Package 'invitroTKdata'

August 19, 2025

Version 0.0.1

Date 2025-07-17

Title In Vitro Toxicokinetic Data Processed with the 'invitroTKstats' Pipeline

Description A collection of datasets containing a variety of in vitro toxicokinetic measurements including -- but not limited to -- chemical fraction unbound in the presence of plasma (f_up), intrinsic hepatic clearance (Clint, uL/min/million hepatocytes), and membrane permeability for oral absorption (Caco2). The datasets provided by the package were processed and analyzed with the companion 'invitroTKstats' package.

Depends R (>= 3.5.0)

Imports Rdpack

RdMacros Rdpack

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LazyData true

Encoding UTF-8

RoxygenNote 7.3.2

URL https://github.com/USEPA/invitroTKdata

BugReports https://github.com/USEPA/invitroTKdata/issues

NeedsCompilation no

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Repository CRAN

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Contents

`crizer2024.clint` *Crizer et al. (2024) Intrinsic Hepatic Clearance Level-2 Data Set*

Description

Mass Spectrometry measurements of intrinsic hepatic clearance (Clint) for cryopreserved pooled human hepatocyte suspensions. Chemicals were per- and polyfluoroalkyl substance (PFAS) samples. The experiments were led by Dr. Crizer.

Usage

```
crizer2024.clint
```

Format

A level-2 data.frame with 7,070 rows and 24 variables:

`Lab.Sample.Name` Sample description used in the laboratory

`Date` Date sample was acquired

`Compound.Name` Compound name

`DTXSID` DSSTox Substance Identifier (CompTox Chemicals Dashboard)

`Lab.Compound.Name` Compound as described in the laboratory

`Sample.Type` Type of Clint sample

`Dilution.Factor` Number of times the sample was diluted

`Calibration` Identifier for mass spectrometry calibration – usually the date

`ISTD.Name` Name of compound used as internal standard (ISTD)

`ISTD.Conc` Concentration of ISTD (uM)

`ISTD.Area` Peak area of internal standard (pixels)

`Hep.Density` The density (units of millions of hepatocytes per mL) hepatocytes in the *in vitro* incubation

`Std.Conc` Concentration of analytic standard (for calibration curve) (uM)

`Clint.Assay.Conc` Intended initial concentration of chemical (uM)

`Time` Time when sample was measured (h)

`Area` Peak area of analyte (target compound)

`Analysis.Method` General description of chemical analysis method

`Analysis.Instrument` Instrument(s) used for chemical analysis)

`Analysis.Parameters` Parameters for identifying analyte peak (for example, retention time)

`Note` Any laboratory notes about sample

`Level0.File` Name of data file from laboratory that was used to compile level-0 data.frame

`Level0.Sheet` Name of "sheet" (for Excel workbooks) from which the laboratory data were read

`Response` Response factor (calculated from analyte and ISTD peaks)

`Verified` If "Y", then sample is included in the analysis. (Any other value causes the data to be ignored.)

References

Crizer DM, Rice JR, Smeltz MG, Lavrich KS, Ravindra K, Wambaugh JF, DeVito M, Wetmore BA (2024). "In Vitro Hepatic Clearance Evaluations of Per-and Polyfluoroalkyl Substances (PFAS) across Multiple Structural Categories." *Toxics*, **12**(9), 672.

`crizer2024.clint.L3` *Crizer et al. (2024) Intrinsic Hepatic Clearance Level-3 Data Set*

Description

Frequentist estimates of intrinsic hepatic clearance (Clint) for cryopreserved pooled human hepatocyte suspensions. Chemicals were per- and polyfluoroalkyl substance (PFAS) samples. The experiments were led by Dr. Crizer.

Usage

```
crizer2024.clint.L3
```

Format

A level-3 data.frame with 60 rows and 13 variables:

`Compound.Name` Compound name

`DTXSID` DSSTox Substance Identifier (CompTox Chemicals Dashboard)

`Lab.Compound.Name` Compound as described in the laboratory

`Calibration` Identifier for mass spectrometry calibration – usually the date

`Clint` Frequentist point estimate for intrinsic hepatic clearance (Clint)

`Clint.pValue` p-value of the estimated `Clint` value

`Fit` Test nominal concentrations in the linear regression fit

`AIC` Akaike Information Criterion (AIC) for the linear regression fit

`AIC.Null` Akaike Information Criterion of the exponential decay assuming a constant rate of decay

`Clint.1` Intrinsic hepatic clearance at 1 uM (frequentist point estimate)

`Clint.10` Intrinsic hepatic clearance at 10 uM (frequentist point estimate)

`AIC.Sat` Akaike Information Criterion of the exponential decay with a saturation probability

`Sat.pValue` p-value of exponential decay with a saturation probability

References

Crizer DM, Rice JR, Smeltz MG, Lavrich KS, Ravindra K, Wambaugh JF, DeVito M, Wetmore BA (2024). "In Vitro Hepatic Clearance Evaluations of Per-and Polyfluoroalkyl Substances (PFAS) across Multiple Structural Categories." *Toxics*, **12**(9), 672.

`crizer2024.clint.L4` *Crizer et al. (2024) Intrinsic Hepatic Clearance Level-4 Data Set*

Description

Bayesian estimates of intrinsic hepatic clearance (Clint) for cryopreserved pooled human hepatocyte suspensions. Chemicals were per- and polyfluoroalkyl substance (PFAS) samples. The experiments were led by Dr. Crizer.

