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

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Poster | Website

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.
- Integrates and documents workflow from literature search and review, to data extraction, evidence synthesis through visualization tools, dose-response analysis, uncertainty characterization, and customized reports.
- Improve integrity of the data and analysis results, greater transparency, standardization of data presentation, and increased consistency.
- Interested parties, including reviewers and stakeholders, have dynamic access to completed and ongoing assessments.
- Creates a clear and concise summary of the results of the assessment, enables online access to literature review, source primary data and/or tabulated study summaries and visual aids that constitute the scientific justification for the assumptions and conclusions.

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

Compatible browsers:
Chrome* | IE 9+
Safari | Firefox
*Recommended browser

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 database
- **Modular architecture** based on key components in assessment process such as literature search, data-extraction, synthesis, and reference-value
- **Integration** with existing tools (BMDS) and information (HERO, PubMed, 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.
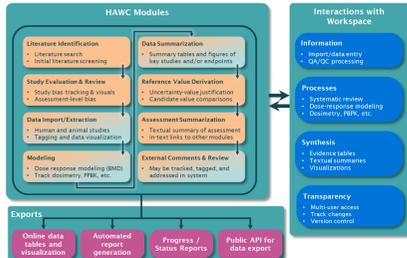
Key modules were upon using the IRIS executive summary framework, as critical components of a human health assessment (EPA 2013). Modules in orange have preliminary prototypes modules, with darker orange for more detailed prototypes.

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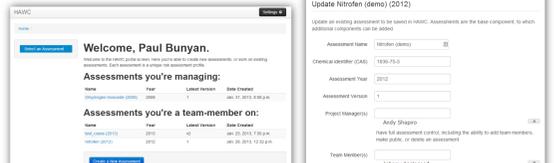
Levels of access:
- **Project managers:** change permissions settings, including who can edit assessment content and which modules are enabled
- **Team-members:** add, edit, and delete content
- **Reviewers:** view assessment and potentially add comments which assessment is not yet public
- **Public:**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

MODULES AND EXAMPLE WORKFLOW

LITERATURE SEARCH AND STUDY BIAS ASSESSMENT

PubMed search and import
Literature searches on PubMed can be conducted internally from HAWC using search terms which can be tracked. HAWC searches PubMed and imports all matches for tagging and screening of relevant data to include/exclude in assessments. Literature can also be imported by specifying PubMed/HERO identifiers and can be tagged for initial study inclusion/exclusion.

Demo link: **Search Queries** | **Reference Search**

Literature screening tags and visualizations
Literature available in HAWC can be evaluated and assigned to custom assessment-specific tags which detail notes for inclusion, exclusion, or other categories specific to an assessment. Multiple tags can be added to each reference, and links to the original resource are also available. Visualizations of the literature database for an assessment are created, and references can easily be identified for further inclusion in an assessment.

Demo links: **Dendrogram** | **Tabular Format (left)**

Study summary and bias. Following many principles from the NTP/OHAT Systematic Review Framework (2013a), metrics can be created and organized by domains for assessment of study bias. Detailed notes on scoring justification can also be saved for each individual score. This module is optional. **Link (above)** | **Details**

Comparative bias analysis. Interactive figure, presenting multiple studies evaluated in an assessment and details for study bias across multiple metrics. By clicking on any row, cell, or column, detailed describing the justification for each metric across studies can be displayed. **Link (above)** | **Summary Plot**

Study-quality integration with dose-response information. This visualization demonstrates how data are shared across modules. A subset of references reviewed in an assessment can be presented in the figure above, with details on study bias associated with each endpoint. **Live link (under development)**

ANIMAL BIOASSAYS

Two methods for loading content:
1. Import from existing database
2. Manually enter data from HAWC interface

Data can be entered into HAWC either manually or via an import. After import or entry of HAWC data, it can be used throughout other HAWC modules.

Animal bioassay data. A subset of references reviewed in the literature search will require quantitative data to be extracted for the animal bioassay. 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. Dose-response data can be visualized in multiple ways. If individual animal data are available, a boxplot can be presented (left). In the center, a collection of related endpoints are presented together, showing LOAEL, doses-tested, and BMD estimates for the selected value. Finally, bar-charts showing statistical significance can also be shown. All visuals are downloadable as SVG, PNG, PDF, or PowerPoint slides for use offline as well..

Demo links: **Boxplots** | **Endpoint Aggregation** | **Dose-Response Plot** | **Dose-Response Barchart**

EPIDEMIOLOGICAL STUDIES

Epidemiological data. When human exposure-data are available, epidemiologic data can be entered into HAWC for display and inclusion in reports. Demographics on the study population and individual exposure-groups can be saved. In addition, odds ratios, relative risks, and other quantitative and qualitative metrics for assessed outcomes can be saved and presented for an assessment. The figures above show epidemiological data, adjustment factors tested and applied to the data, and adjusted odds ratios for multiple exposure groups.

