REACH Compliance Project “Availability of Health and Environmental Data for High Tonnage Chemicals under REACH” – Data Quality of Environmental Endpoints in Registrations

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Methodology – Screening on all dossiers

Example Ecotoxicity
Decision tree: Hierarchy of questions addressing the REACH requirements

1. Long-term depht® fish test!

2. Bioassay: standard 96 h test?

3. Long-term test for missing short-term test?

4. Can long-term test be avoided?

5. Adaptation: Waiting *?

6. Without chronic (QSAR)?

7. Water solubility?

8. Effects: EC50/NOEL ?

9. Ratio: EC50/NOEL ?

10. Long-term fish test?

11. Long-term daphnia test?

12. Non-standard methods applied?

* Scientifically, QSAR, WoE, Read-Across/Grouping, Technically, Exposure, Other

“testing proposal”

“non-compliant”

“without conclusion/complex”

“compliant”
Results

Environmental Endpoints
Environmental endpoints – Results after screening, formal and refined check

Abiotic degradation

Biotic degradation

Bioaccumulation

Ecotoxicity

≥1000 tpa

Screening

Screening + Formal check

Percentage share [%]
Environmental endpoints – Results after screening, formal and refined check

**Abiotic degradation**

- **Screening**:
  - 100-1000 tpa: 47.58%
  - ≥1000 tpa: work in progress

- **Screening + Formal check**:
  - 100-1000 tpa: 47.58%
  - ≥1000 tpa: work in progress

**Biotic degradation**

- **Screening**: 100-1000 tpa: 47.58%
  - ≥1000 tpa: work in progress

- **Screening + Formal check**: 100-1000 tpa: 37.37%
  - ≥1000 tpa: work in progress

**Bioaccumulation**

- **Screening**: 100-1000 tpa: 69.30%
  - ≥1000 tpa: work in progress

- **Screening + Formal check**: 100-1000 tpa: 49.38%
  - ≥1000 tpa: work in progress

**Ecotoxicity**

- **Screening**: 100-1000 tpa: 66.32%
  - ≥1000 tpa: work in progress

- **Screening + Formal + Refined Check**: 100-1000 tpa: 24.44%
  - ≥1000 tpa: work in progress

*Percentage share [%]*

- "compliant"
- "non-compliant"
- "complex"
Screening – Biotic degradation

Main assessment criteria

- Ready biodegradability (OECD TG 301; 310)
- Simulation testing in surface water (OECD TG 309) or in sediment/soil (OECD TG 308, 307)
- Waiving referring to Annex VII, column 2 (no test for inorganic substances)

100-1000 tpa

- Waiving/adaptation (69%)
- Less inorganic substances (11.5%)
  \[\rightarrow\] Lower percentage of “compliant” decisions

- N= 2053

≥1000 tpa

- Waiving/adaptation (69%)
- Less inorganic substances (11.5%)
  \[\rightarrow\] Lower percentage of “compliant” decisions

- N= 1814
Screening – Bioaccumulation

Main assessment criteria

- Bioaccumulation study (OECD TG 305)
- Waiving referring to Annex IX, column 2 (log Kow ≤ 3)

100-1000 tpa

- Less dossiers on inorganic, ionisable or hydrolytically unstable substances (29%)
  → lower percentage of “complex” endpoint decisions
- Waiving/adaptation
  → Majority of registrants used alternative methods to avoid animal testing

≥1000 tpa

- Waiving referring to Annex IX, column 2 (log Kow ≤ 3)

N= 2053

- 29% inorganic, ionisable or hydrolytically unstable
- 69% compliant
- 0.5% non-compliant
- 0.5% complex

N= 1814

- 41% inorganic, ionisable or hydrolytically unstable
- 76% compliant
- 3% non-compliant
- 21% complex
Environmental exposure assessment: Screening

