**FIMIM scoring tool**

Version 1.4

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**Functionality**

This software is used to post-process eTOX database extractions, like those produced by the FIMIM Extraction tools, and produce a QSAR like table, assigning to individual compounds an score representing a certain toxicity endpoint. This score is built by combining the LOEL of a set of findings that the end user must provide as input and which are frequently present in compound positive for this toxicity endpoint. The tool produces the scores in standard tabular formats. In addition a simple graphic generation tool is also included in the package, mainly for debugging purposes.

**Output interpretation**

The scores values indicates the minus logarithm of the minimum dose for which any of the findings associated with the endpoint has been observed, in the provided eTOX database extraction.

**Installation**

The scoring tool is distributed as a self-contained multiplatform package and requires no specific installation. The only pre-requisites are:

* Java Development Kit (JDK) or Java Runtime Environment (JRE) 8 needs to be installed and the java executable must be available in the user PATH. Please refer to https://www.java.com for instructions on how to install these in your platform
* An environment variable called *SCORING\_HOME* must point to the installation path of the scoring tool

**Use**

The tool is run from the command prompt, typing "scoring". The command gives separate access to the three main tool functionalities:

* *scoring endpoints*, for summarizing the findings into a single LOEL value
* *scoring pktransform*, for applying the minus logarithm transform, plus the encoding of non-finding as 0
* *scoring chart*, for generating basic charts of the output results

This command can be executed in sequence, using the output of the previous command as input of the following. The second and third call are optional. A full description of these commands is provided below.

In addition the package provides a convenience script (*scend*) which runs all three above scoring calls using a single command call. Users are encouraged to customize it to meet their own specific requirements.

**Command "endpoints"**

*$SCORING\_HOME/scoring endpoints --findingsLOEL <findings\_file\_etox> --endpoints <endpoints\_definition\_file> --output <endpoints\_file>*

|  |  |
| --- | --- |
| *--findingsLOEL <findings\_file\_etox>* | The <findings\_file\_etox> is a file produced by the FIMIM eTOX database extraction tool. Two examples can be found in the “examples” folder: *histopat\_rat.tsv* and *histopat\_dog.tsv* |
| *--endpoints <endpoints\_definition\_file>* | The <endpoints\_definition\_file> describes a collection of findings (from those represented as columns in the <findings\_file\_etox> file) associated to a certain endpoints. Two examples can be found in the “examples” folder: *steatosis.tsv* and *endpoints.tsv*  The <endpoints\_definition\_file> has a single finding per row, annotated with a 1 or a 0 if it is associated or not with the endpoint, respectively. |
| *--output <endpoints\_file>* | The <endpoints\_file> is the output generated by the command. In this file the findings LOEL (input columns) of the input are replaced with the endpoints LOEL (output columns). The LOEL of an endpoint is the minimum LOEL found for any of the findings associated with the endpoint, as defined in the <endpoints\_definition\_file> above. |

Example:

*$SCORING\_HOME/scoring endpoints --findingsLOEL histopat\_rat.tsv --endpoints steatosis.tsv --output histopat\_rat\_endpoints.tsv*

**Command "pktransform"**

*$SCORING\_HOME/scoring pktransform --endpointsLOEL <endpoints\_LOEL\_file> --output <pks\_LOEL\_file>*

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| --- | --- |
| *--endpointsLOEL <endpoints\_LOEL\_file>* | The <endpoints\_LOEL\_file> is the output file obtained with the "*scoring endpoints*" command (previous command). |
| *--output <pks\_LOEL\_file>* | The <pks\_LOEL\_file> is the output generated by the command. In this file the LOEL values are transformed as minus logarithm and the absence of any finding is encoded as a zero. |

Example:

*$SCORING\_HOME/scoring pktransform --endpointsLOEL histopat\_rat\_endpoints.tsv --output histopat\_rat\_endpoints\_pk.tsv*

The call generates a simple screen output summarizing the number of compounds and some statistics for the endpoints:

*Processed 859 compounds*

*steatosis\_score: 107 positive (12.456%), 1.7 min, 7.0 max, average 0.51*

**Command "chart"**

*$SCORING\_HOME/scoring chart --pks <pks\_LOEL\_file>*

|  |  |
| --- | --- |
| *-pks <pks\_LOEL\_file >* | The *<pks\_LOEL\_file*> is the output of the “*scoring pktransform”* command (previous command)  This command generates an html file (*index-[random-number].html*) containing two charts: a pie chart with positive/negative compounds for the endpoint and a histogram of the distribution of minus logarithm values for the endpoint. The file is automatically shown using the default Internet browser. If no default browser is defined the html file must be opened manually. |

Example:

*$SCORING\_HOME/scoring chart --pks histopat\_rat\_endpoints\_pk.tsv*

**Convenience script "scend"**

*$SCORING\_HOME/scend <file\_LOEL> <file\_endpoints> [-chart]*

This convenience script executes the three previous commands in sequence

|  |  |
| --- | --- |
| *<findings\_file\_etox>* | The <findings\_file\_etox> is a file produced by the FIMIM eTOX database extraction tool. Two examples can be found in the “examples” folder: *histopat\_rat.tsv* and *histopat\_dog.tsv* |
| *<endpoints\_definition\_file>* | The <endpoints\_definition\_file> describes a collection of findings (from those represented as columns in the <findings\_file\_etox> file) associated to a certain endpoints. Two examples can be found in the “examples” folder: *steatosis.tsv* and *endpoints.tsv* |
| ***-****chart* | Optional flag. If present the script will output the charts described in the “*scoring chart*” command. |

Examples:

*$SCORING\_HOME/scend histopat\_rat.tsv steatosis.tsv*

*$SCORING\_HOME/scend histopat\_rat.tsv steatosis.tsv -chart*