Bioaccumulation assessment of ionisable chemicals

When are experimental BCF values necessary?

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For REACH registrations under Annex IX or higher, experimental studies on the bioaccumulation of substances in aquatic species (typically performed on fish) could originally be waived if the registered substance had a Log K_{ow} value below 3 (within a REACH PBT assessment, a Log K_{ow} < 4.5 is even used to conclude that a substance does not meet the B criterion). However, important changes to the REACH legal text in effect as of January 2022, put limitations to the type of substances for which such use of Log K_{ow} is still allowed (see table below). Moreover, substance evaluations have led to requests for aquatic bioaccumulation studies on substances which are ionisable at environmental pH. Such cases have included substances with very low, sometimes negative Log K_{ow} values in their neutral state. Whereas alternative information other than Log K_{ow} can still be used as per Annex XI to REACH, substances in their ionic form are in general believed to accumulate to a lesser extent than their neutral form. As such, an ionisable substance's Log K_{ow} value as determined on its neutral form, should provide a conservative estimation of its aquatic bioaccumulation potential. Moreover, as partitioning to lipids is still considered an important driver of bioaccumulation of ionic substances, a general ban on using Log K_{ow} for such substance's bioaccumulation assessment may be overly restrictive. The analysis presented on this poster examines if it is reasonable to assume that mechanisms other than partitioning to lipids which could play a role for ionic organic substances, could be a deciding factor to consider a substance as bioaccumulative in the aquatic environment.

Original REACH information requirements and column 2 adaptation options for aquatic bioaccumulation

COLUMN 1 : STANDARD INFORMATION REQUIRED	COLUMN 2: SPECIFIC RULES FOR ADAPTATION FROM COLUMN 1
9.3. Fate and behaviour in the environment 9.3.2. Bioaccumulation in aquatic species, preferably fish	9.3.2. **The study need not be conducted if:** – **the substance has a low potential for bioaccumulation** (for instance a log K_{ow} < 3) and/or a low potential to cross biological membranes; or – direct and indirect exposure of the aquatic compartment is unlikely. – (Addition to column 2 for point 9.3.2 since January 2022) The study may not be waived on the basis of low octanol-water partition coefficient alone, unless the potential for bioaccumulation of the substance is solely driven by lipophilicity. For instance, **the study may not be waived on the basis of low octanol-water partition coefficient alone if the substance is surface active or ionisable at environment pH** (pH 4-9).';

Materials & Methods

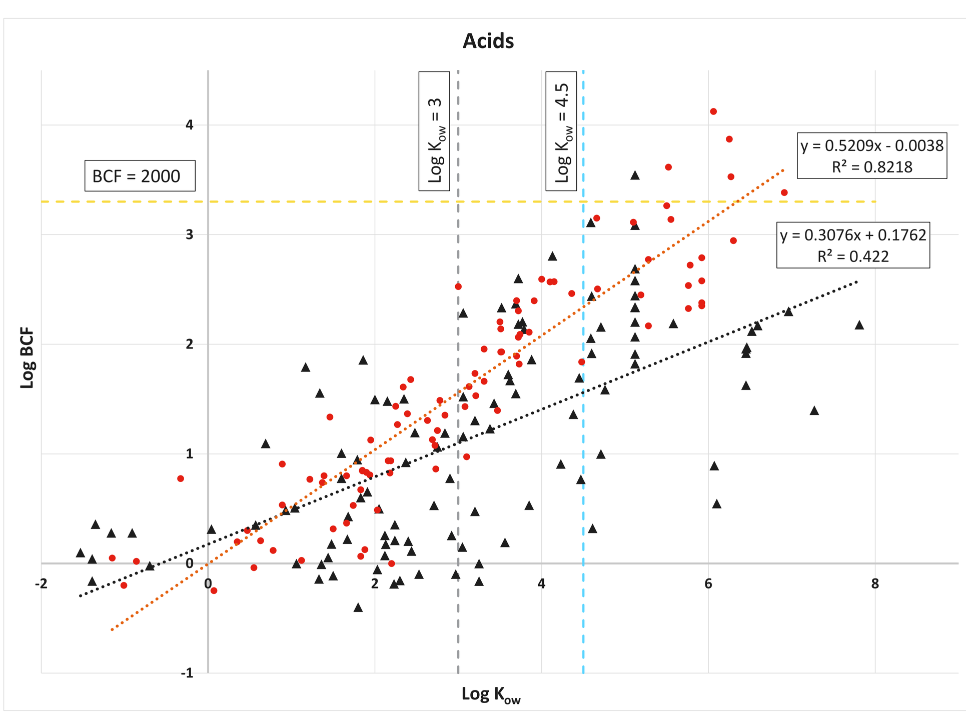
Analysis of experimental Log K_{ow} and BCF data from 2 main papers (Armitage et al., 2013; Fu et al., 2009)

- Armitage et al. (2013): experimental K_{ow} and BCF data on 149 acids and 62 bases
- Fu et al. (2009): experimental K_{ow} and BCF data on 73 acids and 65 bases
- Discussion of the results, partly based on the findings/method from Nendza et al. (2018)

Note: Log K_{ow} as used on this poster always represents the octanol-water partition coefficient as determined (or estimated) on an ionisable substance's neutral form. It is sometimes also denoted as Log Pn.