Main assessment criteria

- Harmonised and/or self-classification
- Availability of environmental exposure scenarios for substances classified or PBT/vPvB (Art. 14(4) REACH)

100-1000 tpa

- “Compliant” exposure assessment not required
- “Non-compliant” classification-related exposure assessment missing
- “Complex” Available exposure scenarios need refined check

![Pie charts showing assessment criteria percentages for 100-1000 tpa and ≥1000 tpa](chart.png)
“Compliant” decisions after screening

- Between 1.3 and 23.6% “compliant” by providing guideline studies

- **Biodegradation**: “compliant” by providing guideline studies, either by
  - 21-23% readily biodegradable in TG 301 or
  - 0.5% studies for simulation testing

- **Abiotic Degradation / Bioaccumulation**: mainly “compliant” because a study was not required (column 2)

- **Ecotoxicity**: 4% “compliant” by providing guideline studies on chronic testing

- **Bioaccumulation/ Ecotoxicity**: Animal testing
Frequency of documented data waiving/adaptation categories

Abiotic degradation

100-1 000 tpa

≥1 000 tpa

work in progress

0% 25% 50% 75% 100%

Biotic degradation

100-1 000 tpa

≥1 000 tpa

0% 25% 50% 75% 100%

Bioaccumulation

100-1 000 tpa

≥1 000 tpa

0% 25% 50% 75% 100%

Ecotoxicity

100-1 000 tpa

≥1 000 tpa

0% 25% 50% 75% 100%

Waiving/adaptation category

- Read Across
- Weight of Evidence
- Qualitative and Quantitative structure-activity relationship ((Q)SAR)
- Endpoint specific, column 2
- Scientifically unjustified
- Technically not possible
- Exposure-driven testing
- Other cases

Angelika Oertel, 23.08.2018, REACH Compliance – Workshop on Data Quality in Registration Dossiers
Data waiving/adaptation used in ca. 65-93% of dossiers (depending on endpoint and tonnage band)

Main categories used for data waiving/adaptation

1. Endpoint specific, Column 2
2. Read Across
3. Weight of Evidence
4. QSAR
5. Other cases (e.g. no reference to REACH Annexes VII-XI)

→ Only minor differences between tonnage bands

Abiotic degradation

≥1 000 tpa

100-1 000 tpa

0%

25%

50%

75%

100%

Bioaccumulation

≥1 000 tpa

100-1 000 tpa

0%

25%

50%

75%

100%

Other cases
Screening/Formal Check – Endpoint-specific waiving (Column 2)

Main assessment criteria

- Endpoint specific rules, e.g.
  - Inorganic substance (BioDeg)
  - Direct or indirect exposure unlikely (BioDeg, Bioaccu)
  - Chemical safety assessment (BioDeg, Ecotox)
  - Log Kow (Bioaccumulation)
  - Water solubility (Ecotox, BioDeg)

→ Bioaccumulation mainly “compliant” because of Log Kow ≤3

→ Biotic Degradation mainly “complex” because of reference to chemical safety assessment

Annex VII-X, Column 2 – Specific rules for adaptation
Screening/Formal Check – Endpoint-specific waiving (Column 2)

Reasons for non-compliance
- Specific rules of REACH Annex VII to X column 2 were not met
  - Required information to justify the column 2 rules were either not provided or not adequately documented
  - Exposure assessment not available although required

Recommendations
- Justification should meet specific rules of REACH Annex VII to X column 2
- Relevant information required to justify rules of column 2 should be available and adequately documented (e.g. log Kow)
- Exposure assessment should be available to demonstrate that exposure is unlikely
71-84% of evaluated Read Across approaches were formally “compliant”

Recommendations for human health endpoints apply here as well

<table>
<thead>
<tr>
<th></th>
<th>Ecotox 100-1 000 tpa</th>
<th>Biotic Degradation 100-1 000 tpa</th>
<th>Bioaccumulation 100-1 000 tpa</th>
</tr>
</thead>
<tbody>
<tr>
<td>Percentage share [%]</td>
<td>71</td>
<td>84</td>
<td>82</td>
</tr>
</tbody>
</table>

