User manual for the PMT screening tool

Introduction
The PMT screening tool is an online tool designed to predict the persistence (P), mobility (M) and human toxicity (T) of substances based on model predictions. The PMT screening tool is available at https://rvszoeksysteem.rivm.nl/PMTscreeningtool (see Figure 1).

Figure 1 Link to the PMT screening tool.

Emissions of substances that are persistent *and* mobile in the aquatic environment *and* hazardous to humans and/or ecosystems (PMT), or that are very persistent *and* very mobile (vPvM) should be avoided. For this purpose, screening approaches are needed to identify PMT/vPvM substances as early as possible. The PMT screening tool can be used by permit officers (responsible for e.g. industrial wastewater discharge permits), risk assessors, drinking water suppliers, industry and others to screen substances for a potential PMT concern.

The PMT screening tool is based on the methodology developed in Hartmann et al. (2023). This user manual summarizes the methodology for this scientific article and provides information on how to use the PMT screening tool.

Methodology of screening approach
The basic approach is to calculate an overall PMT score, based on individual scores for P, M and T, and rank substances between zero (no or very low PMT potential) to 1 (very high PMT potential). Also, for the individual properties P, M, and T as well as for the overall PMT-score, the-scores are constructed to give:

- a score of 0 to 0.33 indicates low to moderate P, M and/or T potential;
- a score of 0.33 to 0.5 indicates high P, M and/or T potential;
- and a score of 0.5 to 1 indicates very high P (vP), M (vM) and/or T potential.
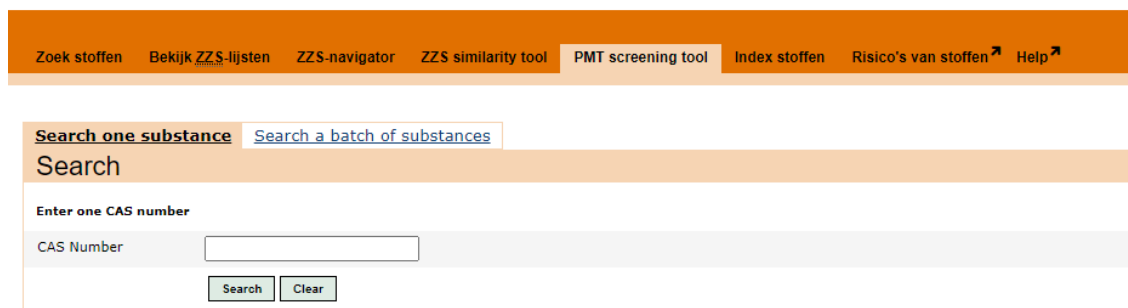
For a concern for PMT properties of a substance, the criteria for the scores of all three individual indicators (P *and* M *and* T) must be met. However, the screening approach might give a substance a high overall PMT-score (≥ 0.33) even if the scores for one of the individual scores on P, M or T is low to moderate. This enables the identification of substances of concern that may not-score high on all three indicators (P, M and T) and could be a borderline case on one of the endpoints, but that do cause a concern based on the combination of (some of) these indicators. From a screening point of view, this more cautious approach is considered valuable.

For details on the screening approach, we refer to Hartmann et al. (2023). A summary of how substances are scored on their P, M and T properties is included at the end of this user manual.

Input
A CAS number of a substance needs to be provided as input. The user can either search a single substance using the tab 'Search one substance' or a list of substances (CAS numbers) using the tab 'Search a batch of substances', see Figure 2. When using a list of substances, CAS numbers need to be divided by a space, a
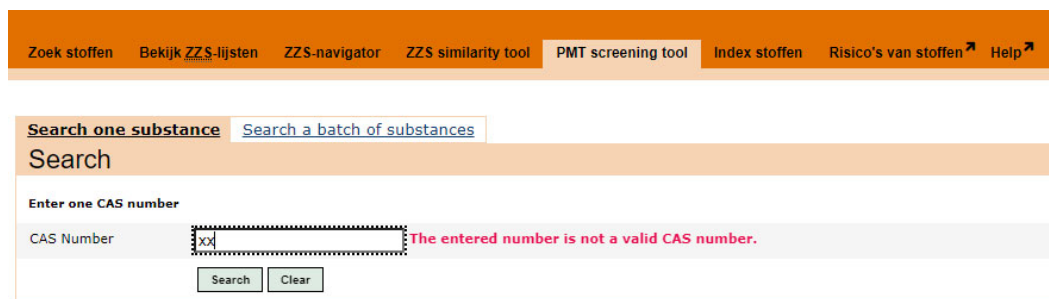
comma, a vertical line (|) or a new line. The user can easily copy and paste a list of CAS numbers directly from an Excel sheet.

