Environmental risk evaluation report: Annex B: Read-across of environmental data between aryl phosphates
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Steve Killeen

Head of Science
Introduction

This annex considers the read-across of data between the triaryl and aryl/alkyl phosphates assessed in this series, to fill in data gaps in the key physico-chemical properties and ecotoxicity data required for environmental risk assessment. The data available for the individual substances are discussed in detail in the main reports.

The approach taken here is to relate the measured physico-chemical properties and ecotoxicity data for the various substances to a parameter that can be easily predicted for all substances considered. In this case, the Syracuse Research Corporation EPI software estimates of log $K_{ow}$ and vapour pressure are used as parameters that can be easily calculated from the chemical structure of the substance. In this way, any missing data values for a given property can be readily predicted from the estimate obtained from the EPI software.

In the analysis, the EPI estimate of log $K_{ow}$ is used to effectively normalise the available measured data on solubility, log $K_{ow}$ and ecotoxicity. There is some logic behind using the estimated log $K_{ow}$ for this process, as many quantitative structure activity relationships relate parameters such as solubility and ecotoxicity to the log $K_{ow}$. For the analysis of vapour pressure data, the EPI estimate for the vapour pressure is used to effect the normalisation.

Table B 1 outlines the measured data available for the various endpoints considered, along with respective estimates for log $K_{ow}$ and vapour pressure obtained from the chemical structure using the EPI software.

Figures B1 to B6 show the plots of the various measured data against EPI-estimated log $K_{ow}$ or vapour pressure. The regression equations obtained from these plots are summarised below.

The use of predictive data needs to be considered with caution. A complicating factor is that most of the commercial substances are complex mixtures, and it is apparent that some mammalian toxicological effects may be influenced by isomerism. Nevertheless, they are all assumed to behave as single substances for the purposes of this review (since this is currently the only practical approach). In addition, many of the correlations obtained are poor and the validity of the approach taken could be questioned on this basis. However, there are a number of gaps in the data available for some aryl phosphate esters and, in the absence of actual test data, the only alternative to the approach taken would be to use the EPI estimates (or other estimates which tend to be based on $K_{ow}$ for solubility, bioconcentration factor (BCF) and toxicity using the estimation methods given in the Technical Guidance Document or TGD) for the various endpoints. As discussed in the individual risk evaluation reports (and is apparent from the plots in this annex), for substances where data are available, the estimated data are often in relatively poor agreement with the measured value, and so using the estimated data alone to fill data gaps would probably lead to substantial errors. Therefore, despite the limitations and uncertainties in the regressions obtained, the approach taken in this annex (essentially normalising the EPI estimates of log $K_{ow}$ to the available measured data) should give more reliable estimates for the data gaps than could be obtained using the EPI or TGD estimates alone.

Where the data derived here are important to the conclusion of the risk assessment (for example, toxicity data), uncertainties in the use of the data are discussed in the main risk evaluation reports and recommendations for reducing this uncertainty are given.
### Table B 1 Data used for estimating missing values.

