations detected in whole water samples (liquid and suspended particulate matter) as part of this monitoring are summarized in Table 1 below along with a comparison to the AA-EQS for 4-tOP (0.10 µg/L). Table 1: Summary of OP Concentration in Water Samples from Monitoring Data Listed in DG-ENV WISE Fact Sheets for 4-tOP (2000-2008) Number of Analyses N = 2795 Range 0 to 1.08 µg/L. Mean ± SD 0.03 ± 0.05 µg/L Median 0.03 µg/L 90th Centile 0.05 µg/L % samples < 0.10 µg/L 96% 0.10 µg/L < % samples < 1.0 µg/L 3.3 % 1.0 µg/L< % samples ≤ 1.08 µg/L 0.7 % The concentrations of 4-tOP reported under the WFD monitoring are taken at discreet moments in time; therefore there were not sufficient data in the Fact Sheets to calculate average values over time in a particular location. Rather than relying on individual sample results, the median and upper 90th percentile concentrations better represent concentrations of 4-t-OP in these waters. 3.3.2 Results for 4-tOP Monitoring Conducted by the Member States under Water Framework Directive Austria Monitoring of 4-tOP concentrations was conducted under the Water Framework Directive by the Austrian Federal Agency for Water Management for the year 2004 (Federal Agency for Water Management, Austria, 2005). Of 403 samples taken from Austrian Waters in 2004, none exceeded the AA-EQS for 4-tOP (0.1 µg/L) and 226 samples (56%) are reported as non-detectable. Switzerland A report on monitoring data from the State of St. Gallen in Switzerland during a 2012 monitoring program where WWTP effluents were	

			measured before dilution in the receiving waters indicates that 4-tOP was found above the detection limit of 0.025 µg/L in only one of 44 WWTP effluents. The one effluent sample where 4-tOP was detected contained 0.14 µg/L 4-tOP. After dilution, this corresponds to a concentration of 0.0001µg/L at this particular waste water treatment plant location (Office of Environment and Energy of the State of St. Gallen, Switzerland, 2013). United Kingdom The Department for Environment, Food and Rural Affairs (DEFRA) in the UK provided data tables with results of monitoring conducted for 4-tOP and OPE in the UK. Only 6 of 4143 samples tested for4-tOP, or 0.1%, are reported at above the method Limit of Detection (LOD), which are listed as 0.1µg/L or 0.05 µg/L depending on the sampling location (UK DEFRA, 2013). Said differently, 99.9% of the UK samples were non-detectable at limits of detection that are less than or equal to the AA-EQS for 4-tOP. Of those samples that were non-detectable, 55% are reported as < 0.05 µg/L. As expected, there are significantly less data reported for OPE. In the UK data tables for OPE, only 15 sample results are reported; however all are reported as non-detectable at LODs of 0.05µg/L (6 samples) , 0.1 µg/L (5 samples) and 0.2 µg/L (4 samples) (UK DEFRA, 2013). 3.4 Monitoring results for 4-tOP reported in the published literature indicate that the majority of surface water samples in the EU contain non-detectable concentrations and those detected are generally below the AA-EQS (0.1 µg/L), which is protective even in chronic exposure situations. Monitoring results for 4-tOP reported in the published, peer-reviewed literature indicate that the majority of surface water samples report non-detectable concentrations of 4-tOP and those detected are generally below the AA-EQS of 0.1 µg/L, which is protective even in chronic exposure situations. Following are summaries of the published monitoring data for 4-tOP in EU waters. Ribeiro et al. (2008) reported monitoring results for 4-tOP in the Mondego River estuary on the west coast of Portugal. Samples were taken at high and low tides and in shallow and deep water at 8 locations. There were 12 sample results reported for 4-tOP. All results were reported at less than the detection limit of 2.0 ng/L, which is 50 time less than the AA-EQS for 4-tOP. Jonkers et al. (2010) reported on the occurrence and concentrations of 4-tOP in Ria de Aveiro, a shallow coastal lagoon area in Portugal from a monitoring campaign that was conducted in 2006. Results (range, median, average) are provided for lagoons, harbors, sea water, sea	

			water near WWTP outfall, city, rivers and WWTP effluent. With the exception of the rivers Caster and Antuã and WWTP effluent, the average and median concentrations of 4-tOP are reported at less than 1 ng/L. For all analytes, including 4-tOP, the highest concentrations were found in the river samples of Rio Caster and Rio Antuã, which the authors explain as being related to flow rates in those rivers. Nevertheless, all median and average results reported for 4-tOP, including in undiluted WWTP effluent, are below the relevant AA-EQS for inland water (0.1µg/L) and other wateri.e., marine (0.01µg/L). Colin et al (2013) reported the occurrence of 4-tOP and OPE2 in raw water and treated water samples from public water systems in a sampling campaign that was performed from October 2011 to May 2012. Sampling was equally distributed across 100 French departments. In total, 291 raw water samples and 291 treated water samples were analyzed in this study, which the authors state represents approximately 20% of the national water supply. Octylphenol monethoxylate (OPE1) and octylphenol ether carboxylate (OPEC) were not detected in any samples. 4-tOP was not detected in any surface water samples. 4-tOP was detected in only one ground water sample at a LOD of 17 ng/L, which is 6 times less than the AA-EQS for 4-tOP. 4-tOP, OPE and OPEC were not detected at all in any treated drinking water samples. Esteban et al , 2013 analyzed a total of 30 compounds with endocrine activity, including natural and synthetic estrogens in the Jarama and Manzanares rivers, the main rivers in the Madrid Region (central Spain), which is the most densely populated area in Spain and also one of the most densely populated areas in Europe. There were 7 samples taken from the Mananares River and 7 samples taken from the Jarama River. Of the 7 samples taken from the Mananares River concentrations of 4-tOP exceeded the AA-EQS of 0.01µg/L for "other" waters in 5 samples. Of the 7 samples from the Jarama River, 1 sample exceeded this AA-EQS. . While there appears to be high contamination of all pollutants in the Mananares River, the sampling in this study was conducted in a limited time frame. The authors note that while 4-tOP was detected at concentrations exceeding the AA-EQS, there were insufficient data to calculate an average over time. The authors suggest that there is a need for further monitoring of this compound in both of these rivers. The authors further note that the total estrogenicity in these two rivers did not exceed 1 ng/L Estradiol Equivalents Quotient (EEQ), which is the lowest level that may cause estrogenic effects in aquatic organisms, in any of the samples - even considering that 30 estrogenically active compounds were monitored. The authors conclude that "the potential	

			estrogenic risk to aquatic organisms in both rivers is low" (Esteban et al , 2013). Kotowska et al. (2013) monitored for phenols and pharmaceuticals in effluent from WWTPs in 9 cities in Poland. The study found that the removal efficiency for 4-tOP was 96% from wastewater. The range of undiluted effluent concentrations for 4-tOP was reported as non-detected to a maximum of 4.02 µg/L. The authors report that in 3 samples out of 172 samples the concentration of 4-tOP was above 1µg/L. More relevant is that the overall mean effluent concentration for 4-tOP is 0.02 µg/L, which is 5 times less than the AA-EQS of 0.1 µg/L and these concentrations will be diluted further in the receiving surface water. Salgueiro-González et al. (2013) analyzed for alkylphenols in surface water, seawater and drinking water in the Coruna area in the northwest of Spain. Concentrations of 4-tOP in surface water were all less than the detection limit of 0.005 µg/L (n=5), which is 20 times less than the AA-EQS of 0.1 µg/L for inland surface waters. Concentrations of 4-tOP in seawater was 0.019 µg/L for one sample and less than the detection limit of 0.007 µg/L for 7 samples; therefore all but one seawater sample was less than the AA-EQS of 0.01µg/L for "other surface water". Concentrations of 4-tOP in six drinking water samples were all below the level of detection for the method, which was 0.020 µg/L. Stalter et al . (2013) reported monitoring for 26 sites impacted by wastewater effluent in several small rivers or streams and one mid-sized river, all in the Hessian Ried close to Frankfurt, Germany. Average concentrations of 4-tOP in water reported in this German study ranged between 12 and 147 ng/L, with an average result of 38 ng/L 4-tOP. With the exception of one sample (147 ng/L) all of the results in this river were below the AA-EQS for 4-tOP (0.1 µg/L). Rocha et al (2013) report concentrations of 4-tOP and other estrogenically active compounds in the Ria Formosa Lagoon in Portugal, which the authors state is highly impacted by discharge from 28 domestic and industrial WWTPs. The authors also note that these WWTPs have functional problems and, along with direct discharges from recreational boats and non-treated sewage, contribute to the pollution in this area. The authors state that this area is impacted by metallurgic industries, which they note is associated with the use of Alkylphenol Ethoxylates (APEs) and represents 25% of the industrial production in the Ria Formosa area (Rocha et al, 2013). This study found that APEs reached their maximal values in summer, which the authors attribute to "the scarcity of water from several riversides that usually supply the lagoon with fresh water and thus possibly dilute these chemicals in the channels" (Rocha, 2013).	