Usage

```
crizer2024.clint.L4
```

Format

A level-4 data.frame with 60 rows and 12 variables:

`Compound.Name` Compound name

`DTXSID` DSSTox Substance Identifier (CompTox Chemicals Dashboard)

`Lab.Compound.Name` Compound as described in the laboratory

`Clint.1.Med` Posterior median intrinsic hepatic clearance at 1 uM

`Clint.1.Low` Posterior 2.5th quantile of intrinsic hepatic clearance at 1 uM (lower credible interval bound)

`Clint.1.High` Posterior 97.5th quantile of intrinsic hepatic clearance at 1 uM (upper credible interval bound)

`Clint.10.Med` Posterior median intrinsic hepatic clearance at 10 uM

`Clint.10.Low` Posterior 2.5th quantile of intrinsic hepatic clearance at 10 uM (lower credible interval bound)

`Clint.10.High` Posterior 97.5th quantile of intrinsic hepatic clearance at 10 uM (upper credible interval bound)

`Clint.pValue` Probability that a chemical concentration decrease is observed

`Sat.pValue` Probability that a lower `Clint` is observed at a higher concentration, i.e. saturation probability

`degrades.pValue` Probability of abiotic degradation

References

Crizer DM, Rice JR, Smeltz MG, Lavrich KS, Ravindra K, Wambaugh JF, DeVito M, Wetmore BA (2024). "In Vitro Hepatic Clearance Evaluations of Per-and Polyfluoroalkyl Substances (PFAS) across Multiple Structural Categories." *Toxics*, **12**(9), 672.

`kreutz2023.clint` *Kreutz et al. (2023) Intrinsic Hepatic Clearance Level-2 Data Set*

Description

Mass Spectrometry measurements of intrinsic hepatic clearance (Clint) for cryopreserved pooled human hepatocyte suspensions. Chemicals were per- and polyfluoroalkyl substance (PFAS) samples. The experiments were led by Dr.s Anna Kreutz and Barbara Wetmore.

Usage

```
kreutz2023.clint
```

Format

A level-2 data.frame with 5,800 rows and 25 variables:

`Lab.Sample.Name` Sample description used in the laboratory

`Date` Date sample was acquired

`Compound.Name` Compound name

`DTXSID` DSSTox Substance Identifier (CompTox Chemicals Dashboard)

`Lab.Compound.Name` Compound as described in the laboratory

`Sample.Type` Type of Clint sample

`Dilution.Factor` Number of times the sample was diluted

`Calibration` Identifier for mass spectrometry calibration – usually the date

`Std.Conc` Concentration of analytic standard (for calibration curve) (uM)

`Clint.Assay.Conc` Intended initial concentration of chemical (uM)

`Time` Time when sample was measured (h)

`ISTD.Name` Name of compound used as internal standard (ISTD)

`ISTD.Conc` Concentration of ISTD (uM)

`ISTD.Area` Peak area of internal standard (pixels)

`Hep.Density` The density (units of millions of hepatocytes per mL) hepatocytes in the *in vitro* incubation

`Area` Peak area of analyte (target compound)

`Analysis.Method` General description of chemical analysis method

`Analysis.Instrument` Instrument(s) used for chemical analysis)

`Analysis.Parameters` Parameters for identifying analyte peak (for example, retention time)

`Note` Any laboratory notes about sample

`Level0.File` Name of data file from laboratory that was used to compile level-0 data.frame

`Level0.Sheet` Name of "sheet" (for Excel workbooks) from which the laboratory data were read

`Response` Response factor (calculated from analyte and ISTD peaks)

`Verified` If "Y", then sample is included in the analysis. (Any other value causes the data to be ignored.)

References

Shibata Y, Takahashi H, Chiba M, Ishii Y (2002). "Prediction of hepatic clearance and availability by cryopreserved human hepatocytes: an application of serum incubation method." *Drug Metabolism and disposition*, **30**(8), 892–896.

Kreutz A, Clifton MS, Henderson WM, Smeltz MG, Phillips M, Wambaugh JF, Wetmore BA (2023). "Category-Based Toxicokinetic Evaluations of Data-Poor Per- and Polyfluoroalkyl Substances (PFAS) using Gas Chromatography Coupled with Mass Spectrometry." *Toxics*, **11**(5), 463.

`kreutz2023.clint.L3` *Kreutz et al. (2023) Intrinsic Hepatic Clearance Level-3 Data Set*

Description

Frequentist estimates of intrinsic hepatic clearance (Clint) for cryopreserved pooled human hepatocyte suspensions. Chemicals were per- and polyfluoroalkyl substance (PFAS) samples. The experiments were led by Dr.s Anna Kreutz and Barbara Wetmore.

Usage

```
kreutz2023.clint.L3
```

Format

A level-3 data.frame with 25 rows and 13 variables:

`Compound.Name` Compound name

`DTXSID` DSSTox Substance Identifier (CompTox Chemicals Dashboard)

`Lab.Compound.Name` Compound as described in the laboratory

`Calibration` Identifier for mass spectrometry calibration – usually the date

`Clint` Frequentist point estimate for intrinsic hepatic clearance (Clint)

`Clint.pValue` p-value of the estimated `Clint` value

`Fit` Test nominal concentrations in the linear regression fit

`AIC` Akaike Information Criterion (AIC) for the linear regression fit

`AIC.Null` Akaike Information Criterion of the exponential decay assuming a constant rate of decay

`Clint.1` Intrinsic hepatic clearance at 1 uM (frequentist point estimate)

`Clint.10` Intrinsic hepatic clearance at 10 uM (frequentist point estimate)

`AIC.Sat` Akaike Information Criterion of the exponential decay with a saturation probability

`Sat.pValue` p-value of exponential decay with a saturation probability

References

Shibata Y, Takahashi H, Chiba M, Ishii Y (2002). "Prediction of hepatic clearance and availability by cryopreserved human hepatocytes: an application of serum incubation method." *Drug Metabolism and disposition*, **30**(8), 892–896.