Database schema. A figure presenting the database schema for storing epidemiology information is shown above. Demographic information can be stored on both the study population as a whole and for individual exposure groups.

Results aggregation. A summary of multiple related effects are shown above, using the HAWC data-pivot feature. Relevant endpoints can be filtered and sorted, and then exposure effects can be viewed. These interactive visualizations also allow for further exploration for the data; clicking a study name will show the study-summary and risk-of-bias, and clicking an individual outcome will show details on adjustment factors and results from all exposure groups.

REPORTS AND COMMENTING

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 uses to create a web-report which summarize 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-bias visualizations, endpoint details, or endpoint-aggregations (see image above). The result is a data-driven report which summarizes key findings but allows uses to view further details easily, instead of referring to appendices.

Demo link: **Nitrofen Summary Report (demonstration-only)**

Commenting
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 a assessment-level basis, making all comments publically viewable, or viewable only to team-members.

Demo links: **Comments Report** | **Study comment**

DATA SUMMARIZATION

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 critical non-cancer effects. **Live link**

Customizable endpoint comparisons. Collections of endpoints can be displayed in multiple ways, with customizable text (based on NTP MetaDataViewer Software).

Demo links: **Feature demo (top)** | **Nitrofen Example (bottom)**

HAWC Crossview Plot. This figure shows all dose-response datasets in a HAWC assessment 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, available in the overlay. **Live link**

### DOSE-RESPONSE ASSESSMENT BY BENCHMARK DOSE MODELING

BMD modeling setup
All animal bioassay dose-response datasets in HAWC are available for BMD modeling. HAWC uses a recompiled version of BMDS 2.40 (for the Linux operating system), 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. The impact of selecting different BMR values can also be examined visually using this approach.

Demo link: **BMD Model Results**

Model Selection Recommendations
BMD model recommendations assist the user in model selection, based up on EPA guidance and recommendation logic in ICF International's BMDS 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 ensure that these cases work; ensure that adding new features don't break existing features [regression testing].
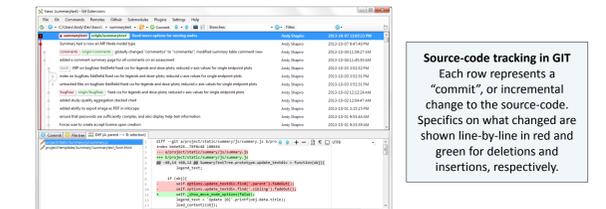
   Source-code tracking in GIT
   Each row represents a "commit", or incremental change to the source-code. Specifics on what changed are shown line-by-line in red and green for deletions and insertions, respectively.

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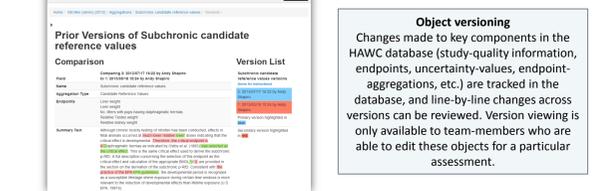
   Object versioning
   Changes made to key components in the HAWC database (study-quality information, endpoints, uncertainty-values, endpoint-aggregations, etc.) are tracked in the database, and line-by-line changes across versions can be reviewed. Version viewing is only available to team-members who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

DATA EXPORT

- Data can be exported in Microsoft Excel® datasets or Microsoft Word® reports
- A browsable application programming interface (API) has also been developed for automatic computer-based querying and retrieval or results
- Capabilities and functionality can be expanded upon request
- Example download shown to the right. **Live link**

TECHNOLOGIES USED

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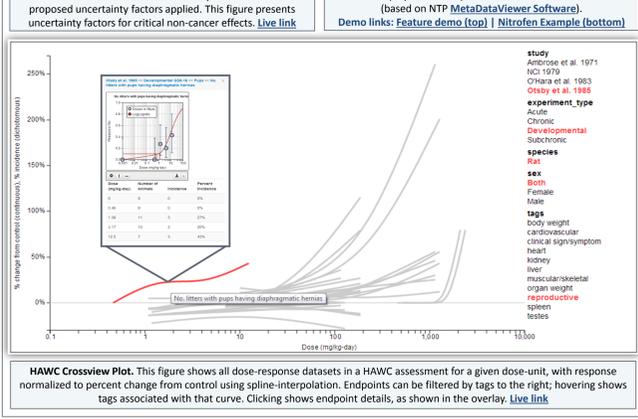- GIT & Bitbucket (software version control)

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