			Concentrations of 4-tOP ranged from 5.9 to 43 ng/L, with 8 of the 10 samples slightly exceeding the AA-EQS (0.01µg/L) for 4-tOP in "other water" but none exceeding the AA-EQS (0.1µg/L) for inland waters. Rocha et al (2013) report that the hormones estone (E1), 17β-estradiol (E2), 17α-ethynylestradiol (EE2), and a phytoestrogen sitosterol (SITOwere measured in considerable amounts in the Ria Formosa Lagoon. The authors also express concern for the total amounts of phosphorous and organophosphorus pesticides, which are present at up to ten fold higher than maximal concentrations recommended for rivers and streams.. These results indicate that discharge conditions in the Ria Formosa Lagoon can result in concentrations of 4-tOP that slightly exceed the AA-EQS for coastal waters. Considering the general pollution, presence of WWTPs "with functional problems", and heavy industrial discharge in this area, it appears that efforts to improve municipal and industry wastewater treatment would benefit this water body. In addition, considering that other compounds appear to pose more risk to this area, prioritizing 4-tOP for authorization on an EU level does not appear to be the most relevant and appropriate approach for 4-tOP or OPEs, both in terms of potential risk and regulatory effectiveness. 4.0 THE PRIORITIZATION PROCESS FOR OPES SHOULD ALSO CONSIDER THAT 4-tOP IS NOT WIDELY DETECTED IN EU WATERS AND, WHEN DETECTED, IS GENERALLY BELOW THE CONSERVATIVE AA-EQS FOR THIS COMPOUND. The Background Document recommending OPEs for prioritization for Annex XIV of REACH calculates a "relatively high" to "high" priority for inclusion in Annex XIV based scores of 0-1 for inherent properties (IP); 7 for high volume (V) and 9 for wide dispersive uses (WDU). However, as noted in section 2.0 of these comments, most uses of OPE are industrial, not consumer applications; therefore the number of sites and scope of dispersiveness is not as great as estimated in the Background Document prioritization. Also, the available environmental monitoring data for waters in the EU indicate that most samples of surface water tested did not detect 4-tOP at the method LOD and, when detected, most measured concentrations are less than the AA-EQS for this compound. Article 58(3) provides for discretion regarding the development and design of a prioritisation approach that in the end provides the Candidate Substances for which the recommendation to include them in Annex XIV is most relevant and appropriate (both in terms of potential risk and regulatory effectiveness) (ECHA, 2010, May 28). Therefore, the prioritization process for OPEs should consider the available monitoring data and the score for dispersiveness should be subject to	

			modification to reflect a lesser degree of dispersiveness and potential risk. 5.0 THERE ARE OTHER REGULATORY INSTRUMENTS IN PLACE IN THE EU TO CONTROL EMISSIONS OF OPES AND 4-tOP . Recent monitoring studies in the EU show that concentrations of 4-tOP that exceed the AA-EQS are associated with specific locations and points in time, which are otherwise polluted or subject to intense or uncontrolled discharges. The following regulations are already in place in the EU to control emissions and environmental risks from OPEs and/or 4-tOP. The Water Framework Directive (European Parliament and Council, 2000, 23 October Directive 2000/60/EC) established a framework for Community action in the field of water policy, which requires the Members States to measure aquatic concentrations relative to established Environmental Quality Standards (EQS) and to take action in case this value is exceeded. The monitoring data described in section 3.0 above notes specific locations and moments in time where concentrations of 4-tOP slightly exceed its AA-EQS. For the most part, these locations have generalized problems with contamination that are most appropriately addressed under the WFD. A UK voluntary industry agreement for the reduction in risk from NP, NPEs and 4-tOP and OPEs was finalized in 2004 (CSI, 2004, April). This agreement, which has impacted the EU market more generally, was taken to reduce the risks from NP/NPEs and 4-tOP/OPEs with the following objectives: • Rapidly reduce the risk from NP/NPE to the environment by making early progress in replacing NP/E in a number of uses and to minimise discharges into the environment in order to reduce existing risks to the environment; • Prevent the development of new risks from 4-tOP/E by preventing the use of 4-tOP/OPEs as substitutes for NP/E for those uses to be phased out; and • Reduce the risks from 4-tOP/OPE by phasing out any dispersive uses of 4-tOP/OPE in sectors targeted by the M&U Directive for NP/NPE The Integrated Pollution Prevention and Control (IPPC) Directive (96/61/EC) lays down measures designed to prevent or, where that is not practicable, to reduce emissions to air, water and land from the activities mentioned in Annex I to the Directive (European Parliament and Council, 1996, September 24). Annex I of the IPPC Directive lists categories of industrial activities subject to regulation by the Directive. Surfactants and surface active chemicals are specifically covered under Annex I. Since OPEs are surfactants they are specifically covered by the IPPC Directive. Other	

			categories of industrial activities that are subject to the IPPC Directive that are relevant to the major use of OPEs in paint and coatings include the chemical industry, including basic polymers and dyes and pigments. Other industrial activities subject to the IPPC directive that may be relevant to other minor uses of OPE include: energy industries, the production and processing of metals, chemical installations for the production of basic plant health products and biocides, installations using a chemical or biological process for the production of basic pharmaceutical products, waste management installations, and landfills. Industrial activities subject to IPPC where OPE use is not expected due to the voluntary agreement mentioned earlier in these comments include industrial plants that process pulp and paper, plants for the pre-treatment or dyeing of fibers and textiles and tanning facilities. In addition, Annex III to the IPPC Directive is a list including the main polluting substances in water to be taken into account, which includes "Substances and preparations which have been proved to possess carcinogenic or mutagenic properties or properties which may affect reproduction in or via the aquatic environment". As noted in section 1.0, neither OPEs nor 4-tOP are C, M or R toxicants; however, if there is concern about the environmental impact of either the IPPC Directive provides an existing regulatory mechanism for addressing these compounds. 6.0 APERC AND CEPAD RECOMMEND THAT OPES DO NOT WARRANT PRIORITIZATION FOR AUTHORIZATION UNDER ANNEX XIV OF REACH BECAUSE THEY DO NOT THEMSELVES MEET THE PRIORITIZATION CRITERIA FOR INHERENT TOXICITY, ARE NOT USED IN WIDELY DISPERSIVE CONSUMER APPLICATIONS AND ARE NOT DETECTABLE WIDELY IN THE WATERS OF THE EU; FURTHERMORE, LOCATIONS WITH EXCEEDANCES OF AA-EQS CAN BE ADEQUATELY CONTROLLED THROUGH EXISTING REGULATIONS OPE themselves do not meet any of the inherent toxicity criteria for prioritization for authorization, therefore on this basis alone should not be subject to prioritization for authorization. Furthermore, uses of these OPEs are generally not dispersive and the focus on OPEs for prioritization over other SVHC compounds is inappropriate. This is confirmed by recent environmental monitoring in the EU, which should be considered in the priority setting process for OPEs. Monitoring indicates that 4-tOP, the compound of actual interest in this case, does not have widespread occurrence in EU waters. Existing regulatory instruments exist in the EU, which are better suited to address specific locations where concentrations of 4-tOP are detectable and of concern relative to the conservative AA-EQS for 4-tOP. 4-tOP, the degradation intermediate of OPE that is the stated	

			concern for prioritization, is already regulated under the Water Framework Directive 2000/60/EC. In addition, 4-tOP and OPE are regulated under the IPPC Directive (96/61/EC) and are subject to a voluntary agreement among manufacturers not to promote the use of OPEs in dispersive uses that lead to entry in the aquatic environment (CSR, 2004, April). These existing regulations provide grounds for an exemption for OPEs from prioritization under Art. 58(2) of Regulation 1907/2006/EEC. As Rocha et al (2013) found in the Ria Formosa Lagoon, concentrations of 4-tOP that slightly exceed the AA-EQS are generally associated with areas impacted by general pollution, i.e., due to WWTPs "with functional problems", and heavy industrial discharge. It appears that efforts to improve municipal and industry wastewater treatment in categories already regulated under the WFD and IPPC Directive would benefit water bodies such as this more effectively than an authorization process for OPE under REACH. Also, considering that other compounds appear to pose more risk to these areas, prioritizing 4-tOP for authorization under REACH is not the most relevant and appropriate approach , both in terms of potential risk and regulatory effectiveness. The basis for given for prioritizing OPE for authorization is a concern for the environmental estrogenic activity of the degradant 4-tOP. Esteban et al , 2013 found that the total estrogenicity in the two rivers with the highest reported concentrations of 4-tOP – as well as 29 other estrogenically active hormones, phytoestrogens and industrial compounds - did not exceed 1 ng/L Estradiol Equivalents Quotient (EEQ). This is the lowest level that may cause estrogenic effects in aquatic organisms, in any of the samples. The authors conclude that "the potential estrogenic risk to aquatic organisms in both rivers is low." Considering this, prioritizing OPE for authorization does not appear to be necessary to address concerns of environmental estrogenicity from 4-tOP. For these reasons, APERC and CEPAD recommend OPE should not be prioritized for authorization under REACH and inclusion in Annex XIV. Reference list is provided in attached document.	
2478	2013/09/23 20:19	ChemSec International NGO Sweden	ChemSec supports the listing and prioritisation of this group of substances (covering well-defined substances and UVCB substances, polymers and homologues) to the Authorisation list (Annex XIV) due to its PB properties, wide dispersive use and high volumes. PBTness: 4-tert-OPnEO has bioaccumulative and persistent properties. A Danish screening survey https://bdkv2.borger.dk/Lovgivning/Hoeringsportalen/dl.aspx?hpid...	Thank you for providing your opinion and for the additional information provided.

