G Model
HAZMAT-17663; No. of Pages 15

ARTICLE IN PRESS

S. Valsecchi et al. / Journal of Hazardous Materials xxx (2016) xxx–xxx

Table 5
Relevant studies used to derive QSs for the different protection objectives. fw = freshwater; sw = saltwater (marine, coastal and transitional waters).

	Relevant study for derivation	AF	QS_{biota}	BCF	BMF	QS_{water}	Reference
PFOA							
MAC-EQS	HC5 of the LC(E)50 SSD function: 22.2 mg L^{-1}	5 (fw)				2220 μg L^{-1} (fw)	
		50 (sw)				450 μg L^{-1} (sw)	
AA-QS	mesocosm study on *Pimephales promelas* (39d); NOEC: 0.3 mg L^{-1}	10 (fw)				30 μg L^{-1} (fw)	[11]
		100 (sw)				3 μg L^{-1} (sw)	
$QS_{biota,secpois}$	LOAEL (mice): 0.01 mg $kg^{-1}{}_{bw}$ d^{-1}	90	0.9 μg $kg^{-1}{}_{fw,biotaww}$	9.4 L kg^{-1}	BMF1: 1	0.1 μg L^{-1} ($QS_{fw,biota,secpois}$)	[24–26]
	bw/DFI: 8.3 kg_{bw} d kg^{-1}		0.18 μg $kg^{-1}{}_{sw,biotaww}$		BMF2: 5	0.02 μg L^{-1} ($QS_{sw,biota,secpois}$)	
	NOEC: 0.083 mg kg^{-1}						
$QS_{biota,hh}$	BMDL10 (rats and mice): 0.3 mg $kg^{-1}{}_{bw}$ d^{-1}	200	91 μg $kg^{-1}{}_{biotaww}$	9.4 L kg^{-1}	BMF1: 1	9.7 μg L^{-1} ($QS_{fw,biota,hh}$)	[22,37]
		TDI: 1.5 μg $kg^{-1}{}_{bw}$ d^{-1}			BMF2: 5	1.9 μg L^{-1} ($QS_{sw,biota,hh}$)	
PFBA							
MAC-EQS	*Brachionus calyciflorus* 24 h LC50: 110 mg L^{-1}	100 (fw)				1100 μg L^{-1} (fw)	[8]
		1000 (sw)				110 μg L^{-1} (sw)	
AA-QS	*Brachionus calyciflorus* 24 h LC50: 110 mg L^{-1}	1000 (fw)				110 μg L^{-1} (fw)	[8]
		10000 (sw)				11 μg L^{-1} (sw)	
$QS_{biota,secpois}$	NOAEL(rat): 6 mg $kg^{-1}{}_{bw}$ d^{-1}	300	200[a] μg $kg^{-1}{}_{biotaww}$				[32]
	bw/DFI: 10 kg_{bw} d kg^{-1}						
	NOEC: 60 mg kg^{-1}						
PFPeA							
MAC-EQS	*Pimephales promelas* 96 h LC50: 31.8 mg L^{-1}	10 (fw)				3180 μg L^{-1} (fw)	[9]
		100 (sw)				318 μg L^{-1} (sw)	
AA-QS	*Pimephales promelas* 96 h LC50: 31.8 mg L^{-1}	1000 (fw)				32 μg L^{-1} (fw)	[9]
		10000 (sw)				3.2 μg L^{-1} (sw)	
PFHxA							
$QS_{biota,secpois}$	NOAEL(rat): 20 mg $kg^{-1}{}_{bw}$ d^{-1}	90	4444[a] μg $kg^{-1}{}_{biotaww}$				[33]
	bw/DFI: 20 kg_{bw} d kg^{-1}						
	NOEC: 400 mg kg^{-1}						
PFBS							
MAC-EQS	*Mysidopsis bahia* 96 h EC50: 372 mg L^{-1}	100 (fw)				3720 μg L^{-1} (fw)	[10]
		1000 (sw)				372 μg L^{-1} (sw)	
AA-QS	*Mysidopsis bahia* 96 h EC50: 372 mg L^{-1}	1000 (fw)				372 μg L^{-1} (fw)	[10]
		10000 (sw)				37 μg L^{-1} (sw)	
$QS_{biota,secpois}$	NOAEL(rat): 60 mg $kg^{-1}{}_{bw}$ d^{-1}	90	13333[a] μg $kg^{-1}{}_{biotaww}$				[34]
	bw/DFI: 20 kg_{bw} d kg^{-1}						
	NOEC: 1200 mg kg^{-1}						

[a] just as Quality Criteria (QC).

Please cite this article in press as: S. Valsecchi, et al., Deriving environmental quality standards for perfluorooctanoic acid (PFOA) and related short chain perfluorinated alkyl acids, J. Hazard. Mater. (2016), http://dx.doi.org/10.1016/j.jhazmat.2016.04.055

G Model
HAZMAT-17663; No. of Pages 15
ARTICLE IN PRESS

data of saltwater aquatic organisms are available, therefore the hazard assessment is based on the freshwater toxicological data. Although chronic data are available for a number of species, the range of taxonomic groups covered is insufficient to enable the use of SSD, and the assessment factor approach is therefore used to derive the AA-QS.

The most sensitive species in acute tests (the marine fish *Psetta maxima*) has not an L(E)C50 value lower than the lowest long term value (e.g. EC10 or NOEC) and long-term toxicity data for species from three trophic levels of the base set (algae, crustacean and fish) are available. In such a case an assessment factor of 10 is applied to the lowest long-term concentration (TGD-EQS).

The lowest chronic toxicological value, from the long-term toxicity dataset, has been reported for a mesocosm study on fish *Pimephales promelas* (39d NOEC 0.3 mg L^{-1}) [11]. When there is only a single model ecosystem study, as in this case, an assessment factor of 5 is recommended (TGD-EQS). Moreover as effects are seen on male plasma concentrations, and it is uncertain which might be the effect on population, a AF of 2 was further applied. Applying the resulting AF of 10 to the NOEC of 0.3 mg L^{-1}, an AA-QS for the freshwater environment of 0.030 mg L^{-1} is obtained (Table 5).

According to TGD-EQS, no additional chronic toxicological data for saltwater aquatic organisms are available and therefore the $QS_{sw,eco}$ can be derived by using the freshwater toxicological data with an extra assessment factor of 10 (TGD-EQS), obtaining an AA-QS for the saltwater environment of 0.003 mg L^{-1} (Table 5).

3.2.4. AA-QSwater, eco for SC-PFAA

When only short-term toxicity data are available for at least algae, invertebrates and fish, as in the case of PFBA and PFPeA, an assessment factor of 1000 is applied to the lowest L(E)C50 value of the relevant data (TGD-EQS). The relevant L(E)C50 values are the same as those used to derive MAC-QS (Table 2) and the application of a AF = 1000 results in the following AA-$QS_{fw,eco}$: 0.11 mg L^{-1} for PFBA and 0.32 mg L^{-1} for PFPeA in freshwater (Table 5). Because insufficient data are available for additional marine taxonomic groups, an additional factor of 10 is applied, giving an AA-$QS_{sw,eco}$ of 0.011 mg L^{-1} for PFBA, of 0.032 mg L^{-1} for PFPeA and 0.14 mg L^{-1} for PFHxA in saltwater environments (Table 5). For PFHxA insufficient data cannot support a robust standard derivation.