Figure 2 Input window of the PMT screening tool

An error can occur when the user searched for a number that is not a valid CAS number (Figure 3). If this error occurs, please correct the entered CAS number and try again. This message is only shown in the input screen when searching for a single substance. When searching for a batch of substances and one or more invalid CAS numbers are used, the error message will be included in the output screen.
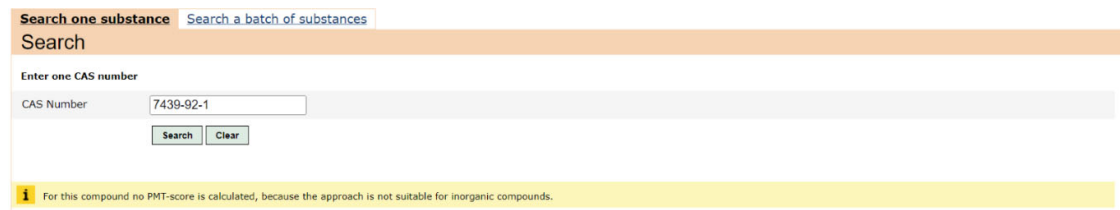

Figure 3 Error message when entered number is not a valid CAS number.

Output

Application domain

The screening approach should not be used for inorganic compounds, because the QSARs/profiles used to derive the PMT scores are not developed for these kind of chemicals. An example is lead (CAS number: 7439-92-1). When the CAS number of an inorganic compounds is used as input, the alert in Figure 4 will be shown.

Figure 4 Alert shown for inorganic compounds.

Search one substance

When searching for one CAS number, the tool will provide the following output:

- the searched CAS-number
- (one of) the substance name(s)
- If available, a link to more detailed substance information

- the overall PMT-score
- the individual P, M and T-scores
- a smiley that indicates the height of the-scores: low to moderate (green smiley), high (orange smiley) and very high (red smiley)
- an explanation for the basis of the overall PMT-score and the individual P, M and T-scores.
  - o the explanation for overall PMT-score and the T-score is static, i.e. the same for all substances
  - o the explanation for the P and M-score are parametrized, i.e. provide information for that specific substance.

Figure 5 gives an example of this output for the substance trifluoracetic acid.

Figure 5 Output for trifluoroacetic acid. Below this output, an explanation of the smileys and the structural formula is given .

If a substance is a Dutch Substance of Very high Concern (in Dutch: Zeer Zorgwekkende Stof), this will be shown as an alert on top of the results section, see Figure 6. For details on this class of substances, we refer to https://rvs.rivm.nl/onderwerpen/zeer-zorgwekkende-stoffen (in Dutch).

Figure 6 Alert message shown if the searched substance is a Dutch Substance of Very High Concern (or Zeer Zorgwekkende Stof in Dutch).

Search a batch of substances

The output for the batch search includes the same information as the single substance search, except for the explanation on the P, M and T-scores. A link to get that information per substance is included. There is also the possibility to download the output of the batch search as a CSV file. Figure 7 shows the output for applying the screening tool to trifluoracetic acid and 1,4-dioxane.
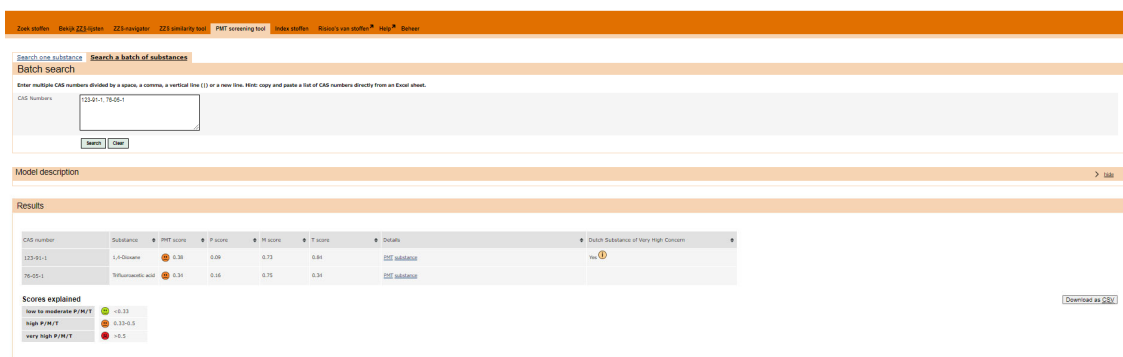
Figure 7 Output of the batch search for trifluoracetic acid and 1,4-dioxane.