			investigated the occurrence of alkylphenolic compounds such as octylphenol (4nOP straight chained isomer and tOP, branched chain mixture), octylphenol monoethoxylate (OP1EO) in the marine and freshwater aquatic environments, and selected alkylphenols in Arctic biota. Further ChemSec has some supporting studies that it has been found in human urine, in human breast milk, in river water, sediment, macroinvertebrates, and in fish bile, in reclaimed water, in bile of Mediterranean fish, in marine snails and oysters, in groundwater and drinking water, in river, estuarine and coastal waters, tissue of estuary-dwelling flounder (Platichthys flesus). It has also been found in plants and vegetables (due to the use of sewage sludge as fertilizer). Sources: Calafat et al 2008, Ademollo et al 2008; CDC 2007; Fiedler et al 2007; Hernandez-Rodriguez et al 2007, Cheng et al 2006; Martin-Skilton et al 2006; Vigano et al 2006; Ye et al 2006; Cantero et al 2006; OSPAR, 2006 Wang et al 2005, OECD SIDS 1995. Wide dispersive use: According to ECHA registration data, 4-tert-OPnEO are used in various applications such as paints (consumer and professional uses), in emulsion for polymerisation and intermediate. The Annex XV report highlights high concentrations of up to 30% in certain household care (consumer) products. The report also highlight uses such as auxiliaries in waste water treatment processes, mould release agent in construction, lubricant in various applications veterinary and pesticide applications. High exposure to workers, consumers and the environment at large are expected, suggesting that there are wide dispersive emissions in the environment. High volumes: 4-tert-OPnEO is manufactured / used in high volumes (up to 100.000tonnes per year). Further a lot of registrants have registered the substance as intermediate. Tonnages of import to the EU are not known. The substance should therefore be prioritised for listing in Annex XIV on this basis.	
2457	2013/09/23 17:44	European Diagnostic Manufacturers Association (EDMA) Industry or trade association	EDMA asks ECHA to recommend against prioritising 4-tert-OPnEO for inclusion on Annex XIV of Regulation 1907/2006/EEC (REACH). Authorisation as a risk management measure is not appropriate given the lack of data underpinning this dossier – particularly given the disproportionate and serious impact it would have on the in vitro diagnostic (IVD) medical device sector. It is difficult to overstate the complexity, risk and potential futility of seeking to substitute 4-tert-OPnEO for alternate surfactants. Due to its presence in multiple forms in small quantities and concentrations across	Thank you for your comments. Intrinsic properties Please see response to comment 2483, this section. Regarding your comment about ECHA disregarding your previous comments

		Belgium	a wide range of IVDs and research products, any search for substitution would trigger the need for re-validation and re-registration on an individual test-by-test basis of affected products both in Europe and internationally. When 1. The evidence to support prioritisation of 4-tert-OPnEO is not based on the substance properties, but on a possible link to their degradation products which are estimated by a possible link to other substances to become a substance of very high concern; 2. The disproportionate impact of Authorisation on the IVD sector which is over 90% SME; and 3. the small volumes used in this sector is weighed against the desired environmental policy outcome, EDMA hopes that regulators will find a proportionate risk management option which will support European manufacturing. Lack of evidence to support prioritisation: In its previous comments for the Registry of Intentions stakeholder consultation (enclosed as a reference), EDMA submitted its grave concerns regarding the evidence given in the Annex XV dossier for 4-tert-OPnEO which was based on 2 linked assumptions: that 4-tert-OPnEO is equivalent to nonylphenol ethoxylates and that they degrade to 4-tert-OP once released as waste. However there is in fact no data to support the claim that the degradation product of 4-tert-OPnEO meets the criteria of a substance of very high concern. The decision to regulate this family of substances is based on the degradation data for another family of chemicals with a significantly different structure. No explanation for why ECHA disregarded EDMA's comments (and similar concerns given by other impacted industry stakeholders) was given by ECHA in their RCOM document and subsequent background document to prioritise 4-tert-OPnEO for potential inclusion on REACH annex XIV. Since we believe that our concerns are both valid and based on careful scrutiny of the annex XV dossier, EDMA both regrets the lack of response and does not understand the rationale for prioritising 4-tert-OPnEO for inclusion on annex XIV at this time. Furthermore, as referenced in the comments submitted to this consultation by CEPAD, the European Council for Alkylphenols and Derivatives and the Alkylphenols Ethoxylates Research Council: The actual monitoring data on the levels of the 4-tert-OP, the substance of concern, in European waterways is not often detectable and when it is, does not exceed levels already regulated under the Water Framework Directive 2000/60/EC for this compound. We therefore continue to support our argument in this submission that the lack of data constitutes grounds for halting the	(and that of other industry stakeholders) – it should be noted that the RCOM document prepared during the SVHC consultations was prepared by the submitting MS (in this case DE) and that a response was provided to your comments on this matter. All comments received were also considered by the MSC when discussing whether this substance meets the criteria set out in Art 57(f) and consequently should be included in the Candidate List. In relation to the intrinsic properties of the substance, ECHA's Draft Background Document fully takes account of the Decision for inclusion of the substance in the Candidate List. <u>Prioritisation of the substance</u> Please see response to comment 2483, this section. With regard to the uses in low concentrations, we would like to note that authorisation is not required for the use of these substances in mixtures below 0.1 %. In accordance with art 58(3) the volume (within the scope of authorisation) is one of the prioritisation criteria. Annex XIV lists substances subject to the authorisation requirement and does not consider specific uses of substances apart from for possible exemptions in accordance with Art 58(2). For these reasons quantities used in certain single applications do not have an impact on the prioritisation. <u>Supply risk due to overlap of sunset date with registration date</u> Good communication in the supply chain is essential to decide the most appropriate

			prioritisation process for potential inclusion on Annex XIV. Supply risk due to overlap of sunset date with registration date: Since the earliest possible sunset date (August 2018) for 4-tert-OPnEO falls shortly after the final registration deadline for phase-in substances, industry will likely be faced with uncertainty of supply. EU manufacturers or importers may choose not to register the substance ahead of the sunset date. Even where EU users apply for Authorisation, supply will not be guaranteed due to lack of a registration within the EU. It is therefore appropriate to delay the prioritisation of 4-tert-OPnEO at this time until after the final registration deadline has passed, and further information on uses of the substance, its chemical properties and degradation product would also be known as a result of registration. Lack of certainty in substance identification: Identifying the appropriate risk management option and implementing chemicals regulation rests on the ability of competent authorities and industry alike to identify which substances are being regulated. Neither the Annex XV dossier nor the background document on 4-tert-OPnEO provides specifics about which compounds are included under this family of substances. EDMA has reached out to suppliers and identified several substances which are likely to be impacted however our association and members still lack certainty over the complete list of impacted 4-tert-OPnEO substances. It is neither possible nor appropriate for ECHA and the EU to regulate a family of substances without providing CAS numbers or other definitive identifiers. This issue has been raised by the European Automotive Manufacturers Association (ACEA) REACH task force at the European Commission technical workshop on the follow-up to the Review of the Regulation in June 2013. ACEA asked for true clarity in the classification of SVHCs with CAS numbers being provided for all impacted chemicals. Without it, full compliance with REACH is not certain for all members of the supply chain – particularly at SME level – and enforcement agencies may disagree on how to regulate at national level. EDMA has identified that some substances in the family of 4-tert-OPnEO are likely to be used under the trade mark of Triton (primarily those in the Triton "X" family although not exclusively). Additionally there are potentially multiple manufacturers using other trade names. The IVD industry uses TX-45, TX-100 (CAS 9002-93-1), TX-114 (CAS 9036-19-5), Triton CF10, TX-102, TX-165, TX-200E, TX-305 and TX-405, TX-705, Nonidet P40, IGEPAL CA-210, IGEPAL CA-520 and IGEPAL CA-720 with the use of TX-100 being the most popular. In some cases multiple substances mentioned here may be used for the same product.	actor(s) to apply for authorisation. This can be manufactures/importer(s) covering their customers' uses; or any downstream user(s) in the supply chain covering their own use, their suppliers' placing on the market and/or their customers' uses; or any combination of these which best meets the needs of the specific supply chain. Regarding the registration status, it appears that no registration has been submitted for 4-tert-OPnEO. However, the reason for this may be that they are considered as polymers (for substances fulfilling the polymer definition there is no registration requirement for the polymer as such; there is instead obligation, under certain conditions, to register monomer substance(s) and other substances from which a polymer is manufactured, e.g. 4-tert-OP). It is noted that registrations have already been submitted for 4-tert-OP. The registration deadline you mention (2018) is potentially relevant only for additional companies, manufacturing / importing 4-tert-OPnEO at volumes ≥1 and <100t/y and under certain conditions (for exact conditions see ECHA's Guidance on polymers and monomers, http://echa.europa.eu/documents/10162/13632/polymers_en.pdf), e.g. provided that no one up the supply chain has registered the monomer substance(s). However, please note that information (e.g. on uses of 4-tert-OPnEO) for priority assessment has already been obtained from the current registrations of 4-tert-OP. For a downstream user who wishes to continue a use and apply for authorisation but is concerned about supply (e.g.