In the case of PFBS, one chronic toxicity value is available in a study on reproduction of the freshwater invertebrate *Daphnia magna* [10] (Table 4). However the algal growth inhibition test of the acute base set (Table 3) is, in principle, a multigeneration test and the NOEC from this test may be used as an additional NOEC to support long term NOECs of species of a further trophic level (TGD-EQS). Including the NOEC for the study on algae inhibition, the log-term toxicity dataset for PFBS comprises two taxonomic groups (algae and crustacean) and the lowest reliable chronic toxicity study from the available dataset for PFBS is a reproduction study on the freshwater invertebrate *Daphnia magna* (21d NOEC 502 mg L^{-1}) [10]. But this NOEC is higher than the lowest acute effect concentration (96 h EC50 372 mg L^{-1} for *Mysidopsis bahia*) [10]. In such cases the QS might be derived by using an assessment factor of 100 to the lowest L(E)C50 of the short-term tests: the derived AA-$QS_{water,eco}$ would result equal to the calculated MAC-$QS_{water,eco}$, so an AF of 1000 is preferred (TGD-EQS). By applying the latter AF to EC50 of 372 mg L^{-1} for *Mysidopsis bahia*, an AA-QS for the freshwater environment of 0.372 mg L^{-1} is derived (Table 5). No long-term toxicity data is available for additional marine taxonomic group and therefore an additional factor of 10 is applied, giving an AA-$QS_{sw,eco}$ of 0.037 mg L^{-1} (Table 5).

3.3. Derivation of QS to protect benthic (sediment dwelling) species

According to TGD-EQS, the general criteria for triggering the development of a $QS_{sediment}$ include log K_{oc} and log K_{ow} properties, toxicity to benthic organisms and evidence of accumulation in sediment.

As many perfluorocarboxylic acids are hydrophobic and lipophobic at the same time, they tend to form three immiscible layers when they are added to an octanol-water system. Thus, it is impossible to directly determine their K_{ow} values using 'regular' methods that are common for organic chemicals[12]. Experimental K_{ow} and K_{oc} data for perfluorocarboxylic acids are therefore scarce [13] and values should have to be calculated by models, even if none of them (e.g., EPISuite) have training sets that include this class of substances. Furthermore, the concept of K_{ow} for PFAA has essentially no meaning or use in an environmental context since in the range of relevant environmental pH values most of the PFAAs will exist as the dissociated anion and not the neutral form of the substance.

No data on the toxicity of any PFAA on sediment dwelling organisms are available and therefore it is not possible to determine whether any PFAA has a toxic impact on benthic organisms.

The final criterion relates to evidence of accumulation in sediments. $K_{sed-water}$ values of all compounds of interest are lower than those measured for legacy POPs such as chlorinated pesticides and are very variable depending on the sediment characteristics (SM1–SM5). Also concentrations data on sediment are very variable depending on the environment, the sediment characteristics and the site-specific pollutant pressures.

3.3.1. $QS_{sediment}$ PFOA

Experimental K_{ow} data for PFOA are reported in [13]. Log K_{ow}s for PFOA, ranging from 4.30 to 6.30 [7,14,15], fulfil the criteria for triggering a $QS_{sediment}$ according to TGD-EQS. Reported log K_{oc} values range from 1.9 to 4. The upper limit value, which overcomes the threshold of 3 recommended by the TGD-EQS, has been obtained in a bank filtration experiment with a sandy sediment which is not really representative of the river bed sediment. Nevertheless the use of log K_{oc} as the key parameter of the adsorption mechanism could not be valid for this substance: in fact the sorption of PFOA at near neutral pH is controlled by the electrostatic sorption on ferric oxide minerals, and not by the sorption to organic carbon [16].

From PFOA dossier (SM1), maximum concentration (7 ng g^{-1} dw) in European freshwater sediments was measured downstream a fluoropolymer plant. Transitional sediments reached 48 ng g^{-1} dw in some estuarial zones, but freshwater and coastal sediments were generally <1 ng g^{-1} dw. From these data we can conclude that the accumulation of PFOA in sediment is limited. Nevertheless, based on the above it is felt that insufficient information is available to support a decision to derive a $QS_{sediment}$ for PFOA.

3.3.2. $QS_{sediment}$ SC-PFAA

The criteria for triggering a $QS_{sediment}$ (log K_{ow} >3) is only partially fulfilled for the SC-PFAA under study. Experimental and modelled log K_{ow}s are variable and range from −0.52 to 2.82 for PFBA, from 0.09 to 3.43 for PFPeA, from 0.70 to 4.37 for PFHxA and from 2.41 to 3.90 for PFBS [7,14,15]. Log K_{oc}s, calculated by EPISuite, are 1.8 for PFBA, 2.4 for PFPeA, 3.1 for PFHxA, and 2.3 for PFBS, while experimental log K_{oc}s are generally <3, a part from some out of range values derived in a single field experiment [17]. Limited accumulation has been measured in freshwater and coastal sediments (0.1-61.2 ng g^{-1} dw for PFBA, <1 ng g^{-1} dw for PFPeA and PFHxA and <1 to 3.5 ng g^{-1} dw), except in a very impacted Chinese lake [18]. Field measured $K_{sed-water}$ values are too variable (0.004–214 for PFBA, 0.04–251 for PFPeA, 0.66–316 for PFHxA and

Please cite this article in press as: S. Valsecchi, et al., Deriving environmental quality standards for perfluorooctanoic acid (PFOA) and related short chain perfluorinated alkyl acids, J. Hazard. Mater. (2016), http://dx.doi.org/10.1016/j.jhazmat.2016.04.055

G Model
HAZMAT-17663; No. of Pages 15
ARTICLE IN PRESS

0.07–759 for PFBS), depending on the sediment characteristics, to infer a definitive conclusion on those compounds.

Based on the above data we can conclude that for PFBA, PFPeA and PFBS there is no need for a $QS_{sediment}$, while for PFHxA the need for a $QS_{sediment}$ is uncertain but insufficient data are anyway available to derive such a threshold.

3.4. Derivation of QS for secondary poisoning ($QS_{biota,secpois}$)

The derivation of a biota standard for the protection of predators from secondary poisoning is triggered by the possibility of accumulation in the food chain in conjunction with hazard properties of the chemical of interest. A biomagnification factor (BMF) >1 or a bioconcentration factor (BCF) $\geq$100 L kg^{-1} is used as indicators of the bioaccumulation potential (TGD-EQS). However, these criteria apply to lipophilic, hydrophobic substances. But perfluorinated compounds do not actually behave as lipophilic compounds that accumulate in fat tissues and this approach should be considered precautionary.

