



HAWC (HEALTH ASSESSMENT WORKSPACE COLLABORATIVE): A MODULAR WEB-BASED INTERFACE TO FACILITATE DEVELOPMENT OF HUMAN HEALTH ASSESSMENTS OF CHEMICALS

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ABSTRACT

HAWC (<https://hawcproject.org/>) is a modular, cloud-ready, content-management system to synthesize multiple data sources into overall human health assessments of chemicals. Developed in collaboration with EPA/NCEA, this system integrates and documents the overall workflow from literature search and review, data extraction and evidence synthesis, dose-response analysis and uncertainty characterization, to creation of customized reports. Crucial benefits of such a system include improved integrity of the data and analysis results, greater transparency, standardization of data presentation, and increased consistency. By including a web-based workspace for assessment teams who can collaborate on the same assessment rather than share files and edits, and a complementary web-based portal for reviewers and stakeholders, all interested parties have dynamic access to completed and ongoing assessments.

HAWC is a prototype website actively under development, feedback is appreciated. Create an account at: <https://hawcproject.org>

RATIONALE AND OBJECTIVES

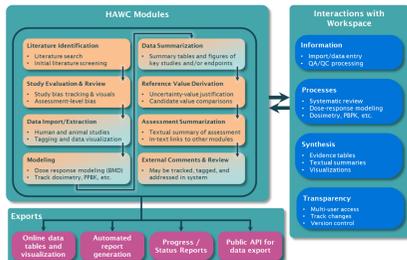
There is a need for increased transparency in the development of human health assessments of chemicals (NRC 2011). HAWC is designed to assist in creating human health assessments of chemicals and displaying the information through an interactive interface that provides access to data, analyses, summaries and supplementary information. Our overall objective is to create a web-based workspace to create, store, share, and display data and analyses by enabling:

- Team collaboration where multiple users can work together on a single assessment using the same datasets
- Automated data presentation, and standardizing the process of building an assessment, based on existing guidance
- Modular architecture based on key components in assessment process such as literature search, data-extraction, synthesis, and reference-value
- Integration with existing tools (BMD5) and information (HERO, ACTOR, etc.)
- Tracking changes over the course of the project, including revisions after review
- Stakeholder participation via engagement, participation, and diving into the details

HAWC makes the process of developing human health assessments TRANSPARENT.

OVERALL FRAMEWORK

HAWC is designed as a collection of modules, with each module being designed to track a key step in the human-health assessment of chemicals. Modules are interconnected, that is, changes in one module are reflected in other modules. Currently HAWC is designed to present animal bioassay data; updates to include other data-types are in-development.

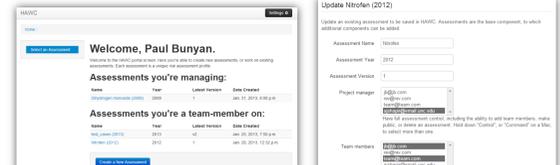


Key modules were using upon the IRIS executive summary framework, as critical components of a human health assessment (EPA 2013). Modules in orange have preliminary prototypes modules, with darker orange for more detailed prototypes.

As a test-case for the application of HAWC, we are using the previously-published EPA PPRTV (provisional peer-reviewed toxicity value) Nitrofen assessment (EPA 2012b). Examples shown here and on the website present results adapted from this assessment.

ASSESSMENT AND PERMISSIONS

HAWC is designed for teams of users to collaboratively work on one or more independent chemical assessments, with multiple layers of access. Users login to personalized login screens to view all assessments which they have access to.



Levels of access:

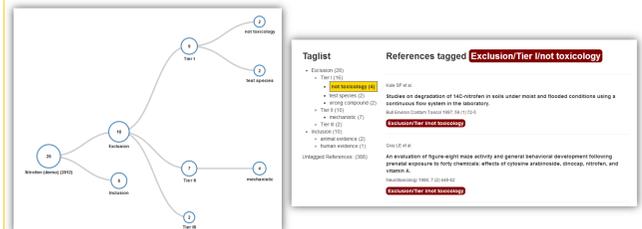
- Project managers: change permissions settings, including who can edit assessment content and which modules are enabled
- Team-members: add, edit, and delete content
- Reviewers: view assessment and potentially add comments which assessment is not yet public
- Public: if a project manager makes an assessment public, the general-public can view and potentially add comments (if commenting is enabled)

MODULES AND EXAMPLE WORKFLOWS

LITERATURE SEARCH AND INITIAL SCREENING

PubMed Literature Search interface showing search results for Nitrofen. Includes search criteria, results for queries, and a demo link for search queries.