Kreutz A, Clifton MS, Henderson WM, Smeltz MG, Phillips M, Wambaugh JF, Wetmore BA (2023). "Category-Based Toxicokinetic Evaluations of Data-Poor Per- and Polyfluoroalkyl Substances (PFAS) using Gas Chromatography Coupled with Mass Spectrometry." *Toxics*, **11**(5), 463.

`kreutz2023.clint.L4` *Kreutz et al. (2023) Intrinsic Hepatic Clearance Level-4 Data Set*

Description

Bayesian estimates of intrinsic hepatic clearance (Clint) for cryopreserved pooled human hepatocyte suspensions. Chemicals were per- and polyfluoroalkyl substance (PFAS) samples. The experiments were led by Dr.s Anna Kreutz and Barbara Wetmore.

Usage

```
kreutz2023.clint.L4
```

Format

A level-4 data.frame with 25 rows and 12 variables:

`Compound.Name` Compound name

`DTXSID` DSSTox Substance Identifier (CompTox Chemicals Dashboard)

`Lab.Compound.Name` Compound as described in the laboratory

`Clint.1.Med` Posterior median intrinsic hepatic clearance at 1 uM

`Clint.1.Low` Posterior 2.5th quantile of intrinsic hepatic clearance at 1 uM (lower credible interval bound)

`Clint.1.High` Posterior 97.5th quantile of intrinsic hepatic clearance at 1 uM (upper credible interval bound)

`Clint.10.Med` Posterior median intrinsic hepatic clearance at 10 uM

`Clint.10.Low` Posterior 2.5th quantile of intrinsic hepatic clearance at 10 uM (lower credible interval bound)

`Clint.10.High` Posterior 97.5th quantile of intrinsic hepatic clearance at 10 uM (upper credible interval bound)

`Clint.pValue` Probability that a chemical concentration decrease is observed

`Sat.pValue` Probability that a lower `Clint` is observed at a higher concentration, i.e. saturation probability

`degrades.pValue` Probability of abiotic degradation

References

Shibata Y, Takahashi H, Chiba M, Ishii Y (2002). "Prediction of hepatic clearance and availability by cryopreserved human hepatocytes: an application of serum incubation method." *Drug Metabolism and disposition*, **30**(8), 892–896.

Kreutz A, Clifton MS, Henderson WM, Smeltz MG, Phillips M, Wambaugh JF, Wetmore BA (2023). "Category-Based Toxicokinetic Evaluations of Data-Poor Per- and Polyfluoroalkyl Substances (PFAS) using Gas Chromatography Coupled with Mass Spectrometry." *Toxics*, **11**(5), 463.

`kreutz2023.uc` *Kreutz et al. (2023) Ultracentrifugation Level-2 Data Set*

Description

Mass Spectrometry measurements of plasma protein binding measured by ultracentrifugation (UC) for per- and poly-fluorinated alkyl substance (PFAS) samples from experiments led by Dr.s Anna Kreutz and Barbara Wetmore.

Usage

```
kreutz2023.uc
```

Format

A level-2 data.frame with 2,955 rows and 23 variables:

`Lab.Sample.Name` Sample description used in the laboratory

`Date` Date sample was acquired

`Compound.Name` Compound name

`DTXSID` DSSTox Substance Identifier (CompTox Chemicals Dashboard)

`Lab.Compound.Name` Compound as described in the laboratory

`Sample.Type` Type of UC sample

`Dilution.Factor` Number of times the sample was diluted

`Calibration` Identifier for mass spectrometry calibration – usually the date

`Standard.Conc` Concentration of analytic standard (for calibration curve) (uM)

`UC.Assay.T1.Conc` Intended concentration of chemical intended in T1 sample (uM)

`ISTD.Name` Name of compound used as internal standard (ISTD)

`ISTD.Conc` Concentration of ISTD (uM)

`ISTD.Area` Peak area of internal standard (pixels)

`Series` Identier for replicate series of UC measurements

`Area` Peak area of analyte (target compound)

`Analysis.Method` General description of chemical analysis method

`Analysis.Instrument` Instrument(s) used for chemical analysis

`Analysis.Parameters` Parameters for identifying analyte peak (for example, retention time)

`Note` Any laboratory notes about sample

`Level0.File` Name of data file from laboratory that was used to compile level-0 data.frame

`Level0.Sheet` Name of "sheet" (for Excel workbooks) from which the laboratory data were read

`Response` Response factor (calculated from analyte and ISTD peaks)

`Verified` If "Y", then sample is included in the analysis. (Any other value causes the data to be ignored.)

References

Howard ML, Hill JJ, Galluppi GR, McLean MA (2010). "Plasma protein binding in drug discovery and development." *Combinatorial chemistry & high throughput screening*, **13**(2), 170–187.

Kreutz A, Clifton MS, Henderson WM, Smeltz MG, Phillips M, Wambaugh JF, Wetmore BA (2023). "Category-Based Toxicokinetic Evaluations of Data-Poor Per- and Polyfluoroalkyl Substances (PFAS) using Gas Chromatography Coupled with Mass Spectrometry." *Toxics*, **11**(5), 463.