According to TGD-EQS the biota-based QS for secondary poisoning is calculated separately for the freshwater and saltwater environment. The $QS_{biota,secpois,fw}$ is derived using the lowest toxicity value for birds or mammals (TOX_{oral} = NOEC) with the appropriate assessment factor, while for the $QS_{biota,secpois,sw}$ the toxicity value should also be divided by the appropriate biomagnification factor (BMF2) to account for an additional trophic level. In some cases, such as e.g. to compare it with other water column standards, select the overall EQS, or fit in with national monitoring regimes that use only water sampling, it can be important to convert the biota standard ($\mu g \cdot kg^{-1}{}_{diet}$) into a water column concentration standard by the application of the appropriate BCF and BMF1 (TGD-EQS).

3.4.1. $QS_{biota,secpois}$ PFOA

Few BCF values are available for PFOA; they have been estimated both for specific fish organs/tissues, such as e.g. blood, liver, and for the whole organism in the case of fish and bivalves. BCFs for whole organisms are <10 L kg^{-1}. Indeed the highest BCF for whole fish (9.4 L $kg^{-1}{}_{ww}$) was calculated for common carp (*Cyprinus carpio* L.) exposed to PFOA in a bioconcentration test according to OECD test guideline 305 in a flow-through fish test [19]. Additionally BMF <1 were reported for PFOA in freshwater fish in laboratory and field biomagnification studies and few and highly variable BMF values were calculated for fish predators in seawater food web (0.6, 7.2 and 31) (SM1). Therefore the numeric criterion as suggested for derivation of a $QS_{biota,secpois}$ is not fulfilled for PFOA. However, PFOA concentrations are generally high in target tissues such as blood or liver (e.g. up to 870 $\mu g\,L^{-1}$ in turtle serum and 84.63 ng g^{-1} in eel liver). Due to its notable water solubility, PFOA is probably quickly excreted via gill permeation and indeed field studies showed that air-breathing organisms are more likely to biomagnify PFOA than the water breathing organisms [20]. Based on the above considerations PFOA has been classified bioaccumulative under REACH by unanimous agreement between EU Member States in July 2013 [21] and, consequently, a secondary poisoning assessment for PFOA was carried out.

The available toxicity data for PFOA were collated and reviewed by a number of organizations, such as Organisation for European Economic Co-operation (OECD) [11], European Food Safety Authority (EFSA) [22] and Environment Canada [23]. Toxicological studies with PFOA include subchronic, developmental/reproductive, and chronic toxicity/carcinogenicity tests in several animal species, in both sexes. Mammalian and avian toxicity studies are reported in Material Table SM9 (references in SM10). Both LOAEL and NOAEL values are tabulated. Three studies in mice showed the highest sensitivity for PFOA, all reporting LOAEL values of 0.01 mg kg_{bw}^{-1} d^{-1} [24,25]. Hines et al. [24] administered APFO to CD-1 mice for 17 d of pregnancy. The lowest exposure level (0.01 mg kg_{bw}^{-1} d^{-1}) significantly increased body weight and serum insulin and leptin in mid-life after developmental exposure. To investigate the low-dose effects of PFOA on offspring, timed-pregnant CD-1 mice were gavage dosed with APFO for half of gestation [25]. At postnatal d 21 the lowest dose at which mammary gland developmental abnormalities were visible in the pups was 0.01 mg kg_{bw}^{-1} d^{-1}. Absolute and relative uterine weights were significantly increased in female offspring of CD-1 dams gavage dosed with 0.01 mg APFO kg_{bw}^{-1} d^{-1} from postnatal d 18 to 20 [26].

The LOAEL of 0.01 mg kg_{bw}^{-1} d^{-1} is therefore used as the basis for the derivation of the $QS_{biota,secpois}$ for PFOA. It is converted, using the conversion factor (bw/DFI) of 8.3 kg_{bw} d kg^{-1} taken from the REACH guidance and included in the TGD-EQS [1], to a no observed effect concentration (NOEC) of 0.083 mg kg^{-1}. Because the selected NOEC value was reported in developmental studies a value of 90 is selected as appropriate assessment factors (AF_{oral}) for the extrapolation of mammalian toxicity data into $QS_{biota,secpois}$ (TGD-EQS).

All available BMFs, collected in wide reviews on PFOA [20], [27,28], are below 1 (0.02–0.63) both in laboratory and field biomagnification studies. However, there are evidences that bioaccumulation in field can occur both in freshwater fish and in organisms at lower trophic levels (BAF ranging from 0.9 to 1585 L kg^{-1}; median 14.0 L kg^{-1}, SM1), suggesting that also the diet contributes to the PFOA accumulation in organisms. Therefore an upper limit value of 1 for BMF1 is chosen.

Few and highly variable BMFs were calculated for fish predators in seawater food web (0.6, 7.2 and 31). However clear biomagnification of PFOA was shown for bottlenose dolphins and polar bears ([20] and references herein). Because of the uncertainties associated with the data available in relation to BMF2 and the frequent detection of PFOA in top predators of seawater food web, a value of 5 is proposed for BMF2.

Concluding, to derive QS based on secondary poisoning of predators in freshwater or saltwater compartments, a TOX_{oral} value of 0.083 mg kg^{-1}, an AF_{oral} value of 90 and a BMF2 value of 5 are used according to TGD-EQS (Eqs. 1 and 2 of SM10). The obtained $QS_{biota,secpois}$ are 0.9 and 0.18 $\mu g\,kg^{-1}{}_{biotaww}$ for fresh- and saltwater respectively (Table 5). These biota standards are converted into an equivalent water concentration using the highest BCF (9.4 L $kg^{-1}{}_{ww}$) found in literature and a BMF1 of 1 according to TGD-EQS (Eqs. 3 and 4 of SM10). This gives a $QS_{fw,secpois}$ of 0.1 $\mu g\,L^{-1}$ and a $QS_{sw,secpois}$ of 0.02 $\mu g\,L^{-1}$ (Table 5).

3.4.2. $QS_{biota,secpois}$ SC-PFAA

The BCF modelled for all examined SC-PFAAs are <10 L kg^{-1} (3.162 L kg^{-1}; BCFWIN v2.17, EPI Suite) and the few field BAF values are, generally, <10 L kg^{-1} (SM2–SM5).

No BCF, BMF1 and BMF2 from laboratory and field studies are available for PFBA. In the case of PFPeA the BCF calculated in a laboratory study with rainbow trout [29] is insignificant and the single BMF value extrapolated with the same species is <0.1 [30]. Concentrations in biota are generally low, ranging from <LOQ to less than 10 ng $g^{-1}{}_{ww}$. Maximum concentrations of 7.62 ng $g^{-1}{}_{ww}$ for PFBA and 9.69 ng $g^{-1}{}_{ww}$ for PFPeA were measured in duckweed and in freshwater fish respectively [17,18].

