

APPENDIX D. HAWC USER GUIDE AND FREQUENTLY ASKED QUESTIONS

D.1 WHAT IS HAWC AND WHAT IS ITS PURPOSE?

The Health Assessment Workspace Collaborative (HAWC) is an interactive, expert-driven, content management system for human health assessments that is intended to promote transparency, trackability, data usability, and understanding of the data and decisions supporting an environmental and human health assessment. Specifically, HAWC is an interface that allows the data and decisions supporting an assessment to be managed in modules (e.g., study evaluation, summary study data, etc.) that can be publicly accessed online (see Section D.2 below and Figure D-1). Following the literature search and screening that are conducted using [HERO](#) and [DistillerSR](#), HAWC manages each study included in an assessment and makes the extracted information available via a web link that takes a user to a web page displaying study-specific details and data (e.g., study evaluation, experimental design, dosing regime, endpoints evaluated, dose-response data, etc., described in further detail below in Sections D.3 to D.6). Finally, all data managed in HAWC is fully downloadable using the blue “Download datasets” link (highlighted in the red box below) also located in the gray navigation bar located on the assessment home page (discussed in Section D.7). Note that a user may quickly navigate HAWC by clicking on the file path (highlighted in the orange, dashed box below) given in the gray row below the HAWC icon and menu bar (see Figure D-1). HAWC aims to facilitate team collaboration by scientists who develop these assessments and enhance transparency of the process by providing online access (no user account required) to the data and expert decisions used to evaluate potential human health hazard and risk of chemical exposures.