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kreutz2023.uc.L3 *Kreutz et al. (2023) Ultracentrifugation Level-3 Data Set*

Description

Frequentist estimates of plasma protein binding measured by ultracentrifugation (UC) for per- and poly-fluorinated alkyl substance (PFAS) samples from experiments led by Dr.s Anna Kreutz and Barbara Wetmore.

Usage

```
kreutz2023.uc.L3
```

Format

A level-3 data.frame with 73 rows and 5 variables:

`Compound.Name` Compound name

`DTXSID` DSSTox Substance Identifier (CompTox Chemicals Dashboard)

`Lab.Compound.Name` Compound as described in the laboratory

`Calibration` Identifier for mass spectrometry calibration – usually the date

`Fup` Frequentist point estimate for fraction unbound in plasma (fup)

References

Howard ML, Hill JJ, Galluppi GR, McLean MA (2010). "Plasma protein binding in drug discovery and development." *Combinatorial chemistry & high throughput screening*, **13**(2), 170–187.

Kreutz A, Clifton MS, Henderson WM, Smeltz MG, Phillips M, Wambaugh JF, Wetmore BA (2023). "Category-Based Toxicokinetic Evaluations of Data-Poor Per- and Polyfluoroalkyl Substances (PFAS) using Gas Chromatography Coupled with Mass Spectrometry." *Toxics*, **11**(5), 463.

kreutz2023.uc.L4 *Kreutz et al. (2023) Ultracentrifugation Level-4 Data Set*

Description

Bayesian estimates of plasma protein binding measured by ultracentrifugation (UC) for per- and poly-fluorinated alkyl substance (PFAS) samples from experiments led by Dr.s Anna Kreutz and Barbara Wetmore.

Usage

```
kreutz2023.uc.L4
```

Format

A level-4 data.frame with 52 rows and 13 variables:

`Compound.Name` Compound name

`DTXSID` DSSTox Substance Identifier (CompTox Chemicals Dashboard)

`Lab.Compound.Name` Compound as described in the laboratory

`Fstable.Med` Posterior median chemical stability fraction

`Fstable.Low` Posterior 2.5th quantile chemical stability fraction (lower credible interval bound)

`Fstable.High` Posterior 97.5th quantile chemical stability fraction (upper credible interval bound)

`Fup.Med` Posterior median fraction unbound in plasma

`Fup.Low` Posterior 2.5th quantile of fraction unbound in plasma (lower credible interval bound)

`Fup.High` Posterior 97.5th quantile of fraction unbound in plasma (upper credible interval bound)

`Fup.point` Point estimate of fraction unbound in plasma

`Unstable` Qualitative determination of chemical stability. "Y" indicates observed chemical stability.

`Uncertain` Qualitative determination of uncertainty about chemical stability. "Y" indicates uncertainty in observed chemical stability.

`CV` Coefficient of variance

References

Howard ML, Hill JJ, Galluppi GR, McLean MA (2010). "Plasma protein binding in drug discovery and development." *Combinatorial chemistry & high throughput screening*, **13**(2), 170–187.

Kreutz A, Clifton MS, Henderson WM, Smeltz MG, Phillips M, Wambaugh JF, Wetmore BA (2023). "Category-Based Toxicokinetic Evaluations of Data-Poor Per- and Polyfluoroalkyl Substances (PFAS) using Gas Chromatography Coupled with Mass Spectrometry." *Toxics*, **11**(5), 463.

`smeltz2023.clint` *Smeltz et al. (2023) Intrinsic Hepatic Clearance Level-2 Data Set*

Description

Mass Spectrometry measurements of intrinsic hepatic clearance (Clint) for cryopreserved pooled human hepatocytes. Chemicals were per- and polyfluoroalkyl substance (PFAS) samples. The experiments were led by Dr.s Marci Smeltz and Barbara Wetmore.

Usage

```
smeltz2023.clint
```

Format

A level-2 data.frame with 625 rows and 24 variables:

`Lab.Sample.Name` Sample description used in the laboratory

`Date` Date sample was acquired

`Compound.Name` Compound name

`DTXSID` DSSTox Substance Identifier (CompTox Chemicals Dashboard)

`Lab.Compound.Name` Compound as described in the laboratory

`Sample.Type` Type of Clint sample

`Dilution.Factor` Number of times the sample was diluted

`Calibration` Identifier for mass spectrometry calibration – usually the date

`Std.Conc` Concentration of analytic standard (for calibration curve) (uM)

`Clint.Assay.Conc` Intended initial concentration of chemical (uM)

`Time` Time when sample was measured (h)

`ISTD.Name` Name of compound used as internal standard (ISTD)

`ISTD.Conc` Concentration of ISTD (uM)

`ISTD.Area` Peak area of internal standard (pixels)

`Hep.Density` The density (units of millions of hepatocytes per mL) hepatocytes in the *in vitro* incubation

`Area` Peak area of analyte (target compound)

`Analysis.Method` General description of chemical analysis method

`Analysis.Instrument` Instrument(s) used for chemical analysis

`Analysis.Parameters` Parameters for identifying analyte peak (for example, retention time)

`Note` Any laboratory notes about sample

`Level0.File` Name of data file from laboratory that was used to compile level0 data table)

`Level0.Sheet` Name of "sheet" (for Excel workbooks) from which the laboratory data were read

`Response` Response factor (calculated from analyte and ISTD peaks)

`Verified` If "Y", then sample is included in the analysis. (Any other value causes the data to be ignored.)

References

Shibata Y, Takahashi H, Chiba M, Ishii Y (2002). "Prediction of hepatic clearance and availability by cryopreserved human hepatocytes: an application of serum incubation method." *Drug Metabolism and disposition*, **30**(8), 892–896.