Also for PFHxA and PFBS the BCF calculated in laboratory studies (rainbow trout for PFHxA [29] and Bluegill sunfish [10]) are <1 L kg^{-1} and the BMFs calculated for PFHxA and PFBS for rainbow trout are «1 [29]. Furthermore monitoring data evidence that occurrence of PFBS and PFHxA in biota is limited with concentrations generally <LOQ and maximum concentrations of 10.8 and 31.4 ng g^{-1} ww respectively [18,31]. Nevertheless the few bioaccumulation data available are highly variable with BAF values ranging from 5.0 to 9 L kg^{-1},120 L kg^{-1} measured in freshwater snails for

Please cite this article in press as: S. Valsecchi, et al., Deriving environmental quality standards for perfluorooctanoic acid (PFOA) and related short chain perfluorinated alkyl acids, J. Hazard. Mater. (2016), http://dx.doi.org/10.1016/j.jhazmat.2016.04.055

G Model
HAZMAT-17663; No. of Pages 15
ARTICLE IN PRESS

PFHxA [31] and from 0.3 to 1736 L kg^{-1} in a freshwater fish for PFBS [17].

Based on the above evidences, PFBA and PFPeA can be considered not bioaccumulable or biomagnificable in the aquatic food web, whereas there is still uncertainty on the bioaccumulation and biomagnification characteristics of PFHxA and PFBS which requires further monitoring data. As a result the requirements to derive $QS_{biota,secpois}$ are not met for these compounds.

Few toxicity studies on mammalian diet and oral exposure are reported for PFBA, PFHxA and PFBS while only one toxicity study for PFPeA has been retrieved (Tables SM9, with references in SM10). Though the number of studies is anyway insufficient to derive a reliable $QS_{biota,secpois}$, we used the lowest NOAEL/LOAEL available to derive Quality Criteria (QC) for freshwater compartment for PFBA, PFHxA and PFBS in order to derive information on the hazard for top predators.

Oral toxicity studies in male rats with ammonium perfluorobutanoate (NH4 + PFBA) showed effects in males such as increased liver weight, slight to minimal hepatocellular hypertrophy; decreased serum total cholesterol; and reduced serum thyroxin with no change in serum thyrotropin [32]. NOAELs were 6 mg kg_{bw}^{-1} d^{-1} for male both in the 28-d and in the 90-d study. This lowest reported NOAEL is converted to an $NOEC_{oral}$ using an bw/DFI of 10 kg_{bw} d kg^{-1} (TGD-EQS). For this short-term test an AF_{oral} of 300 has been applied (TGD-EQS) resulting in a $QC_{biota,secpois,fw}$ for PFBA of 200 μg $kg^{-1}{}_{biotaww}$ (Table 5).

The lowest NOAEL for PFHxA was measured by Loveless et al. [33] in 90-d subchronic toxicity studies with rats. In the study sodium perfluorohexanoate was administered daily to male Crl:CD(SD) rats for approximately 90 d by gavage. The NOAEL was 20 mg kg_{bw}^{-1} d^{-1} based on nasal lesions. This NOAEL for rat is converted by a bw/DFI of 20 kg_{bw} d kg^{-1} (TGD-EQS), giving a $NOEC_{oral}$ of 400 mg kg^{-1}. A $QC_{biota,secpois,fw}$ of 4444 μg $kg^{-1}{}_{biotaww}$ is derived by applying an AF_{oral} of 90 to this $NOEC_{oral}$ (Table 5).

For PFBS similar NOAEL were calculated in subchronic and reproductive studies. A NOAEL of 60 mg kg_{bw}^{-1} d^{-1} based on hematological effects [34] was calculated in a 90-d rat oral gavage study and a NOAEL of 100 mg kg_{bw}^{-1} d^{-1} was extrapolated in P and F1 generation based on general toxicity (increased liver weight, microscopic changes in liver and kidney) [10,35]. A $NOEC_{oral}$ of 1200 mg kg^{-1} is calculated by applying a bw/DFI of 20 kg_{bw} d kg^{-1} for rats to the lowest reported NOAEL of 60 mg kg_{bw}^{-1} d^{-1}. An AF_{oral} of 90 has been applied to this $NOEC_{oral}$, resulting in a $QC_{biota,secpois,fw}$ of 13,333 μg $kg^{-1}{}_{biotaww}$ (Table 5).

3.5. Derivation of QS to protect human health

For humans, the derivation of a biota standard is triggered by the hazardous properties of the chemical of interest. Effects on reproduction, fertility and development are of particular concern since these are long-term effects which could impact on organism populations. Acceptable daily intake (ADI) or tolerable daily intake (TDI) or available mammalian toxicology data are used to assess possible risks to humans.

3.5.1. Human health via consumption of fishery products ($QS_{biota,hh}$)

PFOA has been recently classified as a known or suspected carcinogen (R40) and as a substance known or suspected to affect reproduction (R61) [36], so PFOA meets the criteria to derive QSs to protect human health.

A tolerable daily intake (TDI) of 1.5 μg kg_{bw}^{-1} d^{-1} was proposed by EFSA [22]. The TDI was determined by applying an uncertainty factor of 200 to the BMDL10 of 300 μg kg_{bw}^{-1} d^{-1} [37]. The chosen BMDL10 is the lowest one among a number of studies in mice and male rats looking at the effects on the liver. The overall uncertainty factor of 200 is obtained by multiplying a factor of 100, which takes into account the inter and intra-species differences, with an additional factor of 2, which compensates for uncertainties relating to the internal dose kinetics.

The EFSA's TDI is chosen as human relevant threshold level (TL_{hh}) for PFOA and the $QS_{biota,hh}$ of 91 μg $kg^{-1}{}_{biotaww}$ is calculated (Table 5) using equation 5 reported in SM10. To set the overall EQS, this biota standard is converted to the equivalent water concentration applying a BCF of 9.4 L kg^{-1} and the BMF1 and BMF2 values of 1 and 5, respectively, as discussed above. Inserting these values in equations 6 and 7 reported in SM10, $QS_{fw,hh}$ of 9.7 μg L^{-1} and $QS_{sw,hh}$ of 1.9 μg L^{-1} are derived (Table 5).

No ADI or TDI is available for the other SC-PFAAs and very few toxicity studies on mammalian diet and oral exposure, reporting LOAEL and NOAEL, are available (Tables SM9, with references in SM10). Thereby, at the current state of knowledge, there are insufficient toxicological data to classify SC-PFAAs and derive a $QS_{biota,hh}$ according to the TGD-EQS criteria.

3.5.2. Human health via consumption of drinking water ($QS_{dw,hh}$)

In addition to potential exposure through the consumption of fishery products, a second route for human exposure to substances in water is through drinking water. In principle, existing drinking water standards are adopted, e.g. EU, World Health Organization (WHO) drinking water standards. A treatment factor should be applied to the drinking water standard so that the $QS_{dw,hh}$ relates to the 'raw' water (i.e. it is an 'environmental' standard), before the treatment step. However, since the removal efficiency of the current techniques employed in the drinking water production is generally low and uncertain in the cases of PFOA and SC-PFAA [38], the proposed drinking water standards (QS_{dw}) are considered appropriate for setting $QS_{dw,hh}$ without further correction.

