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Fass.se – the Swedish Prescribing Guide
A Voluntary 
Environmental 
Classification System 
for Pharmaceutical 
Substances

As a consequence of increasing interest in the area of pharmaceuticals in the environment, the Swedish Association of the Pharmaceutical Industry has in collaboration with a range of stakeholders developed an environmental classification scheme for active pharmaceutical ingredients. This article describes the background of the system, its design, and future development.
Background to the initiative to publish environmental data for APIs on Fass.se


Conclusions:

• Large data gaps

• Several substances are environmentally hazardous, but acute environmental risks are limited to ethinyl estradiol and estradiol (sex hormones)

• An environmental classification scheme cannot be introduced on the Swedish market only. Such an initiative would need an EU wide implementation

• A voluntary classification scheme could be introduced in Sweden based on an industry initiative monitored by an independent competent body
Background to the initiative to publish environmental data for APIs on Fass.se (cont.)

• The Swedish Minister of the Environment calls for a round-table discussion

• LIF takes the initiative to develop a system for environmental information on pharmaceutical substances to be introduced on www.fass.se

• Invites stakeholders of concern to participate in the development of the model
Swedish Task Force

- The Swedish Association of Local Authorities and Regions
- Stockholm County Council
- The Swedish Association of the Pharmaceutical Industry
- Medical Products Agency
- The National Corporation of Swedish Pharmacies

Original Members of the International Task Force

- GlaxoSmithKline
- Lilly
- Pfizer
- Roche
- AstraZeneca
- MERCK
Swedish Environmental Classification Scheme for Pharmaceutical Substances

Launched 2005

Data and classifications are updated regularly (at least every third year)

Classifications and data are reviewed by IVL (Swedish Environmental Research Institute). IVL is an impartial body, owned by the foundation SIVL which has a board of directors representing government and industry.

IVL reviews the classifications and environmental data in relation to the guidance document (last revision 2021)

• PEC based on total consumption of a substance in Sweden (data from IQVIA), hence not “product by product”

• Another important difference to EMA ERA Guidance: PEC/PNEC classification based upon RQ from below 0.1 to above 10.
Environmental classification of pharmaceuticals at www.fass.se

Guidance for pharmaceutical companies

2012 v 3.0
The review by IVL results in comments in four categories

**Major deviation** – deficiencies in the submitted material leads to an inaccurate classification of risk or/and hazard and needs to be changed before publication at Fass.se

**Minor deviation** - deficiencies in the submitted material that does not lead to an inaccurate classification of risk or/and hazard but still needs to be changed before publication at Fass.se

**Remarks** – minor deficiencies, correction is recommended (although not mandatory) to be in full compliance with guideline

**No remarks** – no deficiencies found in the submitted material and the document is recommended for publication.
Figure 1. The environmental tab “Miljö” at www.fass.se.

<table>
<thead>
<tr>
<th>Motallt</th>
<th>Pharma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aktiv substans:</td>
<td>Substans A</td>
</tr>
<tr>
<td>ATC-kod:</td>
<td>A91AA</td>
</tr>
<tr>
<td>Utbytarhets:</td>
<td>Utbytbara läkemedel</td>
</tr>
</tbody>
</table>

Läkemedel från Pharma omfattas av Läkemedelsförsäkringen.

### Miljöinformation

Läs mer om miljöpåverkan:

**Substans A**

Målkrav: Användning av Substans A har bedömts medföra försumbar risk för miljöpåverkan.

Neefytningsrisk: Substans A är potentiellt persistent.

Bioackumulering: Substans A har låg potential att bioackumuleras.