Smeltz M, Wambaugh JF, Wetmore BA (2023). "Plasma Protein Binding Evaluations of Per- and Polyfluoroalkyl Substances for Category-Based Toxicokinetic Assessment." *Chemical Research in Toxicology*, **36**(6), 870–881.

`smeltz2023.clint.L3` *Smeltz et al. (2023) Intrinsic Hepatic Clearance Level-3 Data Set*

Description

Frequentist estimate of intrinsic hepatic clearance (Clint) for cryopreserved pooled human hepatocytes. Chemicals were per- and polyfluoroalkyl substance (PFAS) samples. The experiments were led by Dr.s Marci Smeltz and Barbara Wetmore.

Usage

```
smeltz2023.clint.L3
```

Format

A level-3 data.frame with 6 rows and 13 variables:

`Compound.Name` Compound name

`DTXSID` DSSTox Substance Identifier (CompTox Chemicals Dashboard)

`Lab.Compound.Name` Compound as described in the laboratory

`Calibration` Identifier for mass spectrometry calibration – usually the date

`Clint` Frequentist point estimate for intrinsic hepatic clearance (Clint)

`Clint.pValue` p-value of the estimated `Clint` value

`Fit` Test nominal concentrations in the linear regression fit

`AIC` Akaike Information Criterion (AIC) for the linear regression fit

`AIC.Null` Akaike Information Criterion of the exponential decay assuming a constant rate of decay

`Clint.1` Intrinsic hepatic clearance at 1 uM (frequentist point estimate)

`Clint.10` Intrinsic hepatic clearance at 10 uM (frequentist point estimate)

`AIC.Sat` Akaike Information Criterion of the exponential decay with a saturation probability

`Sat.pValue` p-value of exponential decay with a saturation probability

References

Shibata Y, Takahashi H, Chiba M, Ishii Y (2002). "Prediction of hepatic clearance and availability by cryopreserved human hepatocytes: an application of serum incubation method." *Drug Metabolism and disposition*, **30**(8), 892–896.

Smeltz M, Wambaugh JF, Wetmore BA (2023). "Plasma Protein Binding Evaluations of Per- and Polyfluoroalkyl Substances for Category-Based Toxicokinetic Assessment." *Chemical Research in Toxicology*, **36**(6), 870–881.

`smeltz2023.clint.L4` *Smeltz et al. (2023) Intrinsic Hepatic Clearance Level-4 Data Set*

Description

Bayesian estimate of intrinsic hepatic clearance (Clint) for cryopreserved pooled human hepatocytes. Chemicals were per- and polyfluoroalkyl substance (PFAS) samples. The experiments were led by Dr.s Marci Smeltz and Barbara Wetmore.

Usage

```
smeltz2023.clint.L4
```

Format

A level-4 data.frame with 7 rows and 12 variables:

`Compound.Name` Compound name

`DTXSID` DSSTox Substance Identifier (CompTox Chemicals Dashboard)

`Lab.Compound.Name` Compound as described in the laboratory

`Clint.1.Med` Posterior median intrinsic hepatic clearance at 1 uM

`Clint.1.Low` Posterior 2.5th quantile of intrinsic hepatic clearance at 1 uM (lower credible interval bound)

`Clint.1.High` Posterior 97.5th quantile of intrinsic hepatic clearance at 1 uM (upper credible interval bound)

`Clint.10.Med` Posterior median intrinsic hepatic clearance at 10 uM

`Clint.10.Low` Posterior 2.5th quantile of intrinsic hepatic clearance at 10 uM (lower credible interval bound)

`Clint.10.High` Posterior 97.5th quantile of intrinsic hepatic clearance at 10 uM (upper credible interval bound)

`Clint.pValue` Probability that a chemical concentration decrease is observed

`Sat.pValue` Probability that a lower `Clint` is observed at a higher concentration, i.e. saturation probability

`degrades.pValue` Probability of abiotic degradation

References

Shibata Y, Takahashi H, Chiba M, Ishii Y (2002). "Prediction of hepatic clearance and availability by cryopreserved human hepatocytes: an application of serum incubation method." *Drug Metabolism and disposition*, **30**(8), 892–896.

Smeltz M, Wambaugh JF, Wetmore BA (2023). "Plasma Protein Binding Evaluations of Per- and Polyfluoroalkyl Substances for Category-Based Toxicokinetic Assessment." *Chemical Research in Toxicology*, **36**(6), 870–881.

`smeltz2023.red` *Smeltz et al. (2023) Rapid Equilibrium Dialysis Level-2 Data Set*

Description

Mass Spectrometry measurements of plasma protein binding measured by rapid equilibrium dialysis (RED) for per- and poly-fluorinated alkyl substance (PFAS) samples from experiments led by Dr.s Marci Smeltz and Barbara Wetmore.