Though thresholds for PFOA and SC-PFAAs in drinking water have been proposed by some countries, no thresholds have been derived by either EU or WHO. Under these circumstances the TGD-EQS notes that a provisional drinking water standard should be derived using ADI, TDI or the lowest available mammalian toxicology data and Eq. 8 of SM10. TDI (1.5 μg kg_{bw}^{-1} d^{-1}), proposed by EFSA [22], is available only for PFOA and by choosing it as TL_{hh} a QS_{dw} of 5.25 μg L^{-1} is derived. However, because the *long term minimum quality goal* proposed by Italian Institute of Health (0.5 μg L^{-1}) [39] is lower than that one calculated from TDI. QS_{dw}, 0.5 μg L^{-1} is then used as $QS_{dw,hh}$ for PFOA.

For the other SC-PFAAs no ADI or TDI are available and few toxicity studies on mammalian diet and oral exposure are reported (Tables SM9, with references in SM10). At the current state of knowledge, toxicological data are insufficient to derive a standard for drinking water and we used the lowest available national thresholds as the value for $QS_{dw,hh}$.

For PFBA, thresholds in drinking water have been proposed by Germany [40,41] and State of Minnesota, USA [42]. The latter state established a threshold for groundwater of 7 μg L^{-1} as short-term, chronic and sub-chronic Non-Cancer Health Risk Limits and Germany stated a health-related indication value of 7 μg L^{-1} which is used as $QS_{dw,hh}$. For the remaining compounds, the minimum health-related indication values proposed by Germany [41], 3 μg L^{-1} for PFPeA, 1 μg L^{-1} for PFHxA and 3 μg L^{-1} for PFBS, have been set as $QS_{dw,hh}$.

Please cite this article in press as: S. Valsecchi, et al., Deriving environmental quality standards for perfluorooctanoic acid (PFOA) and related short chain perfluorinated alkyl acids, J. Hazard. Mater. (2016), http://dx.doi.org/10.1016/j.jhazmat.2016.04.055

G Model
HAZMAT-17663; No. of Pages 15
ARTICLE IN PRESS

Table 6
Summary of the derived QSs for the different protection objectives. fw = freshwater; sw = saltwater (marine, coastal and transitional waters).

Protection objective	Unit	PFOA	PFBA	PFPeA	PFHxA	PFBS
$AA\text{-}QS_{fw,eco}$ Pelagic community (fw)	[$\mu g\,L^{-1}$]	30	110	32	insufficient data	372
$AA\text{-}QS_{sw,eco}$ Pelagic community (sw)	[$\mu g\,L^{-1}$]	3	11	3.2	insufficient data	37
$QS_{sed,fw}$ Benthic community (fw)	[$\mu g\,kg^{-1}{}_{dw}$]	insufficient data	not required	not required	insufficient data	not required
$QS_{sed,sw}$ Benthic community (sw)	[$\mu g\,kg^{-1}{}_{dw}$]	insufficient data	not required	not required	insufficient data	not required
$QS_{biota,secpois}$ Predators (secondary poisoning)	[$\mu g\,kg^{-1}{}_{biotaww}$]	0.9	not required	not required	not possible to assess if bioaccumulable	not possible to assess if bioaccumulable
	[$\mu g\,L^{-1}$]	0.1 (fw) 0.02 (sw)	– –	– –	– –	– –
$QS_{biota,hh}$ Human health via consumption of fishery products	[$\mu g\,kg^{-1}{}_{biotaww}$]	91	insufficient data	insufficient data	insufficient data	insufficient data
	[$\mu g\,L^{-1}$]	9.7 (fw) 1.9 (sw)	– –	– –	– –	– –
$QS_{dw,hh}$ Human health via consumption of water	[$\mu g\,L^{-1}$]	0.5	7	3	1	3

4. Conclusions: selecting an overall environmental quality standard and environmental risk assessment

QS for water, sediment and biota are derived in the present study for the different protection goals for each examinated PFAS are summarised in Table 6.

$QS_{fw,eco}$ derived from acute and chronic ecotoxicological studies range from 30 $\mu g\,L^{-1}$ for PFOA to 372 $\mu g\,L^{-1}$ for PFBS. Even if, in some cases $QS_{water,\ eco}$ are based on a limited dataset which should be integrated with further studies, nevertheless we may conclude that examined PFAAs have limited toxicity for freshwater and marine organisms.

For compounds with carbon chain <C6 it is not possible to derive a QS for sediments because they do not accumulate in sediment and data are lacking. In other cases (≥C6) it is not possible deriving sediment EQS because data on toxicity on benthic community are lacking.

$QS_{biota,secpois}$ for protection of predators from secondary poisoning have been derived only for PFOA (0.9 $\mu g\,g^{-1}$ ww) and PFBS (13,333 $\mu g\,g^{-1}$ ww), while for PFBA and PFHxA only quality criteria values have been calculated, because of the data lacking. It was possible to derive a $QS_{biota,hh}$ for the protection of human health via consumption of fishery products only for PFOA, but the derived value (91 $\mu g\,g^{-1}$ ww) was 100-fold higher than $QS_{biota,secpois}$. All the QS_{biota} for PFOA have then been back-calculated to water obtaining quality standards expressed in water concentrations.

According to the TGD-EQS, the lowest QS calculated for the different objectives of protection will normally be adopted as the overall quality standard (EQS) for the different aquatic compartments.

For all the compounds, except PFOA, $QS_{dw,hh}$, derived from the drinking water threshold values, are the lowest QS (Table 6). In this case, TGD-EQS warns that $QS_{dw,hh}$ can be adopted as the lowest QS_{water} only for water bodies intended for drinking water use. Italian government decided to adopt $QS_{dw,hh}$ as national overall EQS because most of the water bodies impacted by PFAA pollution are intended for human consumption.

For PFOA the most stringent QS is that related to the protection of predators from secondary poisoning (0.1 $\mu g\,L^{-1}$ for freshwater and 0.02 $\mu g\,L^{-1}$ for saltwater) and it is adopted as EQS (Table 7).

In order to assess the risk connected with the presence of these compounds in the aquatic environment, quality standards may be compared with the occurrence levels, which are collected in the substance dossiers (SM1–SM5).

For all the compounds MAC-EQS are in the order of thousands $\mu g\,L^{-1}$ for freshwaters and hundreds $\mu g\,L^{-1}$ for saltwaters (Table 7) and these levels never occurred in the natural environments, but have been measured for PFOA and PFBS only in the discharge of a fluorochemical factory [43] (see also SM1 and SM5).

Short chain perfluorocarboxylic acids (PFBA, PFPeA and PFHxA) never reach environmental concentrations comparable to proposed EQSs which are in the order of thousands ng L^{-1} for freshwaters (Table 7, SM2–SM4). In the case of PFBS thousands ng L^{-1} were determined only in an Italian river basin directly impacted by a fluorochemical plant [3,43], but concentrations up to 200–400 ng L^{-1} were sometimes measured in rivers in Northern Europe and China (SM5).