- compliant
- non-compliant

Main assessment criteria

<table>
<thead>
<tr>
<th>Annex XI, 1.5</th>
<th>Function group or precursors, breakdown products or constant pattern in the changing of potency</th>
</tr>
</thead>
</table>

Is a justification according to Annex XI 1.5, paragraph 2 given? (or other adequate explanation)

Annex XI, 1.5 – Grouping of substances and read-across approach
Formal Check – (Q)SAR

Main assessment criteria
- (Q)SAR Model Reporting Format (QMRF)
- (Q)SAR Prediction Reporting Format (QPRF)
- Scientific validity
- Applicability domain

Annex XI, 1.3 – Qualitative or Quantitative structure-activity relationship ((Q)SAR)

→ 76-84% of evaluated (Q)SAR approaches were formally “non-compliant”
Formal Check – (Q)SAR

Reasons for “non-compliant”
- QMRF/QPRF (or equal information) is not available
- Scientific validity of the model is not documented
- Evaluation whether substance falls within the applicability domain is missing

Recommendations
- The study summary for a (Q)SAR prediction should be created exactly according to ECHA's practical guide
- The QMRF and QPRF should be attached to the study summary
- A (Q)SAR prediction should not be used if the model is not scientifically validated or if the substance does not fall within the applicability domain
Ecotoxicity – Results after screening, formal and refined check

Main assessment criteria

Screening
- Long-term tests fish & invertebrates  
  (e.g. OECD TG 210, 211)
- Short-term tests fish & invertebrates  
  (e.g. OECD TG 203, 202)
- Water solubility
- Ratio EC50/LC50

Refined Check
- Chemical Safety Assessment

### 100-1000 tpa (N= 500)

<table>
<thead>
<tr>
<th>Screening, Formal/Refined check</th>
<th>&quot;compliant&quot;</th>
<th>&quot;non-compliant&quot;</th>
<th>&quot;complex&quot;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>8</td>
<td>26</td>
<td>66</td>
</tr>
<tr>
<td></td>
<td>32</td>
<td>44</td>
<td>24</td>
</tr>
</tbody>
</table>
Reasons for “non-compliant”

- Test method not suitable as a chronic test
- Water solubility <1 mg/L requires chronic testing unless the substance is highly insoluble
- Assessment factor for PNEC derivation not appropriate
- Environmental exposure assessment not performed although required
- Risk is indicated by PEC/PNEC > 1

Recommendations

- Long-term fish tests (e.g. OECD TG 210) should include sensitive life-stages (juveniles, eggs, and larvae)
- Chronic testing if water solubility <1 mg/L or evidence of highly insolubility
- For derivation of PNECs all available hazard information needs to be evaluated
- Environmental exposure for classified or PBT/vPvB-substances (REACH Art 14(4))
- Risk > 1 should not be indicated
Conclusions on environmental endpoints

Overall results on 100-1000 tpa and ≥1000 tpa after screening

- No general trend on dossier quality
- Intensive use of data waiving / adaptation → Low availability of guideline studies
- Endpoint specific waiving (column 2) most frequently used

After screening and formal check (and refined check for Ecotox)

- ≥1000 tpa: on average 34% compliant; 31% non compliant (AbioDeg excluded)
- 100 -1000 tpa: on average 39% compliant; 24% non compliant (AbioDeg excluded)
  → Data quality slightly improved for particular endpoints (Bioaccumulation, Ecotox)

- On average 36% of endpoints remained “complex”
  → Waiving justifications without reference to REACH Annexes VII-XI
  → Waiving justifications with reference to chemical safety assessment
Overall results and conclusions
Human health and environmental endpoints – Screening results