			Use of 4-tert-OPnEO in the IVD sector: In vitro diagnostic medical devices (IVDs) provide medically useful diagnostic information by examination of a specimen derived from the human body. 4-tert-OPnEO substances are a particularly unique group within the surfactant category. The principal reason for their use in in vitro diagnostic products relates to the nature of the samples being tested. Biological samples such as blood and urine contain proteins which can interfere with the mechanism of the test or "assay". Surfactants are used to prevent unwanted reactions of these proteins with the components of the assay. If these unwanted reactions are not prevented, the accuracy and even the sensitivity of the test are impacted.4-tert-OPnEO substances are used in both wash solutions and reagents. In wash solutions, they are used in one or more of the steps for processing samples taken from patients to remove unbound material like proteins which could interfere with the way the diagnostic test or 'assay' works. EXAMPLE of use of wash solution: Enzyme-linked immunosorbent assay (ELISA) works by the attachment of either the antigen or antibody for an infectious agent to the surface of a polystyrene microtiter plate. When a human sample of for example blood or saliva is applied to the plate, antibodies or antigens of the infectious agent in the sample will bind to the plate with the result that the infectious agent can be detected and diagnosed. The antigen or antibody can only be attached to the plate in a series of delicate steps. Between each step, the plate is typically washed with a mild detergent solution to remove any proteins or antibodies that are not specifically bound. The mild detergent solution contains a specific amount of Triton X-100 (typically <0.1% to 2% concentration) which may vary depending on the infectious agent in question. EXAMPLES of reagent use: Triton X-100 plays an important role in population blood bank screening and virus safety. It inactivates viruses with a lipid coating including HBV, HIV and HCV viruses and allows them to be safely detected. In purified protein reagents, 4-tert-OPnEO substances are often used to help stabilise and solubilise the protein. In the wider industry, 4-tert-OpnEO substances are used not only in IVDs but also: • Research and development, laboratories and in non-CE marked diagnostic tests prepared and performed in house by national health care systems and blood banks; • Non-IVD industries producing commercially marketed	concerned that the suppliers in EU will cease manufacture/import), there is also the possibility to consider importing the substance and submitting (in case required, see guidance above) a registration themselves. <u>Substance Identification</u> Please note that SID aspects have been considered in the context of inclusion of substances in the Candidate List and they are not relevant in the current prioritisation phase. Similar comments on substance identity of 4-tert-OPnEO have been raised during the identification of the substance as SVHC and they have been addressed by the dossier submitter. In brief, ECHA considers that the substance identity information given on the Candidate List and Annex XIV fulfil the requirements set out in art 58(1)(a) REACH. Furthermore, it is to be stressed that the aim of REACH to ensure a high level of protection of human health and the environment which requires also, in ECHA's understanding, a sufficient knowledge from the registrants (and downstream users) of the chemistry and the naming of substances. The knowledge cannot in all cases be summarised by a non-exhaustive list of EC and/or CAS numbers. Therefore, it would not be appropriate to narrow the entries on the Candidate List or on Annex XIV only to those substances which have a CAS or EC number allocated. This is of particular importance as substances without a CAS and EC number covered by the respective entry can exhibit the same properties, hence the same concern exists. The support document for identification of 4-

			diagnostic tests for environmental and food pathogens, forensic or veterinary purposes. Substitution: By proposing 4-tert-OPnEO for prioritization, the ECHA has chosen the class of surfactants most commonly used within the IVD Industry. Because these surfactants are used to overcome matrix effects between patient samples and components within the diagnostic assays, and Authorisation would cover the entire class of these surfactants, it will be difficult to find replacements that meet the same performance requirements. The difficulties are described here in more detail below. Furthermore, unlike human health risks which are straightforward and recognized, it is unclear how likely classification of any given surfactant might be, especially when degradation products come into play. Should work be initiated to replace 4-tert-OPnEO substances with a class of surfactants which is eventually also classified as SVHC, the IVD industry could find itself in an unmanageable position. Continuous redesign/ maintenance of existing products for minute amounts of critical substances which directly impact on the safety and performance of complex and sensitive IVD products is not feasible nor supportive of a continuous and stable supply of diagnostic technologies to the market. Such regulatory uncertainty impacts funding for new diagnostic technologies, places a great burden on SMEs and raises question marks with our companies if they should consider moving manufacturing outside of Europe or limit which products are sold within the European Community. In order to replace 4-tert-OPnEO substances, extensive studies would be required to screen candidate replacements to ensure no change in product performance – in particular sensitivity and specificity testing. Without sufficient testing, the risk arises to have either false negative or false positive tests, which has tremendous and possibly fatal consequences for patients and the health of the population. Because surfactants are commonly used in wash reagents which are used with ALL tests (e.g. which run on the large automated analysers in hospitals or blood banks) a replacement process would impact entire portfolios of diagnostic products. It is important to understand that the extensive studies - validation testing – and re-registration would need to be done on an INDIVIDUAL impacted product-by-product basis. Re-validation means: • Testing of large populations of patients to ensure rare variations in the blood proteins of some patients would not interfere with the safe diagnostic performance of the test, leading to potentially fatal consequences for the individual patient. E.g. in a HIV test;	tert-OPnEO as a SVHC provides a non-exhaustive list of examples of substances covered by the group entry based on submitted pre-registrations and C&L notification. ECHA is looking for possibilities to improve the availability of such non-exhaustive lists (based on REACH and CLP databases) to support the industries. However, it needs to be stressed that for the reasons provided above the list is non-exhaustive and based on REACH and CLP data. <u>Level of risks / suitable alternatives / socio-economic considerations</u> Information on the low level of risk associated to a use or related to the availability and suitability of alternatives, socio-economic considerations regarding the benefits of a use, as well as the (adverse) impacts of ceasing a use are important. Information regarding these topics should be provided as part of the application for authorisation. This information will be taken into account by the Risk Assessment and Socio-Economic Analysis Committees when forming their opinions and by the Commission when taking the final decision. It may impact the decision on granting the applied for authorisation and the conditions applicable to the authorisation, such as e.g. the length of the time limited review period of the authorisation. However, it is to be stressed that the prioritisation for the inclusion in Annex XIV is based on the criteria set out in Art 58(3) and follows the agreed approach described in the general approach document (http://echa.europa.eu/documents/10162/17232/axiv_priority_setting_gen_approac

			• Full stability trials on 3 lots of the reformulated component to ensure the replacement did not adversely impact the products' shelf lives. In many cases, accelerated stability tests will neither be practicable nor possible, necessitating real time tests which may result in additional chemical wastes and delays in product availability of 1-2 years. Without a stable IVD with shelf life lasting several months or even years, diagnostic tests cannot be manufactured centrally and transported across the healthcare market in Europe and globally; • The complexity of substitution is multiplied where several different 4-tert-OPnEO substances are needed in one IVD; • Relicensing in certain markets both EU and non-EU, leading to protracted introduction time and a complex implementation pathway for the products; • Huge costs per product mean decisions to remove some IVDs from the market or manufacture outside EU; • Considerable time and resources to implement a portfolio re-design per impacted product diverted from re-investment into further innovation in diagnostic testing. Application for Authorisation would necessitate the IVD industry checking if substitution is possible. This check would necessitate the extensive sensitivity, specificity and stability testing described above. Therefore the application for Authorisation itself would be a significant burden on our industry which would potentially be prohibitive, jeopardizing the supply of IVDs for health institutions, blood banks and patients as well as stymieing research activities across academic and industrial laboratories. Furthermore, IVD manufacturing is impacted during this same timeline by the proposed prioritisation of N,N-dimethylformamide which, if listed on Annex XIV, would considerably increase the complexity and time needed to address identification of substitutes and redesign products. In many cases, both (sets of) substances are included in the manufacture or formulation of finished IVD products. It is not feasible for one industry to plan for the substitution of multiple different substances that are used in IVDs on the basis that global supply of these devices must be maintained and where validation processes (if viable alternatives exist) are estimated to take up to 10 years for a single substitution. Distortion of EU market and disproportionate impact on SMEs: As over 90% of the European IVD industry is made up of SMEs, the disproportionate cost of Authorisation and in particular the necessity to divert R&D resources into seeking substitution –would fall on those least able to pay for it. Suppliers may choose not to apply for Authorisation in	h_20100701_en.pdf). Consequently information on topics such as the availability and suitability of alternatives, socio-economic considerations regarding the benefits of a use or the (adverse) impacts of ceasing a use as well as information on the low level of risk associated to a particular use are not considered in the prioritisation for recommending substances for inclusion Annex XIV.