EQS_{fw} for PFOA, based on the protection from secondary poisoning, (100 ng L^{-1}) is a more critical threshold which is more often overcome in many surface water bodies. In Italy, for example, where fluorochemical and fluoropolymer plants are present, 90° percentile of concentrations in 35 rivers was 974 ng L^{-1}, with a median of 22 ng L^{-1} [4], while in 121 European rivers a maximun of 174 ng L^{-1} and a 90° percentile of 26 ng L^{-1} were measured [44]. According to the EQS_{fw}, some rivers in Europe can be at risk for PFOA, while only some transitional environments, such as the lagoons in the Po Delta, presented PFOA concentrations close to the EQS_{sw} (20 ng L^{-1}).

EQS for biota have been derived only for PFOA (900 ng g^{-1} for freshwater and 180 ng g^{-1} for saltwater, Table 7), but these concentrations are much higher than those ever measured in whole body or muscle of any fish or mollusks (SM1). Nevertheless it is to be underlined that these levels were measured in target organs and tissues such as liver and serum (SM1).

Please cite this article in press as: S. Valsecchi, et al., Deriving environmental quality standards for perfluorooctanoic acid (PFOA) and related short chain perfluorinated alkyl acids, J. Hazard. Mater. (2016), http://dx.doi.org/10.1016/j.jhazmat.2016.04.055

Table 7
Summary of the proposed Annual Average–EQS (AA-EQS) and Maximum Acceptable Concentration-EQS (MAC-EQS).

	PFOA	PFBA	PFPeA	PFHxA	PFBS
AA-EQS$_{fw}$ [freshwater] [$\mu g\,L^{-1}$]	0.1	7	3	1	3
AA-EQS$_{sw}$ [marine waters] [$\mu g\,L^{-1}$]	0.02	–	–	–	–
AA-EQS$_{biota,fw}$ biota [$\mu g\,kg^{-1}{}_{biotaww}$]	0.9	–	–	–	–
AA-EQS$_{biota,sw}$ biota [$\mu g\,kg^{-1}{}_{biotaww}$]	0.18	–	–	–	–
MAC-EQS$_{fw}$ [freshwater] [$\mu g\,L^{-1}$]	2220	1100	3200	–	3720
MAC-EQS$_{sw}$ [marine waters] [$\mu g\,L^{-1}$]	450	110	320	–	372

In conclusions PFAS with carbon chain ≤C6, due to their low bioaccumulative potential and low acute and chronic aquatic toxicity, do not seem to be a direct concern for aquatic environment. On the contrary, though PFOA shows a low toxicity, because it biomagnifies in air-breathing organisms and is very persistent, it accumulates in target organs even if it is present at moderate concentrations in water.

Acknowledgements

This paper is based on the outcome of the Italian Working Group for EQS in water, coordinated by IRSA-CNR. The work has been partially funded by the Italian Ministry for the Protection of Environment, Territory and Sea, MATTM (Divisione V) within the project "Valutazione del Rischio Ambientale e Sanitario associato alla contaminazione da sostanze perfluoro-alchiliche (PFAS) nel Bacino del Po e nei principali bacini fluviali italiani".

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.jhazmat.2016.04.055.