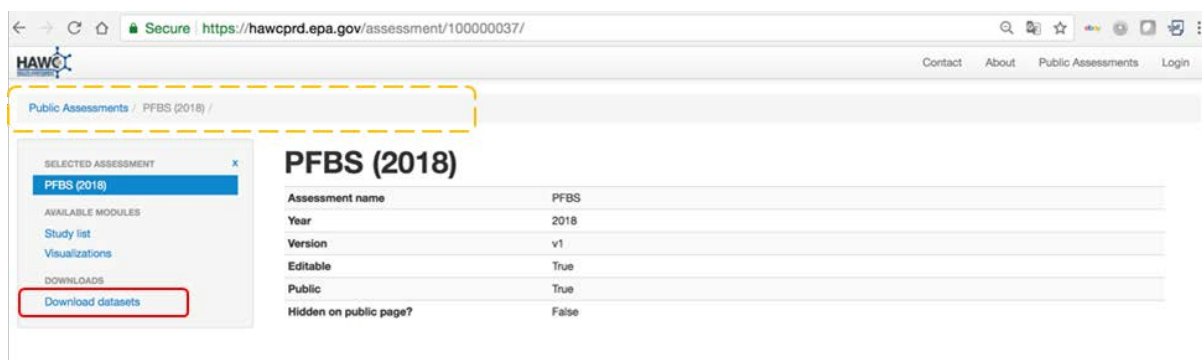


Figure D-1. HAWC Homepage for the Public PFBS Assessment

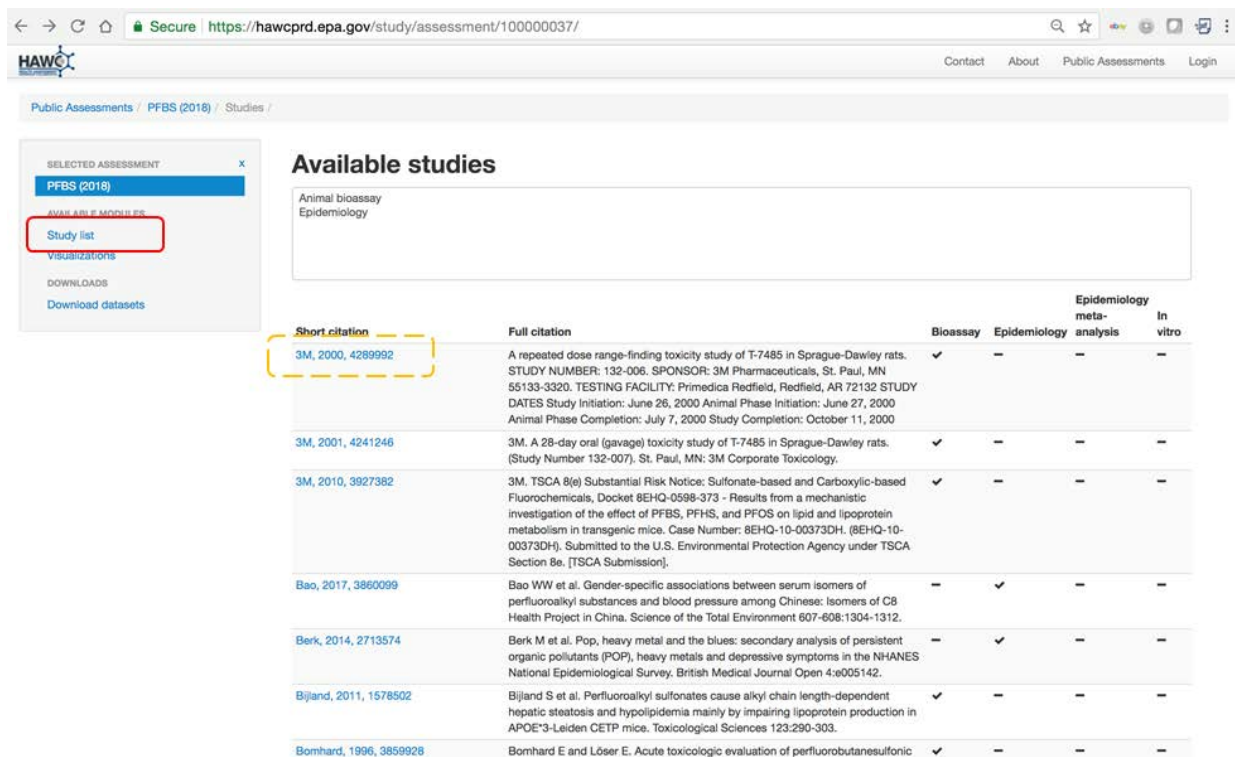
D.2 HOW DO I ACCESS HAWC?

HAWC is an open-source, online application that may be accessed using the following link—<https://hawcprd.epa.gov/assessment/public/>—and then selecting an available assessment. The following browsers are fully supported for accessing HAWC: Google Chrome (preferred), Mozilla Firefox, and Apple Safari. There are errors in functionality when viewed with Internet Explorer. No user account is required for access to public HAWC assessments. The assessments located in HAWC are meant to accompany a textual expert synthesis of the data managed in HAWC. Each written assessment document contains embedded URL links to the evidence in HAWC (e.g., study evaluation, summary study data, visualizations, etc.) supporting

the assessment text. The links embedded in an assessment document can be accessed by a mouse click (or hover while pressing CTRL + right click).

D.3 WHAT CAN I FIND IN HAWC?

HAWC contains a comprehensive landscape of study details and data supporting an assessment. Note that links are provided in the assessment text to guide the reader, but a user may also navigate to the HAWC homepage for an assessment on their own. Once a user lands on an [assessment homepage](#), all studies included in an assessment can be viewed by clicking the blue “[Study list](#)” link (highlighted in the red box below) in the gray navigation pane (see Figure D-2). By clicking the study name listed in blue (under “Short citation”) a user can view the full study details, study evaluation, and experimental details and data. For example, in Figure D-2, a user may click on “3M, 2000, 4289992” (highlighted in the orange, dashed box below). This will take the user to the [3M \(2000d\)](#) study details page that includes a link to the study in [HERO](#) along with study details, study evaluation, and available experimental (animal) and study population (epidemiologic) groups.