			order to market the relatively small volumes of the different 4-tert-OPnEO substances used by the IVD industry, meaning that the cost of application could fall wholly on the IVD industry. Any substitution (if possible) would trigger re-validation and re-registration of thousands of products leading to costs for the industry of well over € 100 million (conservative estimate) – a considerable cost when seen against the total IVD European market revenues of €10.8 billion (2011 figures). Member States could see costs rise considerably or access to new innovative diagnostic products disrupted regardless if Authorisation is granted or a substitute is found. The IVD industry contributes a very small amount of the use of 4-tert-OPnEO in the EU. Amounts used in the EU come to <33 tons per year (conservative estimate based on data from companies). This represents 0.3% of the low end of the tonnage band registered under REACH, as noted in the ECHA OPE background document. While many IVD products and their wash solutions contain 4-tert-OPnEO at a concentration of <0.1 %, there are some that are somewhat higher. Overall therefore the quantity of 4-tert-OPnEO substances used in the IVD sector is minute to negligible. As many wash solutions and reagents containing a 4-tert-OPnEO substance will use <0.1% concentration, these finished products are out of the scope of REACH authorisation according to Regulation 1907/2006/EEC, Article 56.6(a). At the same time, manufacturing products in the EU containing <0.1% concentration becomes impossible without Authorisation to handle the greater amount of product or buy that product from a supplier in order to manufacture a wash solution or reagent mixture with <0.1% concentration. Continued supply itself in the context of the Authorisation process becomes uncertain for such small quantities of use. Authorisation would affect the ability of European companies to compete in our own market. Third country manufacturers exporting IVDs to Europe would be unaffected by the Authorisation requirement. In particular, because the concentration of the surfactants in many final products is usually <0.1%, these same products could be manufactured outside the EU and imported legally into the EU. Therefore, inclusion on Annex XIV would unfairly bias European manufacturing and lead to a distortion of the market. Because re-validation/verification and potentially re-registration would be required for all impacted IVDs the substitution requirements of Authorisation would hit SMEs disproportionately, affect the competitiveness of European IVD manufacturing and impact on innovation and the availability and cost of diagnostic technologies. The cost and resources needed for re-validating/verifying and re-registering	

			thousands of impacted IVDs manufactured in Europe due to the use of minute quantities of 4-tert-OPnEO substances seems disproportionate indeed to the intended policy outcome. Given the hugely positive impact which 4-tert-OPnEO has on diagnostics and healthcare and the uncertainty of the data supporting 4-tert-OPnEO and 4-tert-OP (the substance of interest), EDMA requests that ECHA halt the process to prioritise 4-tert-OPnEO for Annex XIV.	
2422	2013/09/23 14:56	Company Germany	Abbott is a global healthcare company devoted to improving life through the development of products and technologies that span the breadth of healthcare. With a portfolio of leading, science-based offerings in diagnostics, medical devices, nutritionals and branded generic pharmaceuticals, Abbott serves people in more than 150 countries and employs approximately 70,000 people. In the EU, Abbott has major manufacturing facilities in Ireland, United Kingdom, Germany and Spain. Diagnostics: Abbott is a global leader in diagnostics (medical devices and in vitro medical devices (IVDs)) offering a broad range of innovative instrument systems and tests for hospitals, reference labs, blood banks, physician offices and clinics. Our products provide customers automation, convenience and flexibility, all of which lead to cost effective care. Key areas of focus include core laboratory diagnostics, immunoassay and clinical chemistry systems, hematology, molecular diagnostics and point of care diagnostics. Vascular Products: Abbott Vascular is the world's leader in drug eluting stents. Abbott Vascular has an industry-leading pipeline and a comprehensive portfolio of market-leading products for cardiac and vascular care, including products for coronary artery disease, vessel closure, endovascular disease and structural heart disease. Vision care: Abbott Medical Optics is focused on delivering life-improving vision technologies to people of all ages, offering a comprehensive portfolio of cataract, refractive and eye care products. Products in the cataract line include monofocal and multifocal intraocular lenses, phacoemulsification systems, viscoelastics, and related products used in ocular surgery. Products in the refractive line include wavefront diagnostic devices, femtosecond lasers and associated patient interface devices; excimer laser vision correction systems and treatment cards. Products in the eye care line include disinfecting solutions, enzymatic cleaners, lens rewetting drops and artificial tears. Diabetes: Abbott Diabetes Care is a leader in developing, manufacturing and marketing glucose monitoring systems designed to help people better manage their diabetes. N, N-dimethylformamide (DMF) is used in the production of in vitro Diagnostic Medical Device (IVDs) and medical devices that are produced	Thank you for the information provided (in the attachment) regarding 4-tert-OPEOs.

			and marketed in the EU and regulated under the In Vitro Diagnostic Medical Device Directive 98/79/EC and Medical Device Directive 93/42/EEC, and. One of the main objectives of these directives is the maintenance and improvement of the level of health protection attained in the Member States, as well as to allow the free movement of such devices within the EU. Subjecting the use of DMF in manufacture of ingredients used in IVDs to authorisation and forcing their eventual substitution would almost certainly contravene this objective. The use of DMF in the manufacture of these devices as reagents along with the control and calibration of these types of devices is crucial to the continuing production of these devices within the EU. Current manufacturing for many of these lifesaving products occurs in the European Union and supplies the global healthcare market. Thus, the potential authorization requirements for DMF as a process solvent in the manufacture of IVDs, impacts not only the EU healthcare market but the global IVD healthcare market. Substitution of DMF will be a complex, time consuming process subject to approval by many regulatory agencies worldwide. Throughout this substitution, our focus will be to ensure these lifesaving products are available globally without interruption to the public and medical community. Although every effort will be made to achieve appropriate substitution, it is possible that the product critical attributes could be affected (including specificity and sensitivity), thereby affecting the quality of the test results and therefore medical care worldwide. As a result, some manufacturing may need to be deferred to other locations outside the EU to ensure global supply can be uninterrupted. Dimethylformamide is a member of a group of extremely useful and widely used polar aprotic solvents. Within the in-vitro (IVD) medical device industry, DMF and similar solvents (DMAC, NMP) are used as process solvents in the production of IVDs and associated reagents and as standard analytics in laboratory research and development. In some cases, the DMF does not remain as a constituent in the final IVD. While there are other polar aprotic solvents with similar physical and chemical properties that could potentially be used in place of DMF, these alternative solvents also carry essentially the same health hazard as DMF. DMAC and NMP are currently progressing through the committee stages of two separate risk management processes: Authorisation and Restriction. The final decision to include other aprotic solvents (DMAC, EDC) onto Annex XIV is to be taken later this year by EU Committee under ECHAs 4th recommendation. Concurrently, a restriction proposal for NMP has been published for public consultation and is currently being considered	

			by another ECHA committee. Since an iOELV has been set by SCOEL for DMF which has been adopted by several member states into National Legislation, control of occupational exposure below a 'specified level' can already be demonstrated. There is an obvious regulatory inconsistency in so far as similar substances are being treated under different risk management measures for the same uses that could act to undermine the REACH processes that were designed to protect human health and the environment from the harmful effects of chemicals. It would therefore be appropriate that the inclusion of DMF onto Annex XIV be postponed until the outcomes of both Committee procedures are known and a consistent and appropriate risk management approach to the aprotic solvents is agreed. It is anticipated that the use of DMF in IVDs will not be subject to Authorisation in accordance with article 60(2). However, other uses such as a process reagent in the manufacturing of IVDs including use as a solvent in the synthesis of ingredients of reagents which are used in IVDs may not be explicitly exempted from the requirements of authorisation by this article. Authorization of DMF would have a critical impact on the IVD industry as outlined in the section on transitional arrangements. In summary, Abbott strongly opposes the inclusion of DMF onto Annex XIV at this time on the basis that there appears to be a large degree of uncertainty around the application of a consistent REACH regulatory measure for the group of aprotic solvents. Use of the substance in the manufacture of IVDs and medical devices is already regulated under the medical devices directives and occupational exposures are controlled in accordance with the Chemical Agents Directive.	
2369	2013/09/23 04:44	Company United States United Kingdom	The recommendation for 4-(1, 1, 3, 3-tetramethylbutyl) phenol, ethoxylated (4-tert-octylphenol ethoxylates) (4-tert-OPnEO) stated it is "used in high tonnage in products that can be assumed to lead to wide-dispersive emissions to the environment". There was not recognition of use categories where the chemical substance is not present in the final product, and therefore does not negatively impact the environment. The use categories where 4-(1, 1, 3, 3-tetramethylbutyl) phenol, ethoxylated (4-tert-octylphenol ethoxylates) (4-tert-OPnEO) is not present in the final product are subject to legislation imposing risk management measures protecting human health and the environment. Therefore, it is requested the categories of uses including medical research and development, and uses where the final product does not contain the substances and the 'emissions to the environment'' be exempted from the prioritisation.	Regarding prioritisation of the substance, and exemptions please see response to comment 2483, this section. <u>Scientific Research and Development</u> As regards the use of 4-tert-OPEO for medical research and development, this may fall under the general exemption of the use of substances in scientific research and development from the authorisation requirement in accordance with Art. 56(3). We would suggest that you examine whether the mentioned use of your