Results after screening (both tonnage bands)
- 43-96% of dossiers “complex”
- 4-46% of dossiers “compliant”
- 0-28% of dossiers “non-compliant”

→ High rates of “complex” cases
→ Further evaluation of waiving / adaptation needed to increase decision rates
Human health and environmental endpoints – Results after screening and formal check

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Percentage share [%]</th>
<th>&quot;compliant&quot;</th>
<th>&quot;non-compliant&quot;</th>
<th>&quot;complex&quot;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Developmental toxicity 100-1 000 tpa</td>
<td>16</td>
<td>53</td>
<td>49</td>
<td>26</td>
</tr>
<tr>
<td>Developmental toxicity ≥1 000 tpa</td>
<td>18</td>
<td>33</td>
<td>49</td>
<td>43</td>
</tr>
<tr>
<td>Reproductive toxicity 100-1 000 tpa</td>
<td>18</td>
<td>49</td>
<td>49</td>
<td>23</td>
</tr>
<tr>
<td>Reproductive toxicity ≥1 000 tpa</td>
<td>23</td>
<td>54</td>
<td>23</td>
<td>25</td>
</tr>
<tr>
<td>Repeated dose toxicity 100-1 000 tpa</td>
<td>23</td>
<td>43</td>
<td>33</td>
<td>25</td>
</tr>
<tr>
<td>Repeated dose toxicity ≥1 000 tpa</td>
<td>23</td>
<td>43</td>
<td>33</td>
<td>25</td>
</tr>
<tr>
<td>Mutagenicity 100-1 000 tpa</td>
<td>16</td>
<td>45</td>
<td>40</td>
<td>16</td>
</tr>
<tr>
<td>Mutagenicity ≥1 000 tpa</td>
<td>18</td>
<td>47</td>
<td>16</td>
<td>37</td>
</tr>
<tr>
<td>Biotic degradation 100-1 000 tpa</td>
<td>18</td>
<td>56</td>
<td>16</td>
<td>27</td>
</tr>
<tr>
<td>Biotic degradation ≥1 000 tpa</td>
<td>18</td>
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<td>27</td>
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<td>Abiotic degradation 100-1 000 tpa</td>
<td>16</td>
<td>40</td>
<td>12</td>
<td>49</td>
</tr>
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<td>16</td>
<td>40</td>
<td>12</td>
<td>49</td>
</tr>
<tr>
<td>Bioaccumulation 100-1 000 tpa</td>
<td>16</td>
<td>38</td>
<td>14</td>
<td>49</td>
</tr>
<tr>
<td>Bioaccumulation ≥1 000 tpa</td>
<td>16</td>
<td>38</td>
<td>14</td>
<td>49</td>
</tr>
<tr>
<td>Ecotoxicity 100-1 000 tpa</td>
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</tr>
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Results after screening and formal check (both tonnage bands)

- 16-61% of dossiers “complex”
- 18-56% “compliant”
- 2-61% “non-compliant”

→ Still high rates of “complex” cases
→ Further evaluation needed to solve all complex cases

→ Refined check
  - Groups of similar cases
  - “Weight of evidence” case group
  - Other case groups: Aim to identify frequent errors/problems
Human health and environmental endpoints – Results after screening and formal check

### Average on all endpoints (except Muta & AbioDeg)

#### ≥1000 tpa
- 31% “compliant”
- 32% “non-compliant”
- 37% “complex”

#### 100-1000 tpa
- 44% “compliant”
- 19% “non-compliant”
- 37% “complex”

→ **Higher rate of compliance at 100-1000 tpa**
- DevTox / ReproTox lower requirements
- RDT / Ecotox improved compliance

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<table>
<thead>
<tr>
<th>Endpoint</th>
<th>≥1000 tpa</th>
<th>100-1000 tpa</th>
<th>Percentage share [%]</th>
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</thead>
<tbody>
<tr>
<td>Ecotoxicity ≥1 000 tpa</td>
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<tr>
<td>Biotic degradation ≥1 000 tpa</td>
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<tr>
<td>Ecotoxicity 100-1 000 tpa</td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