Results

Figure 1

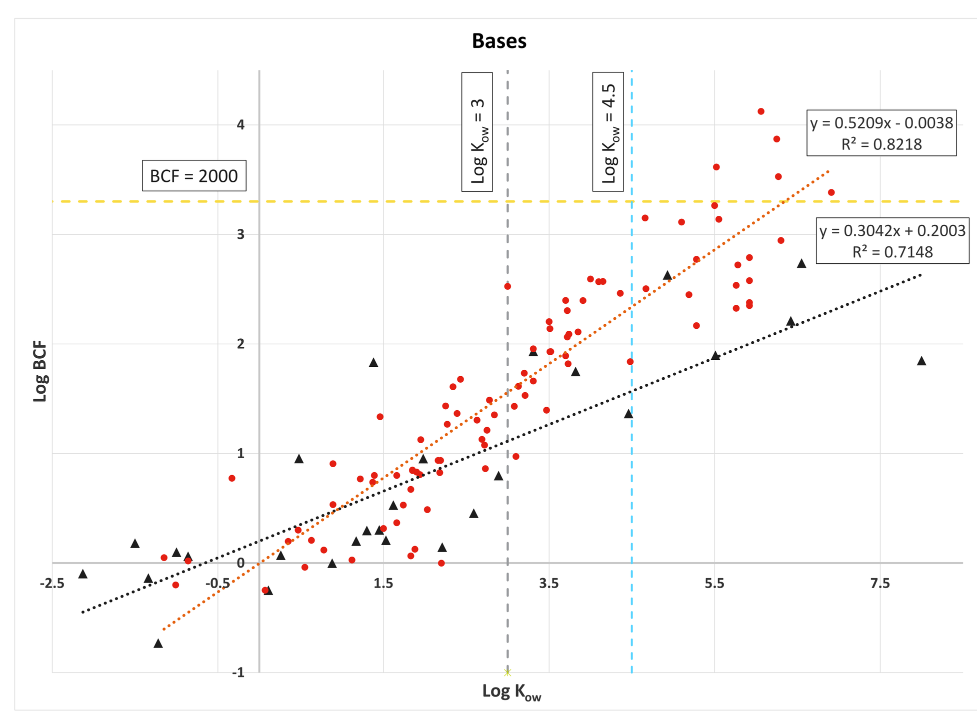


Legend:

▲ *Relation between Log Pn and Log BCF for 110 acids (some acids have multiple entries) expected to be at least partially ionised at pH 7; the black dotted line represents the linear regression line.*

● *Relation between Log Kow and Log BCF for 54 bases and 40 acids expected to be neutral at pH 7; the orange dotted line represents the linear regression line. Data source: Armitage et al. (2013), Fu et al. (2009).*

Figure 2



Legend:

▲ *Relation between Log Pn and Log BCF for 28 bases expected to be at least partially ionised at pH 7; the black dotted line represents the linear regression line.*

● *Relation between Log Kow and Log BCF for 54 bases and 40 acids expected to be neutral at pH 7; the orange dotted line represents the linear regression line. Data source: Armitage et al. (2013), Fu et al. (2009).*

Main findings:

- None of the acids or bases with a Log K_{ow} below 3 had a BCF > 100
- Some acids with a Log K_{ow} below 4.5 had a BCF approaching 1000
- In general, there is no specific reason to assume that a screening bioaccumulation assessment based on Log K_{ow} < 3 (and even Log K_{ow} < 4.5 would be less reliable (and not equally conservative) for an ionic substance
- Some specific chemical classes (e.g., for which it is not possible to reliably determine a K_{ow} value), should be excluded (e.g., PFAS substances, many of which are ionisable; ionic surfactants) (See Figure 3)