				substance can be regarded as SRD in accordance with the definition set out in Article 3(23). Article 3(23) defines SRD as "any scientific experimentation, analysis or chemical research carried out under controlled conditions in a volume less than 1 tonne per year".
2352	2013/09/20 19:35	AdvaMedDx Industry or trade association United States	European Chemicals Agency (ECHA) Annankatu 18 P.O. Box 400 FI-00121 Helsinki, Finland For Electronic Submission to ECHA Website Re: Comments on the Draft Recommendation of Substances for Inclusion in Annex XIV including the Prioritisation of the Substance Name: 4-(1,1,3,3-tetramethylbutyl)phenol, ethoxylated (4-tert-OPnEO) Includes the Triton X-100 family Dear Sir or Madame: On behalf of AdvaMedDx, a Division of the Advanced Medical Technology Association (AdvaMed), we provide these comments on the Draft Recommendation of Substances for Inclusion in Annex XIV of Registration, Evaluation, Authorisation, and Restriction of Chemicals (REACH). Our comments are specific to the 4-(1,1,3,3-tetramethylbutyl)phenol, ethoxylated (4-tert-OPnEO) substance, which includes the Triton X-100 family. AdvaMedDx member companies produce advanced, in vitro diagnostic (IVD) tests that facilitate evidence-based medicine, improve quality of patient care, enable early detection of disease and reduce overall health care costs. Functioning as an association within AdvaMed, AdvaMedDx is the only multi-faceted, policy organization that deals exclusively with issues facing IVD companies in the United States and abroad. Our membership includes manufacturers engaged in the development of innovative technologies supporting the advancement of public health, including manufacturers of IVD products for which the Triton X-100 family is commonly used in reagents and wash solutions. We write to echo strong support for the comments submitted on this topic by the European Diagnostic Manufacturers Association (EDMA). Similarly, AdvaMedDx asks that ECHA recommend against prioritising 4-tert-OPnEO for inclusion in Annex XIV. There is lack of data regarding these substances in the dossier. Furthermore, we are very concerned that the impact would be substantial and disproportionate to the IVD medical device sector with wide-ranging impact on the global supply	Thank you for your comment. Please see response to comments 2483, this section, regarding prioritisation of the substance and 2457, this section, regarding alternatives and socio-economic considerations.

			chain. Patient and health provider access to these critical IVD technologies is fundamental to global health care. AdvaMedDx members have identified that some substances in the family of 4-tert-OPnEO are likely to be used under the trademark of Triton (primarly those in the Triton "X" family although not exclusively). Additionally, there are potentially multiple manufacturers using other trade names. Tritons are very commonly used in the production of IVD medical devices that are produced and marketed worldwide. They have a number of significant uses in the IVD industry including: • As an effective surfactant/wetting agent, it reduces unspecific reactions, prevents protein binding on surfaces, and prevents aggregation of proteins or microparticles. • Promotes solubility and stabilizing hydrophilic proteins allowing their detection. • Lyses cells and inactivates plasma products which are essential in blood diagnostics. • In wash solutions, it is used in one or more of the steps for processing samples taken from patients to remove unbound material from process solutions like proteins that could interfere with the way the test works. By preventing unwanted reactions with components of the assay, they play an important role in assuring accuracy and overall test performance for entire portfolios of diagnostic products. To find replacements for these surfactants will not only be challenging, but it would entail significant studies including validation and reregistration on a product-by-product basis in Europe and internationally for minute amounts of substances that directly impact the safety and performance of IVD products. Uses such as the purification of blood plasma products and use in in vitro diagnostic medical devices represent a very low percentage (estimated at less than 1%) of the use in the EU. This annual usage for IVDs imported into the EU is orders of magnitude below other uses within the scope of Authorisation cited by ECHA in the Annex XV report. At the same, the impact would be profound and wide-ranging with respect to patient care and future access to these innovative technologies and investment in other new IVD product development. Thank you for the opportunity to provide comments. We respectfully request that ECHA not prioritise 4-tert-OPnEO for inclusion in the Annex XIV. A careful consideration should be made to assure that these innovative technologies are available globally without interruption to the public and the medical community. Sincerely,	

			Khatereh Calleja, JD Vice President Technology and Regulatory Affairs	
2334	2013/09/20 15:56	Individual Italy	DiaSorin does not see any basis for such a qualification or, at least, that an exemption from the authorization must be granted for DiaSorin's use of the substance for in vitro diagnostics purposes, as further discussed below.	Article 58(2) exemption Please see response to comment 2483 (section I). In addition, in relation to Council Directive 98/79/EC on in vitro diagnostic medical devices – this Directive sets out a framework for the design (essential requirements) and conformity assessment of devices manufactured & supplied to the EU. This includes reagents and reagent products. REACH Article 60(2) and 62(6) exempt consideration of human health risks in application for authorisations for the use of SVHCs in medical devices covered by this Directive. However, potential environmental risks are not exempted. This implies that specific consideration is needed to judge whether environmental risks arising from such uses are properly controlled. This Directive is not aimed at environmental protection e.g., it does not establish specific emission limits for substances or define risk management measures required to ensure environmental protection. For these reasons Directive 98/79/EC does not appear to be a sufficient justification for exemption under Article 58(2) REACH.
2281	2013/09/19 19:13	Individual France	Diagnostica Stago wishes to comment on public consultation relating to 4-tert-oPnEO. See attached confidental document.	Please see response to comment 2457, this section regarding alternatives / socio-economic considerations. For uses precursor to scientific research and development, please see response to comment 2262 (section III).

				Please also note that in case 4-tert-OPEO is included in A.XIV, uses of mixtures at concentration < 0.1% will be exempted from authorisation (however this exemption does not apply for the production of those mixtures).
2280	2013/09/19 18:55	Individual France	Diagnostica Stago wishes to comment on the public consultation relating to 4-tert-oPnEO (Triton X-100). See attached confidential document.	Please see response to comment 2281 in section I.
2262	2013/09/19 14:11	Company Germany		Thank you for the information provided.
2256	2013/09/19 12:42	Sweden, Member State	We support the prioritisation of 4-tert-octylphenol ethoxylates for inclusion in Annex XIV. The substance has relatively high priority due to high volume and wide dispersive use	Thank you for providing your opinion
2207	2013/09/11 11:10	Norway, Member State	The Norwegian CA supports the prioritisation of including 4-(1,1,3,3-tetramethylbutyl)phenol, ethoxylated (4-tert-OPnEO)] for inclusion in Annex XIV.	Thank you for providing your opinion
2158	2013/08/21 11:58	European Trade Union Confederation Trade union Belgium	ETUC supports the inclusion of 4-(1,1,3,3-tetramethylbutyl)phenol, ethoxylated (4-tert-OPnEO) in the Annex XIV.	Thank you for providing your opinion

II - Transitional arrangements. Comments on the proposed dates:

#	Date	Submitted by (name, Organisation/MSCA)	Comment	Response
2478	2013/09/23 20:19	ChemSec International NGO Sweden	It is assumed that the Commission Regulation including the substances of this 5th Recommendation in Annex XIV would enter into force only in February 2015. Keeping the proposed application date would mean an application date by February 2017 with an extra 18 months to sunset the substance. There is no reason why the date for inclusion in Annex XIV for this substance should be so far ahead, and in this case even deferred by a further 3 months, leading in a delay for the realisation of effective protection objectives i.e. August 2018. Potential applicants are already informed of the likely inclusion of the substance in Annex XIV or will be when a decision on inclusion in Annex XIV is taken. A 2 years preparation period for application submissions should be more than sufficient to prepare for applications. According to REACH (Art 58.1 ii) a minimum 18 months period is only foreseen between the sunset date and the application deadline, but nothing prevents ECHA / the European Commission to foresee an earlier deadline for application. Therefore ChemSec would propose to provide for an effective deadline for application of maximum 2 years from the date of the EU Commission's decision to include the substance in Annex XIV.	ECHA made its proposals for the latest application dates on the basis of discussions by the stakeholder expert group that was following the development of the Guidance for including substances in Annex XIV. This expert group estimated that the time needed for preparation of an authorisation application of sufficient quality might in standard cases be 18 months (roughly 12 months of work-time for drafting the application plus an additional buffer of 6 months for consulting required external expertise). As there is yet no reliable information available that would suggest shortening or prolonging this time interval, we consider that a period of 18 months should normally be given, after inclusion of the substance in Annex XIV, to allow for the preparation of a well-documented application for authorisation. The anticipated workload of the Agency with regard to processing of authorisation applications was accounted for by grouping the proposed substances in 3 lots and spreading the application and sunset dates over a period of six months. 4-tert-OPEO was put in the latest lot for application.
2457	2013/09/23 17:44	European Diagnostic Manufacturers Association (EDMA) Industry or trade association	EDMA does not support Authorisation as the most appropriate risk management option for the reasons mentioned under the 'General Comments' section. If the EU should regardless decide to proceed with including 4-tert-OPnEO on REACH annex XIV, the IVD sector would require 10 years' transition times considering the hundreds of products which would be impacted, the majority SME nature of our sector, and the extensive re-validation and re-	Please note that authorisation, inter alia, is a means to promote the development of alternatives. Article 55 explicitly stipulates that applicants for authorisation shall analyse the availability of alternatives and consider their risks, and the technical and economic feasibility of substitution (this has