References

[1] EC, European Commision Guidance Document No. 27, Technical Guidance For Deriving Environmental Quality Standards, Technical Report—2011-055 in 2011.
[2] S. Castiglioni, S. Valsecchi, S. Polesello, M. Rusconi, M. Melis, M. Palmiotto, A. Manenti, E. Davoli, E. Zuccato, Sources and fate of perfluorinated compounds in the aqueous environment and in drinking water of a highly urbanized and industrialized area in Italy, J. Hazard. Mater. 282 (2015) 51–60.
[3] S. Valsecchi, M. Rusconi, M. Mazzoni, G. Viviano, R. Pagnotta, C. Zaghi, G. Serrini, S. Polesello, Occurrence and sources of perfluoroalkyl acids in Italian river basins, Chemosphere 129 (2015) 126–134.
[4] M. Mazzoni, S. Polesello, M. Rusconi, S. Valsecchi, Investigating the occurrence of C8-based perfluorinated substitutes in Italian waters, Norman Bulletin, Issue 4, March 2015.
[5] H.-J. Klimisch, M. Andreae, U. Tillmann, A systematic approach for evaluating the quality of experimental toxicological and ecotoxicological data, Regul. Toxicol. Pharmacol. 25 (1997) 1–5.
[6] USEPA, SSD: Species Sensitivity Distribution Generator V1-12 (downloaded inoctober 2014) in 2014.
[7] T. Wang, Z. Lin, D. Yin, D. Tian, Y. Zhang, D. Kong, Hydrophobicity-dependent QSARs to predict the toxicity of perfluorinated carboxylic acids and their mixtures, Environ. Toxicol. Pharmacol. 32 (2011) 259–265.
[8] Y. Wang, J. Niu, L. Zhang, J. Shi, Toxicity assessment of perfluorinated carboxylic acids (PFCAs) towards the rotifer *Brachionus calyciflorus*, Sci. Total Environ. 491-492 (2014) 266–270.
[9] R.A. Hoke, L.D. Bouchelle, B.D. Ferrell, R.C. Buck, Comparative acute freshwater hazard assessment and preliminary PNEC development for eight fluorinated acids, Chemosphere 87 (2012) 725–733.
[10] NICNAS, Australian governement (Department of health and ageing), Potassium perfluorobutane sulfonate, Existing Chemical Hazard Assessment Report, https://www.nicnas.gov.au/_data/assets/pdf_file/0004/4927/Potassium_Perfluorobutane_Sulfonate_PDF.pdf, 2005.
[11] OECD, Substance Information Data-Sheet (SIDS). Assessment Profile for Perfluorooctanoic Acid (PFOA), Ammonium Perfluorooctanoate (APFO), 2006.
[12] J.P. Giesy, J.E. Naile, J.S. Khim, P.D. Jones, J.L. Newsted, Aquatic toxicology of perfluorinated chemicals, Rev. Environ. Contam. Toxicol. 202 (2010) 1–52.
[13] G. Ding, W.J.G.M. Peijnenburg, Physicochemical properties and aquatic toxicity of poly- and perfluorinated compounds, Crit. Rev. Anal. Chem. 43 (2013) 598–678.
[14] H.P.H. Arp, C. Niederee, K.-U. Goss, Predicting the partitioning behavior of various highly fluorinated compounds, Environ. Sci. Technol. 40 (2006) 7298–7304.
[15] Z. Wang, M. MacLeod, I.T. Cousins, M. Scheringer, K. Hungerbühler, Using COSMOtherm to predict physicochemical properties of poly- and perfluorinated alkyl substances (PFASs), Environ. Chem. 8 (2011) 389–398.
[16] M.L. Ferrey, J.T. Wilson, C. Adair, C. Su, D.D. Fine, X. Liu, J.W. Washington, Behavior and fate of PFOA and PFOS in Sandy aquifer sediment, Groundwater Monit. Rem. 32 (2012) 63–71.
[17] J. Campo, F. Perez, A. Masia, Y. Pico, M. Farre, D. Barcelo, Perfluoroalkyl substance contamination of the llobregat river ecosystem (Mediterranean area NE Spain), Sci. Total. Environ. 503-504 (2015) 48–57.
[18] Z. Zhou, Y. Liang, Y. Shi, L. Xu, Y. Cai, Occurrence and transport of perfluoroalkyl acids (PFAAs), including short-chain PFAAs in Tangxun Lake China, Environ. Sci. Technol. 47 (2013) 9249–9257.
[19] Y. Inoue, N. Hashizume, N. Yakata, H. Murakami, Y. Suzuki, E. Kikushima, M. Otsuka, Unique physicochemical properties of perfluorinated compounds and their bioconcentration in common carp *Cyprinus carpio* L, Arch. Environ. Contam. Toxicol. 62 (2012) 672–680.
[20] ECHA, Support Document for Identification of Pentadecafluorooctanoic Acid (PFOA) as a Substance of Very High Concern Because of its CMR[1] and PBT[2] Properties, Member State Commitee, 2013.
[21] ECHA, Support Document for identification of pentadecafluorooctanoic acid (PFOA) as a substance of very high concern because of its CMR and PBT properties, http://echa.europa.eu/candidate-list-table/-/substance/305/search/+/term, 2013.
[22] EFSA, Perfluorooctane sulfonate (PFOS), perfluorooctanoic acid (PFOA) and their salts—Scientific Opinion of the Panel on Contaminants in the Food chain, EFSA J. 653 (2008) 1–131.
[23] Canada, Environment Health. Draft Screening Assessment Perfluorooctanoic Acid, its Salts, and its Precursors, 2010.
[24] E.P. Hines, S.S. White, J.P. Stanko, E.A. Gibbs-Flournoy, C. Lau, S.E. Fenton, Phenotypic dichotomy following developmental exposure to perfluorooctanoic acid (PFOA) in female CD-1 mice: low doses induce elevated serum leptin and insulin, and overweight in mid-life, Mol. Cell. Endocrinol. 304 (2009) 97–105.
[25] M.B. Macon, L.R. Villanueva, K. Tatum-Gibbs, R.D. Zehr, M.J. Strynar, J.P. Stanko, S.S. White, L. Helfant, S.E. Fenton, Prenatal perfluorooctanoic acid exposure in CD-1 mice: low-dose developmental effects and internal dosimetry, Toxicol. Sci. 122 (2011) 134–145.
[26] D. Dixon, C.E. Reed, A.B. Moore, E.A. Gibbs-Flournoy, E.P. Hines, E.A. Wallace, J.P. Stanko, Y. Lu, W.N. Jefferson, R.R. Newbold, S.E. Fenton, Histopathologic changes in the uterus, cervix and vagina of immature CD-1 mice exposed to low doses of perfluorooctanoic acid (PFOA) in a uterotrophic assay, Reprod. Toxicol. 33 (2012) 506–512.
[27] USEPA, Revised Draft Hazard Assessment of Perfluorooctanoic Acid and its Salts, Environmental Protection Agency Office of Pollution Prevention and Toxics Risk Assessment Division, 2002.
[28] Canada, Environment Canada, Health Canada, Screening Assessment Report Perfluorooctanoic Acid, its Salts, and its Precursors, 2012.
[29] J.W. Martin, S.A. Mabury, K.R. Solomon, D.C. Muir, Bioconcentration and tissue distribution of perfluorinated acids in rainbow trout (*Oncorhynchus mykiss*), Environ. Toxicol. Chem. 22 (2003) 196–204.
[30] J.W. Martin, S.A. Mabury, K.R. Solomon, D.C.G. Muir, Dietary accumulation of perfluorinated acids in juvenile rainbow trout (*Oncorhynchus mykiss*), Environ. Toxicol. Chem. 22 (2003) 189–195.
[31] Z. Zhou, Y. Shi, W. Li, L. Xu, Y. Cai, Perfluorinated compounds in surface water and organisms from Baiyangdian Lake in North China: source profiles, bioaccumulation and potential risk, Bull. Environ. Contam. Toxicol. 89 (2012) 519–524.
[32] J.L. Butenhoff, J.A. Bjork, S.C. Chang, D.J. Ehresman, G.A. Parker, K. Das, C. Lau, P.H. Lieder, F.M. van Otterdijk, K.B. Wallace, Toxicological evaluation of ammonium perfluorobutyrate in rats: twenty-eight-day and ninety-day oral gavage studies, Reprod. Toxicol. 33 (2012) 513–530.
[33] S.E. Loveless, B. Slezak, T. Serex, J. Lewis, P. Mukerji, J.C. O'Connor, E.M. Donner, S.R. Frame, S.H. Korzeniowski, R.C. Buck, Toxicological evaluation of sodium perfluorohexanoate, Toxicology 264 (2009) 32–44.
[34] P.H. Lieder, S.C. Chang, R.G. York, J.L. Butenhoff, Toxicological evaluation of potassium perfluorobutanesulfonate in a 90-day oral gavage study with Sprague-Dawley rats, Toxicology 255 (2009) 45–52.

Please cite this article in press as: S. Valsecchi, et al., Deriving environmental quality standards for perfluorooctanoic acid (PFOA) and related short chain perfluorinated alkyl acids, J. Hazard. Mater. (2016), http://dx.doi.org/10.1016/j.jhazmat.2016.04.055