Short citation	Full citation	Bioassay	Epidemiology	meta-analysis	In vitro
3M, 2000, 4289992	A repeated dose range-finding toxicity study of T-7485 in Sprague-Dawley rats. STUDY NUMBER: 132-006. SPONSOR: 3M Pharmaceuticals, St. Paul, MN 55133-3320. TESTING FACILITY: Primedica Redfield, Redfield, AR 72132 STUDY DATES Study Initiation: June 26, 2000 Animal Phase Initiation: June 27, 2000 Animal Phase Completion: July 7, 2000 Study Completion: October 11, 2000	✓	-	-	-
3M, 2001, 4241246	3M. A 28-day oral (gavage) toxicity study of T-7485 in Sprague-Dawley rats. (Study Number 132-007). St. Paul, MN: 3M Corporate Toxicology.	✓	-	-	-
3M, 2010, 3927382	3M. TSCA 8(e) Substantial Risk Notice: Sulfonate-based and Carboxylic-based Fluorochemicals, Docket BEHQ-0598-373 - Results from a mechanistic investigation of the effect of PFBS, PFHS, and PFOS on lipid and lipoprotein metabolism in transgenic mice. Case Number: BEHQ-10-00373DH. (BEHQ-10-00373DH). Submitted to the U.S. Environmental Protection Agency under TSCA Section 8e. [TSCA Submission].	✓	-	-	-
Bao, 2017, 3860099	Bao WW et al. Gender-specific associations between serum isomers of perfluoroalkyl substances and blood pressure among Chinese: isomers of C8 Health Project in China. Science of the Total Environment 607-608:1304-1312.	-	✓	-	-
Berk M et al. Pop, heavy metal and the blues: secondary analysis of persistent organic pollutants (POP), heavy metals and depressive symptoms in the NHANES National Epidemiological Survey. British Medical Journal Open 4:e005142.		-	✓	-	-
Bijland, 2011, 1578502	Bijland S et al. Perfluoroalkyl sulfonates cause alkyl chain length-dependent hepatic steatosis and hypolipidemia mainly by impairing lipoprotein production in APOE*3-Leiden CETP mice. Toxicological Sciences 123:290-303.	✓	-	-	-
Bornhard, 1996, 3859928	Bornhard E and Löser E. Acute toxicologic evaluation of perfluorobutanesulfonic	✓	-	-	-

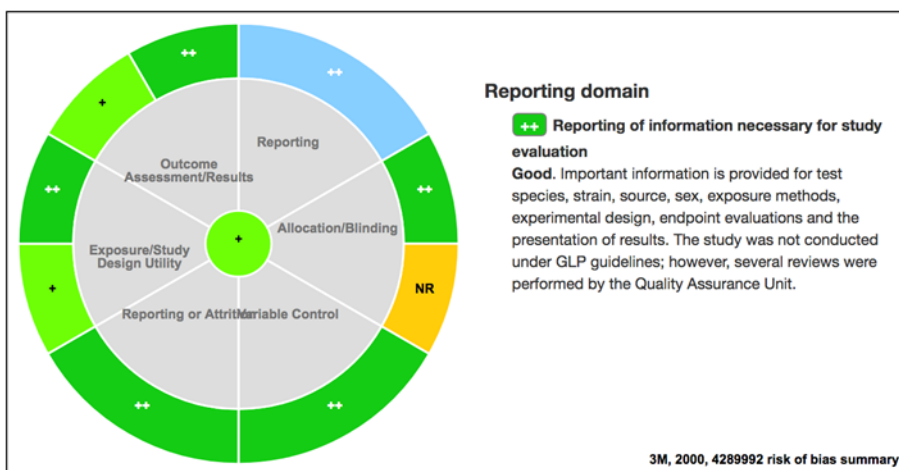
Figure D-2. Representative Study List

D.4 HOW DO I ACCESS STUDY EVALUATION(S)?

Study evaluation is performed to ensure that the studies used in the assessment are conducted in such a manner that the results are credible for each outcome and the ratings are outcome specific. The study evaluation criteria and decisions are fully documented in HAWC and displayed for each study on the study details page. Study evaluation is depicted as a pie chart with each domain and rating making up a piece of the pie that is colored according to the

rating. A user may hover over each piece of the pie, which causes rating metric text to populate to the right of the pie graph (see Figure D-3). For full domain and rating details the user may click the blue “[View details](#)” button (highlighted in the red box below). [Note that this example is given for the [3M \(2000d\)](#)].