Usage

```
smeltz2023.red
```

Format

A level-2 data.frame with 3,955 rows and 25 variables:

`Lab.Sample.Name` Sample description used in the laboratory

`Date` Date sample was acquired

`Compound.Name` Compound name

`DTXSID` DSSTox Substance Identifier (CompTox Chemicals Dashboard)

`Lab.Compound.Name` Compound as described in the laboratory

`Sample.Type` Type of RED sample

`Dilution.Factor` Number of times the sample was diluted

`Calibration` Identifier for mass spectrometry calibration – usually the date

`Std.Conc` Concentration of analytic standard (for calibration curve) (uM)

`Test.Nominal.Conc` Intended concentration of chemical introduced into RED plate (uM)

`Percent.Physiologic.Plasma` Percent of physiological plasma concentration in RED plate (in percent)

`Time` Time of sample measurement (h)

`ISTD.Name` Name of compound used as internal standard (ISTD)

`ISTD.Conc` Concentration of ISTD (uM)

`ISTD.Area` Peak area of internal standard (pixels)

`Replicate` Identifier for replicate series of RED measurements

`Area` Peak area of analyte (target compound)

`Analysis.Method` General description of chemical analysis method

`Analysis.Instrument` Instrument(s) used for chemical analysis

`Analysis.Parameters` Parameters for identifying analyte peak (for example, retention time)

`Note` Any laboratory notes about sample

`Level0.File` Name of data file from laboratory that was used to compile level-0 data.frame

`Level0.Sheet` Name of "sheet" (for Excel workbooks) from which the laboratory data were read

`Response` Response factor (calculated from analyte and ISTD peaks)

`Verified` If "Y", then sample is included in the analysis. (Any other value causes the data to be ignored.)

References

Waters NJ, Jones R, Williams G, Sohal B (2008). "Validation of a rapid equilibrium dialysis approach for the measurement of plasma protein binding." *Journal of pharmaceutical sciences*, **97**(10), 4586–4595.

Smeltz M, Wambaugh JF, Wetmore BA (2023). "Plasma Protein Binding Evaluations of Per- and Polyfluoroalkyl Substances for Category-Based Toxicokinetic Assessment." *Chemical Research in Toxicology*, **36**(6), 870–881.

`smeltz2023.red.L3` *Smeltz et al. (2023) Rapid Equilibrium Dialysis Level-3 Data Set*

Description

Frequentist estimate of plasma protein binding measured by rapid equilibrium dialysis (RED) for per- and poly-fluorinated alkyl substance (PFAS) samples from experiments led by Dr.s Marci Smeltz and Barbara Wetmore.

Usage

```
smeltz2023.red.L3
```

Format

A level-3 data.frame with 15 rows and 4 variables:

`Compound.Name` Compound name

`DTXSID` DSSTox Substance Identifier (CompTox Chemicals Dashboard)

`Calibration` Identifier for mass spectrometry calibration – usually the date

`Fup` Frequentist point estimate for fraction unbound in plasma (fup)

References

Waters NJ, Jones R, Williams G, Sohal B (2008). "Validation of a rapid equilibrium dialysis approach for the measurement of plasma protein binding." *Journal of pharmaceutical sciences*, **97**(10), 4586–4595.

Smeltz M, Wambaugh JF, Wetmore BA (2023). "Plasma Protein Binding Evaluations of Per- and Polyfluoroalkyl Substances for Category-Based Toxicokinetic Assessment." *Chemical Research in Toxicology*, **36**(6), 870–881.

`smeltz2023.red.L4` *Smeltz et al. (2023) Rapid Equilibrium Dialysis Level-4 Data Set*

Description

Bayesian estimate of plasma protein binding measured by rapid equilibrium dialysis (RED) for per- and poly-fluorinated alkyl substance (PFAS) samples from experiments led by Dr.s Marci Smeltz and Barbara Wetmore.

Usage

```
smeltz2023.red.L4
```

Format

A level-4 data.frame with 15 rows and 7 variables:

`Compound.Name` Compound name

`Lab.Compound.Name` Compound as described in the laboratory

`DTXSID` DSSTox Substance Identifier (CompTox Chemicals Dashboard)

`Fup.point` Point estimate of fraction unbound in plasma

`Fup.Med` Posterior median estimate of fraction unbound in plasma

`Fup.Low` Posterior 2.5th quantile of fraction unbound in plasma (lower credible interval bound)

`Fup.High` Posterior 97.5th quantile of fraction unbound in plasma (upper credible interval bound)

References

Waters NJ, Jones R, Williams G, Sohal B (2008). "Validation of a rapid equilibrium dialysis approach for the measurement of plasma protein binding." *Journal of pharmaceutical sciences*, **97**(10), 4586–4595.

Smeltz M, Wambaugh JF, Wetmore BA (2023). "Plasma Protein Binding Evaluations of Per- and Polyfluoroalkyl Substances for Category-Based Toxicokinetic Assessment." *Chemical Research in Toxicology*, **36**(6), 870–881.

smeltz2023.uc *Smeltz et al. (2023) Ultracentrifugation Level-2 Data Set*

Description

Mass Spectrometry measurements of plasma protein binding measured by ultracentrifugation (UC) for per- and poly-fluorinated alkyl substance (PFAS) samples from experiments led by Dr.s Marci Smeltz and Barbara Wetmore.

Usage

```
smeltz2023.uc
```

Format

A level-2 data.frame with 10,133 rows and 23 variables:

`Lab.Sample.Name` Sample description used in the laboratory

`Date` Date sample was acquired

`Compound.Name` Compound name

`DTXSID` DSSTox Substance Identifier (CompTox Chemicals Dashboard)

`Lab.Compound.Name` Compound as described in the laboratory

`Sample.Type` Type of UC sample

`Dilution.Factor` Number of times the sample was diluted

`Calibration` Identifier for mass spectrometry calibration – usually the date

`Standard.Conc` Concentration of analytic standard (for calibration curve) (uM)

`UC.Assay.T1.Conc` Intended concentration of chemical in T1 sample (uM)

`ISTD.Name` Name of compound used as internal standard (ISTD)

`ISTD.Conc` Concentration of ISTD (uM)

`ISTD.Area` Peak area of internal standard (pixels)

`Series` Identifier for replicate series of UC measurements

`Area` Peak area of analyte (target compound)

`Analysis.Method` General description of chemical analysis method

`Analysis.Instrument` Instrument(s) used for chemical analysis

`Analysis.Parameters` Parameters for identifying analyte peak (for example, retention time)

`Note` Any laboratory notes about sample

`Level0.File` Name of data file from laboratory that was used to compile level-0 data.frame

`Level0.Sheet` Name of "sheet" (for Excel workbooks) from which the laboratory data were read

`Response` Response factor (calculated from analyte and ISTD peaks)

`Verified` If "Y", then sample is included in the analysis. (Any other value causes the data to be ignored.)