[35] P.H. Lieder, R.G. York, D.C. Hakes, S.C. Chang, J.L. Butenhoff, A two-generation oral gavage reproduction study with potassium perfluorobutanesulfonate (K + PFBS) in Sprague Dawley rats, Toxicology 259 (2009) 33–45.
[36] ECHA, Opinion proposing harmonised classification and labelling at Community level of Perfluorooctanoic acid (PFOA), European Chemicals Agency, Committee for Risk Assessment, ECHA/RAC/DOC No CLH-O-0000002227-78-01/F, 2011.
[37] J.L. Butenhoff, G.L. Kennedy Jr., S.R. Frame, J.C. O'Connor, R.G. York, The reproductive toxicology of ammonium perfluorooctanoate (APFO) in the rat, Toxicology 196 (2004) 95–116.
[38] C. Eschauzier, E. Beerendonk, P. Scholte-Veenendaal, P. De Voogt, Impact of treatment processes on the removal of perfluoroalkyl acids from the drinking water production chain, Environ. Sci. Technol. 46 (2012) 1708–1715.
[39] Veneto-Region, Deliberazione della Giunta Regionale della Regione del Veneto n. 618 del 29 aprile 2014 Approvazione di 'Primi indirizzi operativi per l'utilizzo dei pozzi privati ai Comuni delle Province interessate dalla presenza di sostanze perfluoroalchiliche (PFASs) nelle acque destinate al consumo umano' che prende atto dei livelli di performance indicati dal Ministero della Salute con nota prot. n. 2565-P-DGPRE del 29.01. 2014 e dei limiti fissati dall'EFSA da impiegare fino a nuova e diversa indicazione. (Bur del Veneto n. 52 del 20 maggio 2014). http://bur.regione.veneto.it/BurvServices/pubblica/SommarioSingoloBur.aspx?num=52&date=20%2f05%2f2014.
[40] TWK, Provisional evaluation of PFT in drinking water with the guide substances perfluorooctanoic acid (PFOA) and perfluorooctane sulfonate (PFOS) as examples, Drinking Water Commission of the German Ministry of Health at the Federal Environment Agency, 2006.
[41] M. Wilhelm, S. Bergmann, H.H. Dieter, Occurrence of perfluorinated compounds (PFCs) in drinking water of North Rhine-Westphalia, Germany and new approach to assess drinking water contamination by shorter-chained C4-C7 PFCs, Int. J. Hyg. Environ. Health 213 (2010) 224–232.
[42] US, State of Minnesota Health Risk Limits for Groundwater Adopted: 2011. http://www.health.state.mn.us/divs/eh/risk/rules/water/.
[43] M. Mazzoni, M. Rusconi, S. Valsecchi, C.P.B. Martins, S. Polesello, An on-Line solid phase extraction-Liquid chromatography-tandem mass spectrometry method for the determination of perfluoroalkyl acids in drinking and SurfaceWaters, J. Anal. Methods Chem. (2015) 13.
[44] R. Loos, B.M. Gawlik, G. Locoro, E. Rimaviciute, S. Contini, G. Bidoglio, EU-wide survey of polar organic persistent pollutants in European river waters, Environ. Pollut. 157 (2009) 561–568.
[45] A. Latala, M. Nedzi, P. Stepnowski, Acute toxicity assessment of perfluorinated carboxylic acids towards the Baltic microalgae, Environ. Toxicol. Pharmacol. 28 (2009) 167–171.
[46] I. Rodea-Palomares, F. Leganes, R. Rosal, F. Fernandez-Pinas, Toxicological interactions of perfluorooctane sulfonic acid (PFOS) and perfluorooctanoic acid (PFOA) with selected pollutants, J. Hazard. Mater. 201-202 (2012) 209–218.
[47] I. Colombo, W.d. Wolf, R.S. Thompson, D.G. Farrar, R.A. Hoke, J. L'Haridon, Acute and chronic aquatic toxicity of ammonium perfluorooctanoate (APFO) to freshwater organisms, Ecotoxicol. Environ. Saf. 71 (2008) 749–756.
[48] R. Rosal, I. Rodea-Palomares, K. Boltes, F. Fernandez-Pinas, F. Leganes, A. Petre, Ecotoxicological assessment of surfactants in the aquatic environment: combined toxicity of docusate sodium with chlorinated pollutants, Chemosphere 81 (2010) 288–293.
[49] G. Ding, M. Wouterse, R. Baerselman, W.J. Peijnenburg, Toxicity of polyfluorinated and perfluorinated compounds to lettuce (*Lactuca sativa*) and green algae (*Pseudokirchneriella subcapitata*), Arch. Environ. Contam. Toxicol. 62 (2012) 49–55.
[50] S. Yang, F. Xu, F. Wu, S. Wang, B. Zheng, Development of PFOS and PFOA criteria for the protection of freshwater aquatic life in China, Sci. Total Environ. 470–471 (2014) 677–683.
[51] C. Hu, Q. Luo, Q. Huang, Ecotoxicological effects of perfluorooctanoic acid on freshwater microalgae *Chlamydomonas reinhardtii* and *Scenedesmus obliquus*, Environ. Toxicol. Chem. 33 (2014) 1129–1134.
[52] R. Ji, Y. Kim, S. Oh, B. Ahn, H. Jo, K. Choi, Toxicity of perfluorooctane sulfonic acid and perfluorooctanoic acid on freshwater macroinvertebrates (*Daphnia magna*) and *Moina macropoca*) and fish (*Oryzias latipes*), Environ. Toxicol. Chem. 27 (2008) 2159–2168.
[53] G.H. Ding, T. Fromel, E.J. van den Brandhof, R. Baerselman, W.J. Peijnenburg, Acute toxicity of poly- and perfluorinated compounds to two cladocerans, *Daphnia magna* and *Chydorus sphaericus*, Environ. Toxicol. Chem. 31 (2012) 605–610.
[54] M.H. Li, Toxicity of perfluorooctane sulfonate and perfluorooctanoic acid to plants and aquatic invertebrates, Environ. Toxicol. 24 (2009) 95–101.
[55] L. Zhang, J. Niu, Y. Li, Y. Wang, D. Sun, Evaluating the sub-lethal toxicity of PFOS and PFOA using rotifer *Brachionus calyciflorus*, Environ. Pollut. 180 (2013) 34–40.
[56] M. Ulhaq, G. Carlsson, S. Orn, L. Norrgren, Comparison of developmental toxicity of seven perfluoroalkyl acids to zebrafish embryos, Environ. Toxicol. Pharmacol. 36 (2013) 423–426.
[57] A. Hagenaars, L. Vergauwen, W. De Coen, D. Knapen, Structure-activity relationship assessment of four perfluorinated chemicals using a prolonged zebrafish early life stage test, Chemosphere 82 (2011) 764–772.
[58] E. Mulkiewicz, B. Jastorff, A.C. Skladanowski, K. Kleszczynski, P. Stepnowski, Evaluation of the acute toxicity of perfluorinated carboxylic acids using eukaryotic cell lines, bacteria and enzymatic assays, Environ. Toxicol. Pharmacol. 23 (2007) 279–285.
[59] L. Mhadhbi, D. Rial, S. Perez, R. Beiras, Ecological risk assessment of perfluorooctanoic acid (PFOA) and perfluorooctanesulfonic acid (PFOS) in marine environment using *Isochrysis galbana* Paracentrotus lividus, *Siriella armata* and *Psetta maxima*, J. Environ. Monit. 14 (2012) 1375–1382.
[60] M.L. Hanson, J. Small, P.K. Sibley, T.M. Boudreau, R.A. Brain, S.A. Mabury, K.R. Solomon, Microcosm evaluation of the fate, toxicity, and risk to aquatic macrophytes from perfluorooctanoic acid (PFOA), Arch. Environ. Contam. Toxicol. 49 (2005) 307–316.
[61] M.-H. Li, Chronic effects of perfluorooctane sulfonate and ammonium perfluorooctanoate on biochemical parameters, survival and reproduction of *Daphnia magna*, J. Health Sci. 56 (2010) 104–111.

Please cite this article in press as: S. Valsecchi, et al., Deriving environmental quality standards for perfluorooctanoic acid (PFOA) and related short chain perfluorinated alkyl acids, J. Hazard. Mater. (2016), http://dx.doi.org/10.1016/j.jhazmat.2016.04.055

170230018050