		Belgium	registration required both in the EU and internationally. IVD manufacturing is impacted during this same timeline by the proposed prioritisation of N,N-dimethylformamide which, if listed on Annex XIV, would considerably increase the complexity and time needed to address identification of substitutes and redesign products. In some cases, both (sets of) substances are included in the manufacture or formulation of the finished IVD products. It is not feasible for one industry to plan for the substitution of multiple different substances that are used in IVDs on the basis that global supply of these devices must be maintained and validation processes (if viable alternatives exist) are estimated to take up to 10 years for a single substitution. Should both (sets of) substances be listed on Annex XIV, the IVD industry would potentially need much longer than 10 years to test for candidates and engage in re-validation/registration processes.	to be included in the analysis of alternatives to be submitted as part of the authorisation application in accordance with Art. 62 (4e)). Therefore, the present lack of alternatives to (some of) the uses of a substance (as well as established validation / registration processes, safety requirements or performance standards) and the need to complete R&D programmes to get qualified alternatives to it are not viable reasons for postponing the subjection of a substance or some of its uses to authorisation. Information regarding lack of alternatives (as well as established validation / registration processes, safety requirements or performance standards) is however important information for inclusion in an authorisation application. This information will be taken into account by the Risk Assessment and Socio-Economic Analysis Committees when forming their opinions and by the Commission when taking the final decision. It may impact the decision on granting the applied for authorisation and the conditions applicable to the authorisation, such as e.g. the length of the time limited review period of the authorisation.
2422	2013/09/23 14:56	Company Germany	Abbott strongly opposes the inclusion of DMF onto Annex XIV and asks ECHA to consider more appropriate risk management options in the context with the whole group of other polar aprotic substances (as outlined in the general comments), due to the criticality of the use in the IVD industry. However, if ECHA decides to proceed towards authorization, Abbott requests ECHA to consider longer transitional arrangements on the basis that substitution of DMF is a complex, time consuming process subject to approval by many regulatory agencies worldwide. In order to replace key substances used in manufacturing of IVD tests or as test constituent, extensive studies would be required	This comment primarily relates to DMF. In this regard, please see response at the respective comment in the RCOM document for DMF. Regarding 4-tert-OPEO, please firstly note that the sunset date does not need to consider the timeframe in which it may be possible to *substitute* the substance in question in its uses. See also response to comment 2457 (in this section) regarding alternatives / validation processes.

			to screen candidate replacements to ensure no change in product performance – in particular sensitivity and specificity testing. This may include testing of large populations of patients, in order to make sure that rare variations in the blood proteins of some patients wouldn't interfere with the safe diagnostic performance of the test, leading to potentially fatal consequences for an individual patient. e.g., in a HIV test. Additionally, full stability trials on 3 lots of the reformulated component would be necessary to introduce such a change. Any change such as this would mean relicensing in certain markets, leading to protracted introduction time and a complex implementation pathway for the products. The validation testing studies– and re-registration would need to be done on an individual product-by-product basis. Because the test constituents produced using DMF can be used in several different final products (IVD test kits) other tests which run on the same large automated analysers in a hospital or blood bank can be impacted also. That means, a replacement process could impact entire portfolios of diagnostic tests on this analyser, i.e. all the different blood parameters or disease markers. The time to implement such a portfolio redesign would be considerable. The complexity of substitution, the resources needed and the costs incurred could cause companies to evaluate whether to remove some products from the market and/ or to relocate manufacturing outside the EU. Furthermore, IVD manufacturing is likely to be impacted to some extent during this same timeline by the proposed prioritisation of 4-tert- OPnEO which increases the complexity and time needed to address identification of substitutes. In some cases, both DMF and 4-tert OPnEO are included in the manufacture or formulation of the finished IVD products. Abbott therefore requests longer transitional arrangements on the basis that the medical devices sector is potentially impacted by EU activity on these substances and as well as proposed activity on other aprotic polar solvents. In addition, should authorisation be required, multiple, parallel applications could be necessary. It is not feasible for one company to plan for the substitution for multiple substances that are used in IVDs on the basis that global supply of these devices must be maintained and validation processes are estimated to take up to 10 years (see attached table on confidential attachments).	Furthermore, note that in accordance with Art. 62(1, 2) applications for authorisation may be made by the manufacturer(s), importer(s) and/or downstream users of a substance (or any combination thereof) and that they may be made for one or several uses. Applications may be made for the applicant's own uses and/or for uses for which he intends to place the substance on the market. From these specifications of Art. 62 it is evident that not each actor on the market has to apply for authorisation of his use(s). A supplier (manufacturer, importer or downstream user) may cover in his application use(s) of his downstream users. Furthermore, it is possible to submit joint applications by a group of actors. To get the required application(s) ready in time is therefore also a matter of communication, organisation and agreement between the relevant actors in the supply chain and efficient allocation of work. For 4-tert-OPEO in fact ECHA recommends a LAD of 24 months after inclusion in A.XIV, which is 6 months more than the time estimated (by the stakeholder expert group that was following the development of the guidance for including substances in Annex XIV) as required to prepare an authorisation application of sufficient quality (18 months).

2281	2013/09/19 19:13	Individual France	Diagnostica Stago wishes to comment on public consultation relating to 4-tert-oPnEO. See attached confidental document.	Please see response to comment 2281 in section I
2280	2013/09/19 18:55	Individual France	Diagnostica Stago wishes to comment on the public consultation relating to 4-tert-oPnEO (Triton X-100). See attached confidential document.	Please see response to comment 2281 in section I
2256	2013/09/19 12:42	Sweden	We agree with the proposed dates.	Thank you for providing your opinion.

III - Comments on uses that should be exempted from authorisation, including reasons for that:

#	Date	Submitted by (name, Organisation/MSCA)	Comment	Response
2478	2013/09/23 20:19	ChemSec International NGO Sweden	ChemSec supports the proposal of ECHA to not allow any exemptions.	Thank you for providing your opinion.
2457	2013/09/23 17:44	European Diagnostic Manufacturers Association (EDMA) Industry or trade association Belgium	EDMA does not support Authorisation as the most appropriate risk management option for the reasons mentioned under the 'General Comments' section. EDMA notes that 4-tert-OP, the actual substance of interest, is already regulated under the Water Framework Directive 2000/60/EC. This is grounds for an exemption under Art. 58(2) of Regulation 1907/2006/EEC: since the relevant exposure scenario (presence of the presumed degradation product in the water stream) is already addressed, REACH should not add additional requirements. If the EU should regardless decide to proceed with including 4-tert-OPnEO on REACH Annex XIV, an exemption for PPORD up to 10 tons per annum would be required.	Regarding Art 58(2) exemption, please see response to comment 2483. PPORD As regards the requested exemption for PPORD, we would like to make reference to REACH Article 55, in which the progressive replacement of SVHCs where this is technically and economically viable is mentioned as one of the objectives of authorisation. Therefore, we consider that any further PPORD activities which may require the use of a substance included in Annex XIV should in principle aim at developing alternative substances and technologies to replace the SVHC in question or to further develop processes to improve the control of risks until feasible alternatives are available. However, ECHA notes that actors can apply for a use of a substance (included in Annex XIV) for any PPORD activity and the pertinence of a PPORD activity with a substance identified as SVHC should be justified in an authorisation application and be scrutinized and decided in the authorisation granting process in accordance with Article 60.

2422	2013/09/23 14:56	Company Germany	Abbott anticipates that its use of the substance DMF in the production and subsequent use of medical devices and IVDs regulated under Directives EC Nos. 93/42/EEC and 98/79/EEC will be exempted from the requirements of Authorisation in accordance with article 60(2) of REACH, however exemptions are requested for the following other associated uses of the substance. Exemptions requested under Article 56(3): Clinical Chemistry and Quality Control Testing DMF is used as a solvent in test reagents used for the quality control testing of materials and components used during manufacture of in vitro diagnostic reagents. DMF is also specified in many analytical tests that are required by the EU Pharmacopeia (see list in confidential attachments). It is also used in stock solutions used in the preparation of labelled probes and conjugates and for the storage of labelled compounds prior to further formulation into diagnostic reagents. We consider that article 56(3) of REACH that exempts substances listed on Annex XIV from the requirements of Authorisation where the use is for scientific research and development, applies to analytical and quality control uses for instance in use in medical laboratories where the diagnostic technique specifies the use of the substance. These uses are carried out in laboratory settings under controlled conditions (as detailed in the IVD and Medical Device Directives) and in quantities of less than 1 tonne per year.	This comment relates to DMF. A response has been provided in the RCOM document for DMF instead.
2369	2013/09/23 04:44	Company United States United Kingdom	These substances have a critical use as a surfactant in laboratory scale bio-chemistry processes involving proteins, lipids, DNA and cell-membranes. Therefore, these are essential ingredients and process chemicals in the manufacture of laboratory reagents for further Lifesciences research. Use exemptions should apply to: - Use applications where the volume is < 1000 litres per year per use. - Where the final products do not contain the 4-(1, 1, 3, 3-tetramethylbutyl) phenol, ethoxylated (4-tert-octylphenol ethoxylates) (4-tert-OPnEO) - Where the end products are used in scientific research & development, by cancer research institutes, medical research organisations, universities and pharmaceutical companies to investigate cellular disease processes, with a goal of developing	Thank you for your comment. Regarding exemptions in general please see response to comment 2483, section I. Regarding scientific R&D please see response to comment 2369, section I. Regarding PPORD please see response to comment 2457, this section.