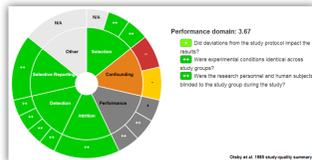
Initial literature screening tags interface. Shows a list of tags for current reference and a detailed view of a tag, including exclusion and tier information.



Example dendrogram visualization of reference tags for an assessment, and the number of references with each tag. The size of circle is area-weighted to the relative number of references with the specified tag. The interactive version allows for clicking on any circle to examine all references with this tag. To the right, the same data are presented in tabular format, showing all references and in an assessment. Searching by reference is also available (link below). Demo links: Visualization | Tabular Format | Reference Search

STUDY EVALUATION AND REVIEW

A key step in the review process of studies is clearly displaying study-evaluation criteria and justification for which studies are to be included in the assessment. Following many principles from the OHAT Systematic Review framework (2013a), HAWC displays study quality information for studies in an assessment.



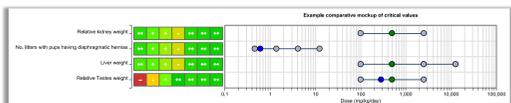
Study summary of bias. Individual-study summary bias, presented by metric and organized by domain. Detailed notes on scoring justification can also be saved for each individual score. Live link



Comparative analysis of bias. Interactive figure shows all studies evaluated in assessment and assigned score for metric; by clicking on a row/column score and detailed justification for each study or metric is presented. Live link



Assessment-level bias summary. Presents overall bias for assessment, including ratings for all evaluated studies (consistent with OHAT 2013b). Live link



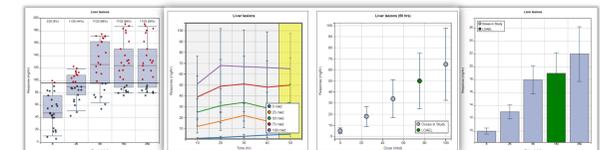
Study-quality integration with dose-response information. Subset of endpoints can be viewed, displaying both critical effect levels and study-quality metrics. Live link (under development)

DATABASE AND VISUALIZATIONS

Two methods for loading assessment content:
1. Import from existing database (in-development)
2. Manually enter data from HAWC interface

Database and visualizations interface showing subchronic rats, available animal groups, female rats, dosing regime, and liver weight endpoint details with a plot.

Animal bioassay data. A subset of references reviewed in the literature search will require quantitative data to be extracted for the assessment. Each reference may have multiple experiments (top-left). An experiment may consist of multiple animal groups, or sets of comparable animals (bottom-left). Relationships can also be saved across animal groups, which is required for reproductive and developmental studies (parent, children, siblings, etc.). Finally, multiple dose-response endpoints can be saved for each animal group. Standardized tags can also be applied to endpoint datasets for easier searching (right). Demo links: Experiment | Animal Group | Endpoint | Endpoint Search



Dose-Response Dataset Visualization. Individual dose-response data can be visualized in multiple ways. If individual animal data are available, a boxplot is shown. If multiple time-points were collected for the same dataset, dose-response at each time point can be viewed interactively. Finally, bar- and scatter-plots are available. All visuals can be downloaded. Demo links: Boxplots | Dose+Response+Time Plots | Dose-Response Plot | Dose-Response Barchart

REPORTS AND COMMENTING

Reports and commenting interface showing animal studies, provisional value derivation, and summary reports for Nitrofen.

Summary Reports Previous modules shown here demonstrate HAWC enabling users to display individual data and decisions made in the process of human-health assessment of chemicals. The summary report module allows users to create a web-report which summarizes conclusions from the assessment. Headers and sub-headers can be created, similar to a standard report. However, "smart-tags" can dynamically link text to other HAWC components, such as study-quality visualizations, endpoint details, or endpoint-aggregations (see inserts above). The result is a data-driven report which summarizes key findings but allows users to view further details easily, instead of referring to appendices. Demo link: Nitrofen Summary Report (demonstration-only)

Commenting interface showing a comment summary for a specific assessment, including user information and comment text.