Risk of bias visualization



[View details](#)

Figure D-3. Representative Study Evaluation Pie Chart with the Reporting Domain Selected and Text Populating to the Right of Pie Chart

D.5 HOW DO I ACCESS STUDY-SPECIFIC INFORMATION ON EXPERIMENTAL AND STUDY POPULATION DETAILS AND EXTRACTED ENDPOINT DATA?

Specific information on experimental design, dosing (if animal bioassay), outcomes and exposure (if epidemiology), and extracted endpoint data can be accessed from the study details page by clicking on [for the [3M \(2000d\)](#) study] “[available animal bioassay experiments](#)” at the bottom of the study details page. A user may click on the experiment name (highlighted in blue, [10-day oral](#)) to view dosing/exposure details and available groups. Clicking on available animal groups (e.g., [male Sprague-Dawley](#) or [female Sprague-Dawley](#)) will take the reader to a new page with experimental group information (e.g., species/strain/sex, dosing regimen information, and available/additional endpoints information for animal studies; and outcome and exposure information for epidemiologic studies). If a study reports data, then the data are extracted and managed as “available endpoints.” If the study authors include endpoints in the methods and results but do not report data, the endpoint is listed under “additional endpoints” without dose-response data. All endpoints are also clickable and contain an endpoint description, methods, and (if data are reported) a clickable data plot (e.g., [alanine aminotransferase \[ALT\]](#)). The description of endpoints, methods, and data are often copied directly from the study report and, therefore, can contain study author judgments and may not necessarily include U.S. EPA judgments on the endpoint data that would be included in the assessment.

D.6 WHAT ARE VISUALIZATIONS AND HOW DO I ACCESS THEM?

The data managed in HAWC is displayed using visualizations that are intended to support textual descriptions within an assessment. All visualizations can be accessed using the blue “[Visualizations](#)” link (highlighted in the red box below) also found in the gray navigation pane (see Figure D-4A). *Note that the available visualizations are at the discretion of the chemical manager and are meant to accompany the assessment text.* Visualizations are fully interactive. Hovering and clicking on records in the rows and columns and data points on a plot will cause a pop-up window to appear (see Figure D-5B). This pop-up window is also interactive and clicking on blue text within this pop-up will open a new web page with descriptive data.



Figure D-4A. Visualization Example for PFBS
 (Note that the records listed under each column [study, experiment endpoint, units, study design, observation time, dose] and data within the plot are interactive.)

NTP 2018, 4309741 / 28 Day Oral / Male Harlan Sprague Dawley Rat / Tetraiodothyronine (T4), Free

Study Experiment Animal Group Endpoint

Endpoint name	Tetraiodothyronine (T4), Free
System	Endocrine
Organ	Thyroid
Effect	Hormone
Effect subtype	Thyroid Hormone
Observation time	Day 28
Data reported?	✓
Data extracted?	✓
Values estimated?	—
Location in literature	R07-Hormone Summary
Expected response adversity direction	any change from reference/control group
LOAEL	62.6 mg/kg-day
Monotonicity	not-reported
Statistical test description	Jonckheere (trend) and Shirley or Dunn (pairwise) tests
Trend result	not reported
Power notes	Statistical analysis performed by Jonckheere (trend) and Shirley or Dunn (pairwise) tests Statistical significance for a treatment group indicates a significant pairwise test compared to the vehicle control group Statistical significance for the control group indicates a significant trend test * Statistically significant at P <= 0.05 ** Statistically significant at P <= 0.01

Close

Figure D-4B. Example Pop-Up Window after Clicking on Interactive Visualization Links (In Figure D-4A, the red circle for study [NTP \(2019\)](#); male at a dose of 500 mg/kg-day was clicked leading to the pop-up shown above. Clicking on the blue text will open a new window with descriptive data.)

D.7 HOW DO I DOWNLOAD DATA SETS?

A user may download any available data set by first clicking on the blue “[Download datasets](#)” link (highlighted in the red box below) in the gray navigation pane on the assessment homepage. This takes the user to a new page where the desired data set may be selected for download as an Excel file (see representative image in Figure D-6).