References

Howard ML, Hill JJ, Galluppi GR, McLean MA (2010). "Plasma protein binding in drug discovery and development." *Combinatorial chemistry & high throughput screening*, **13**(2), 170–187.

Smeltz M, Wambaugh JF, Wetmore BA (2023). "Plasma Protein Binding Evaluations of Per- and Polyfluoroalkyl Substances for Category-Based Toxicokinetic Assessment." *Chemical Research in Toxicology*, **36**(6), 870–881.

`smeltz2023.uc.L3` *Smeltz et al. (2023) Ultracentrifugation Level-3 Data Set*

Description

Frequentist estimate of plasma protein binding measured by ultracentrifugation (UC) for per- and poly-fluorinated alkyl substance (PFAS) samples from experiments led by Dr.s Marci Smeltz and Barbara Wetmore.

Usage

```
smeltz2023.uc.L3
```

Format

A level-3 data.frame with 107 rows and 5 variables:

`Compound.Name` Compound name

`DTXSID` DSSTox Substance Identifier (CompTox Chemicals Dashboard)

`Lab.Compound.Name` Compound as described in the laboratory

`Calibration` Identifier for mass spectrometry calibration – usually the date

`Fup` Frequentist point estimate for fraction unbound in plasma (fup)

References

Howard ML, Hill JJ, Galluppi GR, McLean MA (2010). "Plasma protein binding in drug discovery and development." *Combinatorial chemistry & high throughput screening*, **13**(2), 170–187.

Smeltz M, Wambaugh JF, Wetmore BA (2023). "Plasma Protein Binding Evaluations of Per- and Polyfluoroalkyl Substances for Category-Based Toxicokinetic Assessment." *Chemical Research in Toxicology*, **36**(6), 870–881.

smeltz2023.uc.L4 *Smeltz et al. (2023) Ultracentrifugation Level-4 Data Set*

Description

Bayesian estimate of plasma protein binding measured by ultracentrifugation (UC) for per- and poly-fluorinated alkyl substance (PFAS) samples from experiments led by Dr.s Marci Smeltz and Barbara Wetmore.

Usage

```
smeltz2023.uc.L4
```

Format

A level-4 data.frame with 69 rows and 7 variables:

`Compound.Name` Compound name

`DTXSID` DSSTox Substance Identifier (CompTox Chemicals Dashboard)

`Lab.Compound.Name` Compound as described in the laboratory

`Fup.Med` Posterior median fraction unbound in plasma

`Fup.Low` Posterior 2.5th quantile of fraction unbound in plasma (lower credible interval bound)

`Fup.High` Posterior 97.5th quantile of fraction unbound in plasma (upper credible interval bound)

`Fup.point` Point estimate of fraction unbound in plasma

References

Howard ML, Hill JJ, Galluppi GR, McLean MA (2010). "Plasma protein binding in drug discovery and development." *Combinatorial chemistry & high throughput screening*, **13**(2), 170–187.

Smeltz M, Wambaugh JF, Wetmore BA (2023). "Plasma Protein Binding Evaluations of Per- and Polyfluoroalkyl Substances for Category-Based Toxicokinetic Assessment." *Chemical Research in Toxicology*, **36**(6), 870–881.

wambaugh2019.clint *Wambaugh et al. (2019) Intrinsic Hepatic Clearance Level-2 Data Set*

Description

Mass spectrometry measurements of intrinsic hepatic clearance (Clint) measured using *in vitro* suspensions of pooled primary human hepatocytes (Shibata et al. 2002).

Usage

```
wambaugh2019.clint
```

Format

A data.frame with 22898 rows and 26 variables:

`Lab.Sample.Name` Sample description used in the laboratory

`Date` Date sample was acquired

`Compound.Name` Compound name

`DTXSID` DSSTox Substance Identifier (CompTox Chemicals Dashboard)

`Lab.Compound.Name` Compound as described in the laboratory

`Sample.Type` Type of Clint sample

`Dilution.Factor` Number of times the sample was diluted

`Calibration` Identifier for mass spectrometry calibration – usually the date

`ISTD.Name` Name of compound used as internal standard (ISTD)

`ISTD.Conc` Concentration of ISTD (uM)

`ISTD.Area` Peak area of internal standard (pixels)

`Area` Peak area of analyte (target compound)

`Analysis.Method` General description of chemical analysis method

`Analysis.Instrument` Instrument(s) used for chemical analysis

`Analysis.Parameters` Parameters for identifying analyte peak (for example, retention time)

`Note` Any laboratory notes about sample

`Level0.File` Name of data file from laboratory that was used to compile level-0 data.frame

`Level0.Sheet` Name of "sheet" (for Excel workbooks) from which the laboratory data were read

`Time` Time when sample was measured (h)

`Test.Compound.Conc` Measured concentration of analytic standard (for calibration curve) (uM)

`Test.Nominal.Conc` Expected initial concentration of chemical added to donor side (uM)

`Hep.Density` The density (units of millions of hepatocytes per mL) hepatocytes in the *in vitro* incubation

`Biological.Replicates` Identifier for measurements of multiple samples with the same analyte

`Technical.Replicates` Identifier for measurements of one sample of a compound

`Response` Response factor (calculated from analyte and ISTD peaks)

`Verified` If "Y", then sample is included in the analysis. (Any other value causes the data to be ignored.)