Interpretation of output

It should be noted that a low or high PMT-score is only a first indication that the substance is of potential low or high concern (for having PMT properties). The higher the overall PMT-score, the higher the possibility that the substance is indeed a concern for PMT. The screening approach should be used as a first step, which needs to be followed by further investigation of the properties .

The follow-up can, for instance, include collection of emission data and/or experimental data on persistence, mobility and/or toxicity. When evaluating the presented output, it is advised to not only look at the smiley indicators but to pay attention to the underlying-scores.

Finally, it should be noted that a prediction of a low PMT concern (or absence of any prediction) does not mean that this substance can be used safely. Other effects or properties might not be included. Substances with high P and/or T-scores, but low M-scores, might still be of potential concern for human and/or the environmental health, e.g. because of persistent, bioaccumulative and toxic (PBT) properties or Carcinogenic, Mutagenic and/or Reprotoxic (CMR) properties.

Scoring contaminants on their potential persistence (P)

The P-score is based on the estimated half-life in freshwater using the BIOWIN3 model of EPISuite™. The output of BIOWIN3 was converted to a continuous estimate of half-lives in water using the approach introduced by Rorije et al. (2011). Next a sigmoid function was constructed that transforms the half-life in freshwater in days to a value between 0 and 1, so that persistent substances with a half-life between 40 and 60 days in freshwater get-scores between 0.33 and 0.5, whereas very persistent substances with a half-life in excess of 60 days get a-score of 0.5 or higher. The benchmark values of 40 and 60 days were chosen based on the criteria for persistent (half-life in surface water ≥ 40 days) and very persistent (half-life in surface water ≥ 60 days) substances according to Annex XIII of REACH. The P-score thereby indicates a substance's potential to persist in the aquatic environment on a scale from 0 to 1.

Scoring contaminants on their potential mobility (M)

The M-score is based on the substance's organic carbon/water partition coefficient (Koc) using the KocWIN model of EPISuite™. Mirroring the persistence scoring approach described above, a sigmoid function was constructed that covers the degree of fulfilment of the mobility criterion as a function of log Koc. The sigmoid function was constructed using benchmark values for mobile and very mobile substances. Here, mobile substances are substances with an estimated log Koc of 3 or lower (i.e. a-score of 0.33), whereas very mobile substances have a log Koc of 2 or lower (i.e. a-score of 0.5 or higher). For details see Hartmann et al. (2023).

Scoring contaminants on their potential toxicity (T)

The T-score was based on the indicators for five human health endpoints: carcinogenicity (c), mutagenicity (m), reprotoxicity (r), endocrine disruption (ED) and general repeated dose systemic toxicity. Structural alerts for these endpoints taken from the OECD QSAR Toolbox™ and Toxtree™ were used as indicators of potential human toxicity. Substance similarity values to Substances of Very High Concern (SVHC) with c, m and/or r properties were also included. Transformation functions were developed to translate the presence of alerts and similarity to the existing SVHCs to values between 0 and 1. Subsequently, all values were also aggregated to an overall T-score, again ranging from 0 to 1. For details see Hartmann et al. (2023).

Overall PMT-score

The overall PMT-score is calculated using the following equation:

$$\mathrm{PMT} - \mathrm{score} = P - \mathrm{score}^{a} * M - \mathrm{score}^{b} * T - \mathrm{score}^{c}$$

where the sum of the weights (∑a,b,c) should be 1. Here, we used equal weights: a=1/3 , b=1/3 and c=1/3.