<table>
<thead>
<tr>
<th>Phosphate ester</th>
<th>Measured vapour pressure at 20°C (Pa)</th>
<th>Measured water solubility at room temperature (mg/l)</th>
<th>Measured Log $K_{ow}$</th>
<th>Measured BCF (l/kg)</th>
<th>Long-term NOEC for aquatic organisms (mg/l)</th>
<th>EPI Estimates</th>
<th>Fish</th>
<th>Invertebrates</th>
<th>Algae</th>
<th>Vapour pressure at 25°C (Pa)</th>
<th>Log $K_{ow}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Triphenyl phosphate</td>
<td>$1.2 \times 10^{-3}$</td>
<td>1.9</td>
<td>4.63</td>
<td>420</td>
<td>0.037</td>
<td>0.1</td>
<td>2.8</td>
<td>$10^{-5}$</td>
<td>4.70</td>
<td>$2.7 \times 10^{-6}$</td>
<td>7.98</td>
</tr>
<tr>
<td>Trixylenyl phosphate</td>
<td>$[4.7 \times 10^{-4}]^a$</td>
<td>0.89</td>
<td>5.63</td>
<td>1,300-1,900</td>
<td>0.1</td>
<td></td>
<td>2.7</td>
<td>$10^{-6}$</td>
<td></td>
<td>7.98</td>
<td></td>
</tr>
<tr>
<td>Tricresyl phosphate</td>
<td>$3.5 \times 10^{-5}$</td>
<td>0.36</td>
<td>5.11</td>
<td>800</td>
<td>0.00032</td>
<td>0.1</td>
<td>3.4</td>
<td>$10^{-6}$</td>
<td>6.34</td>
<td>$1.4 \times 10^{-6}$</td>
<td>5.24</td>
</tr>
<tr>
<td>Cresyl diphenyl phosphate</td>
<td>$3.3 \times 10^{-5}$</td>
<td>2.6</td>
<td>4.51</td>
<td>200</td>
<td>0.1</td>
<td></td>
<td>1.4</td>
<td>$10^{-6}$</td>
<td></td>
<td>5.24</td>
<td></td>
</tr>
<tr>
<td>Tris(isopropylphenyl) phosphat e</td>
<td>$2.3 \times 10^{-6}$</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.024</td>
<td>5.3</td>
<td>$10^{-6}$</td>
<td>9.07</td>
<td>$2.7 \times 10^{-6}$</td>
<td>9.07</td>
</tr>
<tr>
<td>Isopropylphenyl diphenyl phosphat e</td>
<td>$9.5 \times 10^{-6}$</td>
<td>2.2</td>
<td>5.30</td>
<td>[7,266]$^a$</td>
<td>0.024</td>
<td>0.006</td>
<td>5.3</td>
<td>$10^{-6}$</td>
<td>6.16</td>
<td>$5.3 \times 10^{-6}$</td>
<td>6.16</td>
</tr>
<tr>
<td>Tertbutylphenyl diphenyl phosphat e</td>
<td>$7.8 \times 10^{-5}$</td>
<td>0.04-3.2</td>
<td>5.12</td>
<td>778</td>
<td>0.093</td>
<td>0.010</td>
<td>3.5</td>
<td>$10^{-6}$</td>
<td>6.61</td>
<td>$3.5 \times 10^{-6}$</td>
<td>6.61</td>
</tr>
<tr>
<td>2-Ethylhexyl diphenyl phosphat e</td>
<td>$3.4 \times 10^{-4}$</td>
<td>0.38-1.9</td>
<td>5.73</td>
<td>934</td>
<td>0.021</td>
<td>0.018</td>
<td>2.5</td>
<td>$10^{-6}$</td>
<td>6.30</td>
<td>$2.5 \times 10^{-6}$</td>
<td>6.30</td>
</tr>
<tr>
<td>Isodecyl diphenyl phosphat e</td>
<td>$[3.8]^a$</td>
<td>0.03-0.75</td>
<td>5.44</td>
<td>335</td>
<td>0.057</td>
<td>0.004</td>
<td>6.3</td>
<td>$10^{-6}$</td>
<td>7.28</td>
<td>$6.3 \times 10^{-6}$</td>
<td>7.28</td>
</tr>
<tr>
<td>Tetrphenyl resorcinol diphenyl phosphat e</td>
<td>$0.69$</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2.7</td>
<td>$10^{-6}$</td>
<td></td>
<td>7.41</td>
<td></td>
</tr>
</tbody>
</table>

**Notes:**
- a) These values are uncertain (see main risk assessment reports) and have not been included in the estimation analysis.
- b) Assumes these two products have similar toxicity.
- c) Revised solubilities used in the individual risk assessment reports, the values here are used in the estimation analysis.
Physico-chemical properties

Vapour pressure

The plot (Figure B1) was constructed omitting the data point for isodecyl diphenyl phosphate (which appears to be out of line with the other available data). A reasonable correlation was obtained between the log (measured vapour pressure at 20°C (Pa)) and the log (EPI-estimated vapour pressure at 25°C (Pa)). The following regression equation was obtained:

\[ \log (\text{measured vapour pressure at } 20\degree \text{C (Pa)}) = 1.6671 \times \log (\text{EPI estimate (Pa)}) + 4.2214 \]

Using this equation, the vapour pressures at 20°C can be estimated for the data gaps as follows:

- Tris(isopropylphenyl) phosphate: \( 8.5 \times 10^{-5} \text{ Pa} \)
- Isopropylphenyl diphenyl phosphate: \( 1.1 \times 10^{-4} \text{ Pa} \)
- Isodecyl diphenyl phosphate: \( 3.6 \times 10^{-5} \text{ Pa} \)
- Tetraphenyl resorcinol disphosphate: \( 8.7 \times 10^{-6} \text{ Pa} \)
- Trixylenyl phosphate: \( 8.7 \times 10^{-6} \text{ Pa} \)

**Figure B1: Plot of log (measured vapour pressure (Pa)) against log (EPI estimated vapour pressure (Pa)).**
**Water solubility**

A poor correlation (Figure B2) was obtained between the log (measured water solubility (mg/l)) and the log (EPI-estimated $K_{ow}$). The following regression equation was obtained:

$$\log (\text{measured water solubility}) = -0.2801 \times \log (\text{EPI-estimated } K_{ow}) + 1.634$$

Using this equation, the water solubility at room temperature can be estimated for the data gaps as follows:

- Tris(isopropylphenyl) phosphate $0.12 \text{ mg/l}$

**Figure B2: Plot of log (measured solubility (mg/l) at 20°C) against log $K_{ow}$ (EPI estimate).**

**Log $K_{ow}$**

A reasonable correlation (Figure B3) was obtained between the log (measured $K_{ow}$) and the log (EPI-estimated $K_{ow}$). The following regression equation was obtained:

$$\log (\text{measured } K_{ow}) = 0.3381 \times (\text{EPI-estimated } K_{ow}) + 3.045$$