### Bilder och delbarhet

Läs mer
Environmental Risk Phrases

PEC/PNEC < 0.1
Use of the medicine has been considered to result in insignificant environmental risk

0.1 < PEC/PNEC < 1
Use of the medicine has been considered to result in low environmental risk

1 < PEC/PNEC < 10
Use of the medicine has been considered to result in moderate environmental risk

PEC/PNEC > 10
Use of the medicine has been considered to result in high environmental risk

No or limited data:
Risk of environmental impact cannot be excluded due to lack of data
Risk of environmental impact cannot be excluded, however some ecotoxicity data are available
PEC is below the action limit of 0.01 μg/L

For some APIs, data may be lacking due to limited use/low dose which, in turn, means the action limit in the EU EMA Environmental Risk Assessment guideline (EMA/CHMP/SWP/4447/00) of PEC < 0.01 μg/L is not triggered and, consequently, an environmental risk assessment may not have been undertaken. In these cases, the following phrase should be included in the detailed background information:

According to the European Medicines Agency guideline on environmental risk assessment of medicinal products (EMA/CHMP/SWP/4447/00), use of *name of the substance* is unlikely to represent a risk for the environment, because the predicted environmental concentration (PEC) at the time of registration was below the action limit 0.01 μg/L.
Exempted substances

According to the EU EMA guideline for Environmental Risk Assessment of pharmaceuticals (Ref. 1), vitamins, electrolytes, amino acids, peptides, proteins, carbohydrates and lipids are exempted because they are unlikely to result in significant risk to the environment. Similarly, vaccines and herbal medicinal products are also exempted due to the nature of their constituents.

There might also be other pharmaceuticals on the Swedish market that could be exempted due to the nature of their constituents e.g. activated carbon. In these cases, the companies should supply the reviewer with enough information to justify the exemption. Substances that, due to their volatility or other physical parameters, cannot be assessed for aquatic environmental fate and effects are also exempted. The justification of the exemption should be included in the detailed background information.
Degradation and Bioaccumulation Phrases

**Bioaccumulation:** No significant bioaccumulation potential or Potential to bioaccumulate in aquatic organisms

**Degradation:** The medicine is degraded in the environment, or The medicine is slowly degraded in the environment, or The medicine is potentially persistent

If the pharmaceutical fulfills the criteria for PBT (Persistent, Bioaccumulative and Toxic) and/or vPvB (very Persistent and very Bioaccumulative), the following phrase should be added:

*According to the established EU criteria, the compound should be regarded as a PBT/vPvB substance*
Some strengths and some challenges

- Classifications reviewed by impartial body (IVL)
- Publicly available
- Total PEC
- Several thresholds (0.1, 1, 10) allow for larger differentiation between substances

- Different classifications for the same substance may be published by companies
  - In the summary slides, we present the “toughest” classification
- PNEC vs EQS – not necessarily comparable
Summary of API Classifications on Fass.se

- **1171**: Number of products that have some environmental information published
- **944**: Unique substances
- **621**: Exempted products (452 unique substances)
- **286**: Risk classified products (270 unique substances)
- **264**: Data are missing/limited (222 unique substances)
944 unique substances

- Classified substances: 29%
- Exempted substances: 48%
- Reviewed but lack of data: 24%
Environmental Risk Phrases for 270 unique substances

Worth noticing:
There are another 452 unique substances exempted from classification due to “unlikely to result in significant risk to the environment”
Bioaccumulation Phrases

Low potential to bioaccumulate

High potential to bioaccumulate
Degradation Phrases

- Degrades: 20%
- Degrades slowly: 10%
- Potentially persistent: 70%
Reduce environmental impacts of pharmaceuticals along the value chain

Needs, requirements and use of product-specific environmental information by different actors and for different applications

Ann-Christin Flisberg, Peter Öfrin, Lisa Persson

In cooperation with The Research-Based Pharmaceutical Industry (LIF)

Some ideas for future development of the classification scheme
Proposed model for environmental assessment of pharmaceutical products

Environmental risk

Production of Raw materials

API production process

Environmental risk management and assessment of local emissions of API covers environmental risks in production process steps where API can be/is released to the environment

Formulation process & Packaging

Distribution and delivery

Use

End-of-life

Production of Raw materials

Production of Pack materials

Current Environmental classification of pharmaceuticals at Fass.se covers environmental risks from release of API from patient excretion in Swedish water recipients

Carbon footprint of pharmaceutical products covers greenhouse gas emissions for partial or full life cycle; from "cradle to gate" or "cradle to grave"

Developed in a two-year collaboration project (Oct 2017 – July 2019), jointly funded by LIF and SIVL (Foundation of the Institute for Water and Air Research).
The information may be used in different ways, to drive improvements along the value chain.
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