			more effective pharmaceuticals and therapies. - Uses in PPORD and medical R&D by public and private institutions where the 4-(1, 1, 3, 3-tetramethylbutyl) phenol, ethoxylated (4-tert-octylphenol ethoxylates) (4-tert-OPnEO). Use descriptors: o PROC15 Use as laboratory reagent o PC21 Laboratory chemicals o PC19 Intermediate	
2281	2013/09/19 19:13	Individual France	Diagnostica Stago wishes to comment on public consultation relating to 4-tert-oPnEO. See attached confidental document.	Please see response to comment 2281 in section I
2280	2013/09/19 18:55	Individual France	Diagnostica Stago wishes to comment on the public consultation relating to 4-tert-oPnEO (Triton X-100). See attached confidential document.	Please see response to comment 2281 in section I
2262	2013/09/19 14:11	Company Germany	The packaging/refilling of the pure substances as well as the formulation/packaging/refilling of mixtures for scientific R&D purposes into small packages should be exempted from authorisation. The packaging/refilling of the pure substances as well as the formulation/packaging/refilling of mixtures into small packages for virus inactivation for the production of plasma as well as for cell lysis and cleaning and preservative applications should be exempted from authorisation. Use of octylphenol ethoxylates for plasma products Human plasma is the source of over 700 proteins of considerable therapeutic value such as albumin, clotting factors, immunoglobulins, fibrinogen and others. The process used to extract and purify these proteins is known as plasma fractionation. A critical step, viral clearance, ensures the removal of viruses such as parvovirus, hepatitis and HIV. 4-tert-Octylphenol ethoxylates (e.g. Triton X-100) are used in the solvent/detergent treatment for the inactivation of enveloped viruses and removal procedures intended to assure the viral safety of human blood plasma products. For virus inactivation normally a concentration of 0.1 % of the octylphenol ethoxylate is used. An established procedure for virus inactivation is the Solvent/Detergent (S/D) treatment (see "Attachment 01_ BioPharm_Solvent_Detergent Treatment.pdf).	Thank you for your comment. Regarding exemptions in general please see response to comment 2483 in section I. Regarding use in scientific R&D please see response to comment 2369 in section I. Regarding use in IVD medical devices please see response to comment 2334 in section I. Regarding use in medicinal products, Regulation (EC) No 726/2004 establishes the operation of European authorisation procedures for the placing of medicinal products on the market in the European Union (EU). Each application for authorisation must be accompanied by the particulars and documents referred to in Directive 2001/83/EC on the Community code relating to medicinal products for human use or in Directive 2001/82/EC relating to the production, placing on the market, labelling, distribution and advertising of veterinary medicinal products.

			Solvent/detergent treatment using Triton-X 100, Octoxinol 10 is mentioned in several guidelines, e.g. "Guideline on plasma-derived medicinal products published" by the European Medicines Agency (see "Attachment 02_EMA_Guideline on plasma-derived medicinal products"), Annex IV to "Guidelines on viral inactivation and removal procedures intended to assure the viral safety of human blood plasma products" published by the WHO (see "Attachment 03_WHO_TRS_924_A4_Guideline on viral inactivation and removal procedures"). Also the European Pharmacopoeia describes this type of substances for virus inactivation in its monographs (see "Attachment 04_European Pharmacopoeia_7.7_Human plasma pooled and treated for virus inactivation"). It is reported that the worldwide experience with S/D-treated products indicates that the proteins present in S/D-plasma will circulate and function normally in vivo (see "Attachment 09_Solvent_detergent treated plasma "). Inactivation of HIV, HBV and HCV and of many other enveloped viruses has been demonstrated by using 4-tert-octylphenol ethoxylates (e.g. Triton X-100) (see "Attachment 09_Solvent_detergent treated plasma ", "Attachment 05_Info DRK - virusinaktiviertes Humanplasma" and "Attachment 06_RKI_HIV_Inaktivierung"). When the treatment is complete, the solvent/detergent reagents must be removed. The permitted residual levels of Triton X-100 are generally 3–25 ppm (see "Attachment 03_WHO_TRS_924_A4_Guideline on viral inactivation and removal procedures"). Use in detection of viruses Octylphenol ethoxylates are also used in the detection of viruses in donated plasma. Testing of plasma, e.g. for HIV and hepatitis is required by the European Directive 2002/98/EC "setting standards of quality and safety for the collection, testing, processing, storage and distribution of human blood and blood components and amending Directive 2001/83/EC" (see "Attachment 07_Directive 2002_98_EC"). The description of an ELISA test kit for the detection of HIV can be found in "Attachment 08_HIV p24 confirmatory reagents". Use in biochemical R&D Octylphenol ethoxylates (e.g. Triton X-100) are widely used in very small volumes in biochemical applications on R&D scale: One application is degradation of viruses or lysis of bacteria to isolate proteins and nucleic acids. Another application is as	Whilst measures may be in place to control the residual amount of solvents in the final product, these pieces of legislation may not control risks to human health or the environment arising from the use of the substance at production stage of these products or, in particular, from the use and disposal of 4-tert-OPnEO. Therefore, they may be not regarded as a sufficient basis for exempting uses of 4-tert-OPnEO from authorisation in accordance with Article 58(2) of the REACH Regulation. <u>Formulation/packaging/refilling for SRD</u> Although uses for scientific research and development of a substance are exempted from the authorisation requirement in accordance with Article 56(3) this appears to only apply to its final use for SRD purposes under the conditions defined in Article 3(23). However, use of an SVHC included in Annex XIV, on its own or in a mixture (in the case of 4-tert-OPnEO, at or above the concentration limit of 0.1%), with the intention to supply them for SRD purposes, would probably require authorisation.

			solubility promoter and stabilizer for hydrophobic proteins. For lysing cells, typically a concentration of 0.1 % in water is sufficient. Use in biochemical analysis Analysis of membrane proteins is an essential task in pharma research for the evaluation of drug targets. Since these proteins are generally not soluble under low salt conditions alternative reagents must be used for their isolation. Different membrane proteins may require different detergents for solubilization. Octylphenol ethoxylates, especially Triton X-100, are widely used among others for solubilization. Test kits provided to professionals typically contain solutions with a concentration of 1% of Triton X-100. Use in cleaning and preservative applications Octylphenol ethoxylates are used in low concentrated aqueous mixtures in the cleaning of medicinal equipment. Use as solubility promoter In several mixtures used for routine analysis, organic substances with low solubility are solubilized by the addition of nonionic surfactants like Triton X-100. All formulations mentioned in the uses described above are used in the laboratory by industrial and professional users that are well-trained.	
2207	2013/09/11 11:10	Norway, Member State	Norway considers that no exemptions from the authorisation requirement should be proposed	Thank you for providing your opinion

IV - Comments on uses for which review periods should be included in Annex XIV, including reasons for that:

#	Date	Submitted by (name, Organisation/MSCA)	Comment	Response
2478	2013/09/23 20:19	ChemSec International NGO Sweden	ChemSec supports the proposal of ECHA to not allow any review periods.	Thank you for providing your opinion
2457	2013/09/23 17:44	European Diagnostic Manufacturers Association (EDMA) Industry or trade association Belgium	EDMA does not support Authorisation as the most appropriate risk management option for the reasons mentioned under the 'General Comments' section. If the EU should regardless decide to proceed with including 4-tert-OPnEO on REACH Annex XIV, the IVD sector would require 10 year review periods considering the hundreds of products which would be impacted, the majority SME nature of our sector, and the extensive re-validation and re-registration required both in the EU and internationally.	Thank you for your comment. Please note that setting 'upfront' review periods for any uses requires that the Agency has access to adequate information on different aspects relevant for a decision on the review period. ECHA currently assessed that the information available is not sufficient to conclude upfront on specific review periods. Therefore, ECHA did not propose such review periods. It is to be stressed that all authorisation decisions will include specific review periods which will be based on concrete case specific information provided in the applications for authorisation. Furthermore, note that guidance on the type of information in an application for authorisation which may impact the review period when granting authorisation can be found in RAC's and SEAC's approach for establishing the length of the review period.(http://echa.europa.eu/documents/10162/13580/seac_rac_review_period_authorisation_en.pdf)
2281	2013/09/19 19:13	Individual France	Diagnostica Stago wishes to comment on public consultation relating to 4-tert-oPnEO. See attached confidental document.	Please see response to comment 2281 in section I.
2280	2013/09/19	Individual	Diagnostica Stago wishes to comment on the public	Please see response to comment 2281

#	Date	Submitted by (name, Organisation/MSCA)	Comment	Response
	18:55	France	consultation relating to 4-tert-oPnEO (Triton X-100). See attached confidential document.	