"compliant"  "non-compliant"  "complex"
Conclusions

Mean average of compliant endpoints higher in 100-1000 tpa (44%) compared to ≥1000 tpa (31%)

Potential reasons

- Requirements less comprehensive for DevTox and ReproTox
- Higher frequency of compliant justifications on data waiving / adaptions (RDT, Ecotox)

→ Indicates improvement of data quality

Data gaps and inappropriate waiving/adaptations identified in registrations

- ≥1000 tpa: 12-61% of the examined endpoints “non-compliant”
- 100-1000 tpa: 2-44% of the examined endpoints “non-compliant”

→ There is a need for improvement of registrations.

Conclusions on the examined endpoints not possible for all dossiers (remained “complex”)

Note on project results

- Do not represent the Compliance Check done by ECHA
- “Compliant” endpoints may still require an in-depth (scientific) analysis of studies and justifications (e.g. Read Across)
Recommendations to registrants ≥1000 tpa

Aim
- Evidence-based assistance to registrants

Structure
- General recommendations, e.g.:
  - for identity/similarity of substance and test material
  - Data adjustments according to REACH Annex XI
- Endpoint specific recommendations
  - Human health
  - Environmental endpoints

→ 33 recommendations published soon
→ Recommendations also applicable to 100-1000 tpa
Example Bioaccumulation – Reasons for “non-compliance” and development of recommendations

### Report on ≥1000 tpa

<table>
<thead>
<tr>
<th>Waiving/adaptation category</th>
<th>Main reason(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Q)SAR (28 %)</td>
<td>Insufficient model was used</td>
</tr>
<tr>
<td></td>
<td>ESR not provided</td>
</tr>
<tr>
<td></td>
<td>Reporting of model and prediction were insufficient</td>
</tr>
<tr>
<td>Technically not feasible (21 %)</td>
<td>Substance is UVCB</td>
</tr>
</tbody>
</table>

### Recommendations on ≥1000 tpa

<table>
<thead>
<tr>
<th>Problems</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Validation data on the (Q)SAR model and prediction results are not available</td>
<td>• OCED validation criteria should be met</td>
</tr>
<tr>
<td>Testing is not required because the substance is a UVCB substance</td>
<td>• Model and prediction reporting formats should be used</td>
</tr>
<tr>
<td></td>
<td>• ESR for each (Q)SAR required</td>
</tr>
<tr>
<td></td>
<td>• UVCB could contain CMR substances and/or PBT- substances, e.g. PAHs, and should be analysed</td>
</tr>
<tr>
<td></td>
<td>• Deficiencies in substance identity should be tackled or justified</td>
</tr>
<tr>
<td></td>
<td>• Validation of analytical methods for UVCB but also for UVCB in environmental matrices</td>
</tr>
</tbody>
</table>
Outlook – Publications and information

≥1000 tpa
- Final Report part 1 and part 2 (soon available)
- Recommendations to registrants (soon available)

100-1000 tpa
- Final report (in preparation)

ECHA-Newsletter

Information and downloads on the project
http://www.bfr.bund.de/de/verfuegbarkeit_von_gesundheits_und_umweltdaten_fuer_hochtonnagige_chemikalien_unter_reach_reach_iii_-202836.html
https://www.umweltbundesamt.de/publikationen/reach-compliance-data-availability-of-reach
http://www.reach-info.de/reach-compliance.htm
Thank you for your attention

Angelika Oertel

Acknowledgements to
• Documentary assistants Paulina Heinze, Michael Panitz, Kerstin Schlegel, Uwe Ramm
• Former project colleagues Andrea Springer, Dana Sittner, Henning Hermann, Anna Lena Kronsbein, Katrin Maul, Anne-Katrin Müller, Uta Herbst

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