The screenshot shows a web browser window with the URL <https://hawcprd.epa.gov/assessment/10000037/downloads/>. The page title is "PFBS (2018) downloads". On the left, a sidebar menu includes "SELECTED ASSESSMENT" (PFBS (2018)), "AVAILABLE MODULES" (Study list, Visualizations), and "DOWNLOADS" (Download datasets, highlighted with a red box). The main content area lists several data categories with "Download" buttons:

- Literature-review**: Download (Microsoft Excel spreadsheet)
- Study evaluation report**: Download (Microsoft Excel spreadsheet)
- Animal bioassay data**: Complete export, Endpoint summary (Microsoft Excel spreadsheet)
- Epidemiology data**: Download (Microsoft Excel spreadsheet)
- Epidemiology meta-analysis data**: Download (Microsoft Excel spreadsheet)
- In-vitro data**: Download (Microsoft Excel spreadsheet)
- Visualizations**: Visualizations can be exported into SVG, PNG, PDF, and PPTX formats; you can download each individual visualization when being viewed.

Figure D-5. Representative Data Download Page

D.8 HOW DO I ACCESS THE BENCHMARK DOSE MODELING OUTPUTS?

Benchmark dose (BMD) modeling is performed on an endpoint-by-endpoint basis at the discretion of the chemical manager. Those endpoints for which BMD modeling has been completed are referenced in the assessment text and are available for viewing. To access BMD modeling outputs the user can click on links included in the assessment text. Alternatively, the user may navigate to the BMD modeling outputs by clicking on a study [e.g., [Feng et al. \(2017\)](#)] of interest from the [study list](#), an available animal bioassay experiment (in this example, the [20-day oral gestation study](#)), an available animal group ([P₀ female ICR mice](#)), and an endpoint of interest ([tetraiodothyronine \[T₄\], free](#)). Next navigate to the blue “Actions” button, click, and scroll to “[View session](#)” (highlighted in the red box below) under BMD Modeling (see Figure D-7A). The [BMD setup](#), [results](#), and [model recommendation and selection](#) (highlighted in the orange, dashed box in Figure D-8B) are available for viewing. Selecting the BMD setup tab will display the modeled dose-response data, the selected models and options, and all benchmark modeling responses (BMRs). The results tab will display the BMD modeling output summary for all models. A user may hover over a selected model row to visualize the model fit to the data. In addition, a user may obtain the Benchmark Dose Software (BMDS) output text by clicking the “View” button under the “Output” column for each model that was run. The “Model recommendation and selection” tab displays all models, warnings when appropriate, and the recommendation for which models are valid, questionable, or failed to fit.