Using this equation, the log $K_{ow}$ can be estimated for the data gaps as follows:

- Tetraphenyl resorcinol diphosphate $5.5$
- Tris(isopropylphenyl) phosphate $6.1$
Environmental fate and behaviour

*Bioconcentration factor, BCF*

A reasonable correlation (Figure B4) was obtained between the log (measured BCF) and the log (EPI-estimated \(K_{ow}\)) when the data for isopropylphenyl diphenyl phosphate is omitted (this data point is considered an outlier). The following regression equation was obtained:

\[
\log (\text{measured BCF}) = 0.1878 \times \log (\text{EPI-estimated } K_{ow}) + 1.5947
\]

Using this equation, the BCF can be estimated for the data gaps as follows:

- Tetraphenyl resorcinol diphosphate \(\text{BCF} = 969 \text{ l/kg}\)
- Tri(isopropylphenyl) phosphate \(\text{BCF} = 1,986 \text{ l/kg}\)
- Isopropylphenyl diphenyl phosphate \(\text{BCF} = 564 \text{ l/kg}\)
- Tertbutylphenyl diphenyl phosphate \(\text{BCF} = 686 \text{ l/kg}\)
- Trixylenyl phosphate \(\text{BCF} = 1,240 \text{ l/kg}\)
Ecotoxicity

Long-term toxicity to fish

A plot of the log (no observed effect concentration (NOEC) for fish (mole/l)) against the log (EPI-estimated K_{ow}) is shown as Figure B5. The analysis combines the data from long-term fish growth/mortality studies and fish early life-stage studies. No clear trend with EPI-estimated K_{ow} was seen. This indicates that as a first approximation, the toxicities of the various trialkyl and trialkyl/aryl phosphates to fish are similar when expressed on a mol/l basis. The one exception appears to be tricresyl phosphate that has a fish NOEC considerably lower than the other phosphate esters considered here.

Assuming that all of the substances considered have a fish NOEC equivalent to around 4.2\times10^{-8} \text{ mol/l} (equivalent to the intercept of -7.3729 on Figure B5), the NOECs for the following substances for which data are not available can be estimated using the equation given in Figure B5:

- Tetraphenyl resorcinol diphosphate: NOEC ~ 0.024 mg/l
- Cresyl diphenyl phosphate: NOEC ~ 0.014 mg/l
- Trixylenyl phosphate: NOEC ~ 0.017 mg/l
- Tertbutylphenyl diphenyl phosphate: NOEC ~ 0.016 mg/l
- Isodecyl diphenyl phosphate: NOEC ~ 0.016 mg/l
- Isopropylphenyl diphenyl phosphate: NOEC ~ 0.015 mg/l
- Tris(isopropylphenyl) phosphate: NOEC ~ 0.019 mg/l
One of the NOEC values (for tricresyl phosphate with *Gasterosteus aculeatus*) appears to be much lower than the other data. This substance/data point could therefore be considered an outlier. However, this value was obtained with a species for which data are lacking for the other aryl phosphate esters, and the other available long-term toxicity data for tricresyl phosphate with other fish species are not out of line with the data on other aryl phosphates. Therefore, it is not clear whether a) *Gasterosteus aculeatus* is particularly sensitive to aryl phosphates in general or b) if tricresyl phosphate shows a specific mode of action to *Gasterosteus aculeatus*. The above regression plot and equation was derived from the dataset including the tricresyl phosphate NOEC for *Gasterosteus aculeatus*. If this value is excluded, the regression equation becomes:

\[
\log \text{NOEC (mol/l)} = -0.0485 \times \log (\text{EPI-estimated K}_{\text{ow}}) - 6.6916 \quad (R^2 = 0.0713)
\]

**Long-term toxicity to invertebrates**

A poor correlation was obtained between the log (NOEC for invertebrates (mol/l)) and the log (EPI-estimated \(K_{\text{ow}}\)). The following regression equation was obtained:

\[
\log (\text{measured BCF}) = -0.2279 \times \log (\text{EPI-estimated K}_{\text{ow}}) - 5.9317
\]

Using this equation, the log \(K_{\text{ow}}\) can be estimated for the data gaps as follows:

- Tetraphenyl resorcinol diphosphate\(^1\) NOEC = 0.014 mg/l
- Cresyl diphenyl phosphate NOEC = 0.025 mg/l
- Trixylenyl phosphate NOEC = 0.007 mg/l
- Triphenyl phosphate NOEC = 0.032 mg/l

\(^1\) The available long-term invertebrate data for tetraphenyl resorcinol diphosphate show that the actual NOEC is 0.021 mg/l; as there is some uncertainty in this value (undissolved test substance may have been present), it was not included in the analysis in Figure B6.
**Long-term toxicity to algae**

There are insufficient data to generate a regression equation for the algal NOEC. However, the available data indicate that algae appear to be much less sensitive than fish and invertebrates to triaryl and trialkyl/aryl phosphates and so an assessment based on the long-term fish and invertebrate data should also be protective for algae.
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