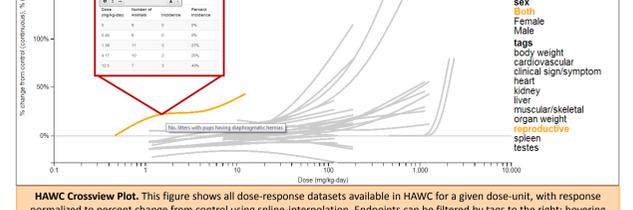
If commenting is enabled for an assessment, logged-in users can post comments on specific portions of an assessment. These comments can be applied to a particular study, endpoint, endpoint-aggregation, etc. Alternatively, comments can be targeted to specific headers or subheaders of summary-text (shown above). Visibility of comments can be controlled on an assessment-level basis, making all comments publically viewable, or viewable only to team-members. Demo links: Comments Report | Study comment

DATA SUMMARIZATION

Data summarization interface showing uncertainty factor values, summary text, and customizable endpoint comparisons.

Uncertainty factor derivation. NRC 2011 candidate reference values recommended evaluation of multiple critical effects and proposed uncertainty factors applied. This figure presents uncertainty factors for key effects. Live link

Customizable endpoint comparisons. Collections of endpoints can be displayed in multiple formats with customizable text (based on NTP MetaDataViewer Software). Demo links: Forest-plot (top) | Data Pivot Example (bottom)



HAWC Crossview Plot. This figure shows all dose-response datasets available in HAWC for a given dose-unit, with response normalized to percent change from control using spline-interpolation. Endpoints can be filtered by tags to the right, hovering shows tags associated with that curve. Clicking shows endpoint details, as shown in the overlay. Live link

DOSE-RESPONSE ASSESSMENT BY BENCHMARK DOSE MODELING

BMD modeling setup interface showing model options, BMD modeling setup, and BMD modeling results.

BMD modeling setup All dose-response datasets in HAWC are available for BMD modeling. HAWC uses a recomputed version of BMD 2.40, with all BMDs 2.40 input options available. The figures to the right show a dataset to be modeled, and individual model customization for dataset. Demo link: BMD Model Setup

Modeling Results Full BMDs model outputs are available including detailed output files. Multiple model-fits can be visually compared to the dose-response datasets to assist in BMD model selection. Demo link: BMD Model Results

Model Selection Recommendations interface showing BMD model recommendations to assist in model selection, based on EPA guidance and recommendation logic in ICF International's BMD5 Wizard (ICF International 2013, US EPA 2012).

Model Selection Recommendations BMD model recommendations assist the user in model selection, based on EPA guidance and recommendation logic in ICF International's BMD5 Wizard (ICF International 2013, US EPA 2012). Recommendation logic is fully customizable and consistent for all endpoints in an assessment. Demo link: BMD Model Recommendations

Quality Assurance

Provides quality of assessment generation through multiple levels of quality assurance.
1. Internally, source-code tracking using GIT software version-control. Unit-testing framework applied when developing new functionality in HAWC (write test-cases and ensuring that these cases work; ensure that adding new features don't break existing features).

Source-code tracking in GIT Each row represents a "commit", or incremental change to the source-code. Specifics on what changed are shown line-by-line in red and green for deletions and insertions, respectively.

2. Tracks keys changes to all data stored in HAWC. All changes to text and objects stored in HAWC are saved in the database, including who changed the content and at what time. Team-members with editing access to the can view these incremental changes, to see how content has evolved over time.

Prior Versions of Subchronic candidate reference values interface showing comparison and version list of assessment data.

Object versioning Changes made to key components in the HAWC database (study-quality information, endpoints, uncertainty-values, endpoint-aggregations, etc.) are tracked in the database, and line-by-line changes across versions can be reviewed. Version viewing is only available to team-members who are able to edit these objects for a particular assessment.

3. Provide mechanisms for both public and internal review. Comments can be posted by the general public and/or expert reviewers. These comments can then be processed internally, and may also be made available to the public for transparency.

FUTURE WORK

- Expansion of the prototype modules, including more flexible visualizations, tables, and reports
- Incorporation of additional datastreams critical to a chemical health assessment including epidemiological information and in-vitro datasets
- Importing abilities to load data from other data sources
- Expanding exporting functionality include improved and expanded Microsoft Word® reports, and Microsoft Excel® exports

TECHNOLOGIES USED

- Diango Web Framework (Python)
- Diango REST Framework (Python)
- PostgreSQL (Database)
- Memcached (Caching)
- jQuery & jQuery UI (Javascript)
- D3.js (Javascript Visualization)
- Inkscape (SVG conversion)
- GIT & Bitbucket (software version control)

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DISCLAIMER: The views expressed are those of the authors and do not necessarily represent the views and/or policies of the U.S. Environmental Protection Agency or NTP/NIHES.

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