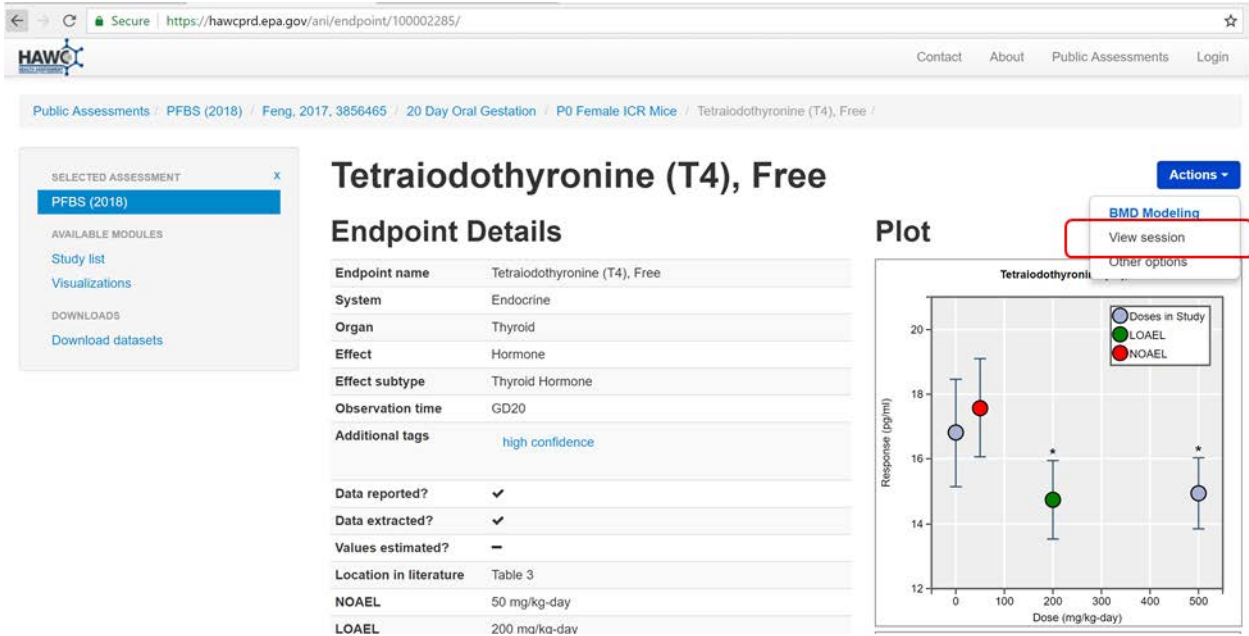


Figure D-6A. Example BMD Modeling Navigation

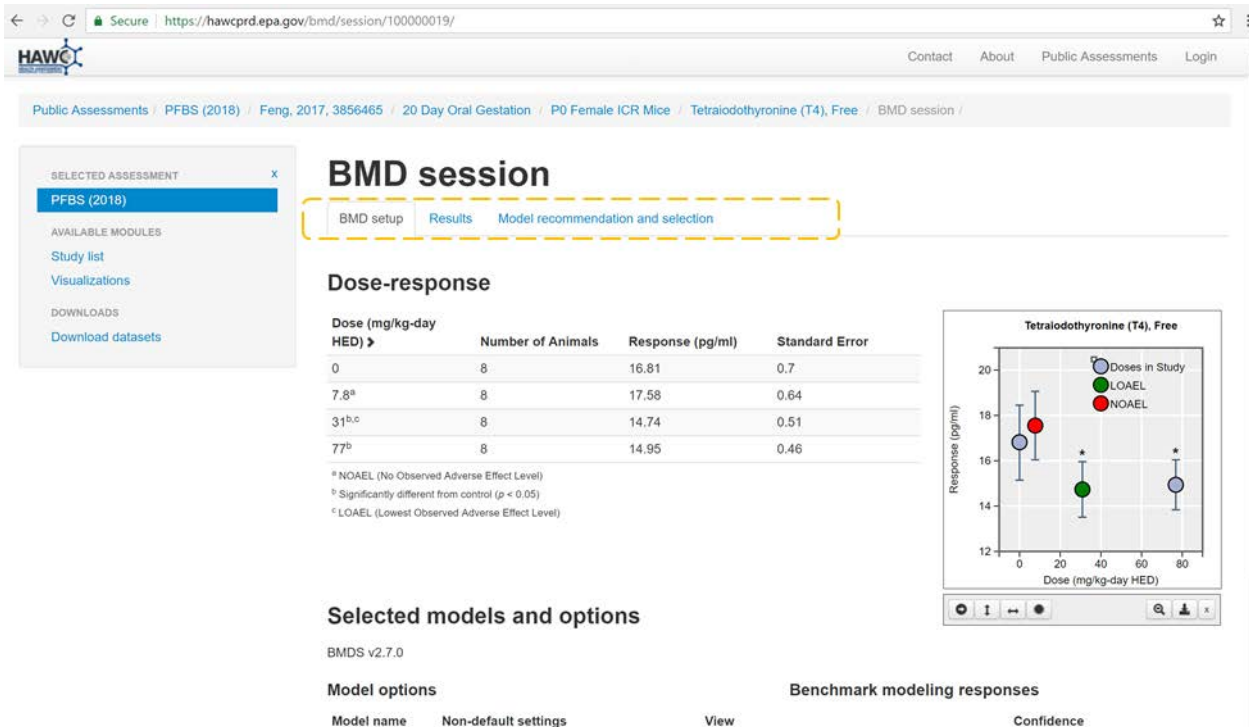


Figure D-6B. Example BMD Session