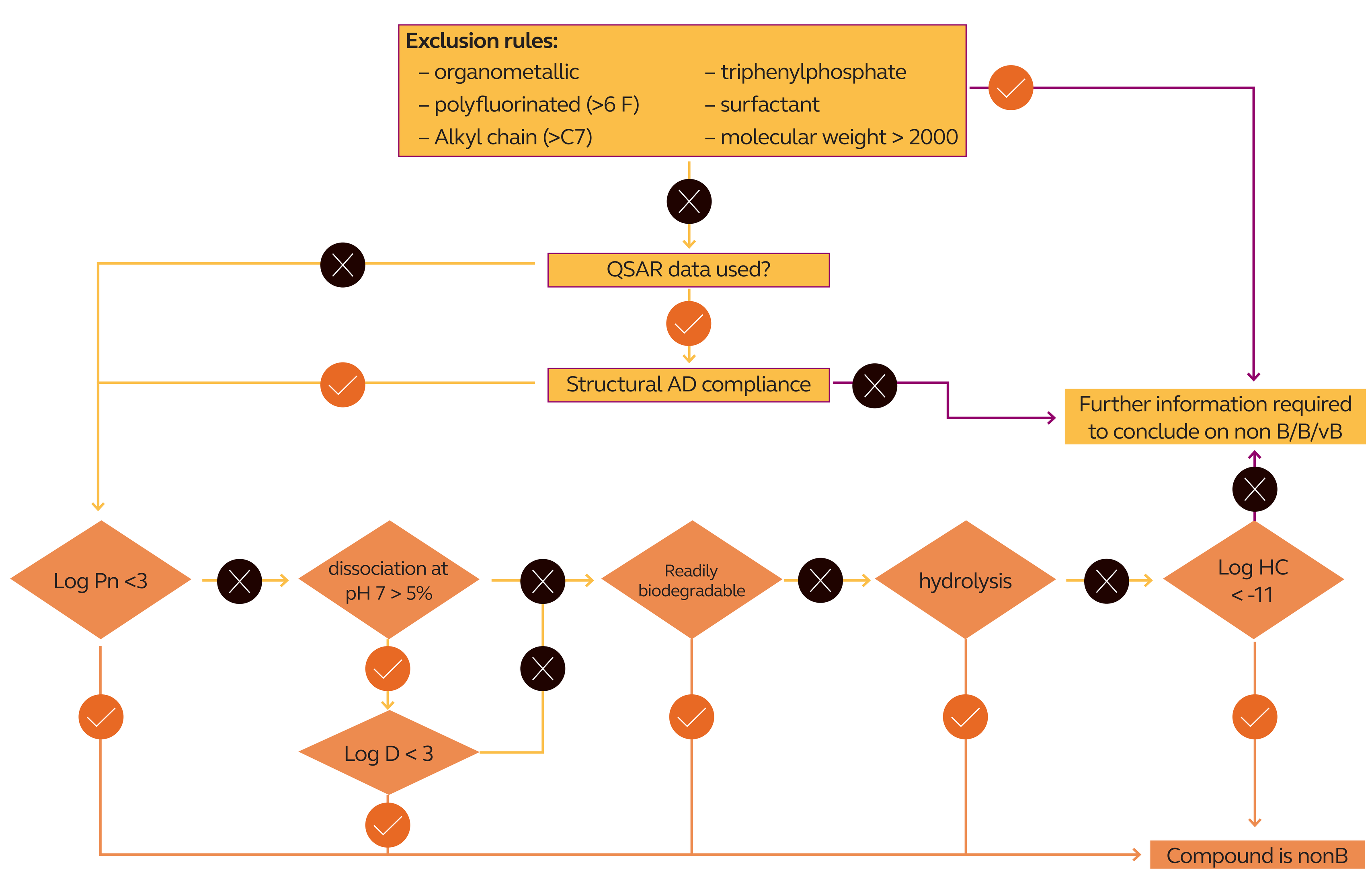


Figure 3. BCF waiving scheme, adapted from Nendza et al. (2018). Log Pn = Log K_{ow}

Conclusion

For ionisable organic compounds, the results of our analysis suggest that a (conservative) screening assessment of aquatic bioaccumulation potential is possible based on reliable experimental (or modeled) Log K_{ow} data alone.

References

Armitage JM, Arnot JA, Wania F, Mackay D (2013) Development and evaluation of a mechanistic bioconcentration model for ionogenic organic chemicals in fish. Environmental Chemistry 32(1): 115-128.

Nendza M, Kühne R, Lombardo A, Strempel S, Schüürmann G (2018) PBT assessment under REACH: Screening for low aquatic bioaccumulation with QSAR classifications based on physicochemical properties to replace BCF in vivo testing on fish. Science of the Total Environment 616-617: 97-106.

Fu W, Franco A, Trapp S (2009) Methods for estimating the bioconcentration factor of ionizable organic chemicals. Environmental Chemistry 28(7): 1372-1379.