Source

Wambaugh et al. (2019)

References

Shibata Y, Takahashi H, Chiba M, Ishii Y (2002). "Prediction of hepatic clearance and availability by cryopreserved human hepatocytes: an application of serum incubation method." *Drug Metabolism and disposition*, **30**(8), 892–896.

Wambaugh JF, Wetmore BA, Ring CL, Nicolas CI, Pearce RG, Honda GS, Dinallo R, Angus D, Gilbert J, Sierra T, others (2019). "Assessing toxicokinetic uncertainty and variability in risk prioritization." *Toxicological Sciences*, **172**(2), 235–251.

`wambaugh2019.clint.L3` *Wambaugh et al. (2019) Intrinsic Hepatic Clearance Level-3 Data Set*

Description

Frequentist estimate of intrinsic hepatic clearance (Clint) measured using *in vitro* suspensions of pooled primary human hepatocytes (Shibata et al. 2002).

Usage

```
wambaugh2019.clint.L3
```

Format

A data.frame with 473 rows and 13 variables:

`Compound.Name` Compound name

`DTXSID` DSSTox Substance Identifier (CompTox Chemical Dashboard)

`Lab.Compound.Name` Compound as described in the laboratory

`Calibration` Identifier for mass spectrometry calibration - usually the date

`Clint` Frequentist point estimate for intrinsic hepatic clearance (Clint)

`Clint.pValue` p-value of the estimated `Clint` value

`Fit` Test nominal concentrations in the linear regression fit

`AIC` Akaike Information Criterion (AIC) for the linear regression fit

`AIC.Null` Akaike Information Criterion of the exponential decay assuming a constant rate of decay

`Clint.1` Intrinsic hepatic clearance at 1 uM (frequentist point estimate)

`Clint.10` Intrinsic hepatic clearance at 10 uM (frequentist point estimate)

`AIC.Sat` Akaike Information Criterion of the exponential decay with a saturation probability

`Sat.pValue` p-value of exponential decay with a saturation probability

Source

Wambaugh et al. (2019)

References

Shibata Y, Takahashi H, Chiba M, Ishii Y (2002). "Prediction of hepatic clearance and availability by cryopreserved human hepatocytes: an application of serum incubation method." *Drug Metabolism and disposition*, **30**(8), 892–896.

Wambaugh JF, Wetmore BA, Ring CL, Nicolas CI, Pearce RG, Honda GS, Dinallo R, Angus D, Gilbert J, Sierra T, others (2019). "Assessing toxicokinetic uncertainty and variability in risk prioritization." *Toxicological Sciences*, **172**(2), 235–251.

`wambaugh2019.clint.L4` *Wambaugh et al. (2019) Intrinsic Hepatic Clearance Level-4 Data Set*

Description

Bayesian estimate of intrinsic hepatic clearance (Clint) measured using *in vitro* suspensions of pooled primary human hepatocytes (Shibata et al. 2002).

Usage

```
wambaugh2019.clint.L4
```

Format

A level-4 data.frame with 473 rows and 12 variables:

`Compound.Name` Compound name

`DTXSID` DSSTox Substance Identifier (CompTox Chemicals Dashboard)

`Lab.Compound.Name` Compound as described in the laboratory

`Clint.1.Med` Posterior median intrinsic hepatic clearance at 1 uM

`Clint.1.Low` Posterior 2.5th quantile of intrinsic hepatic clearance at 1 uM (lower credible interval bound)

`Clint.1.High` Posterior 97.5th quantile of intrinsic hepatic clearance at 1 uM (upper credible interval bound)

`Clint.10.Med` Posterior median intrinsic hepatic clearance at 10 uM

`Clint.10.Low` Posterior 2.5th quantile of intrinsic hepatic clearance at 10 uM (lower credible interval bound)

`Clint.10.High` Posterior 97.5th quantile of intrinsic hepatic clearance at 10 uM (upper credible interval bound)

`Clint.pValue` Probability that a chemical concentration decrease is observed

`Sat.pValue` Probability that a lower `Clint` is observed at a higher concentration, i.e. saturation probability

`degrades.pValue` Probability of abiotic degradation

Source

Wambaugh et al. (2019)

References

Shibata Y, Takahashi H, Chiba M, Ishii Y (2002). "Prediction of hepatic clearance and availability by cryopreserved human hepatocytes: an application of serum incubation method." *Drug Metabolism and disposition*, **30**(8), 892–896.

Wambaugh JF, Wetmore BA, Ring CL, Nicolas CI, Pearce RG, Honda GS, Dinallo R, Angus D, Gilbert J, Sierra T, others (2019). "Assessing toxicokinetic uncertainty and variability in risk prioritization." *Toxicological Sciences*, **172**(2), 235–251.

wambaugh2019.red *Wambaugh et al. (2019) Rapid Equilibrium Dialysis Level-2 Data Set*

Description

Mass spectrometry measurements of plasma protein binding using the rapid equilibrium dialysis (RED) assay method (Waters et al. 2008).

Usage

```
wambaugh2019.red
```

Format

A data.frame 15990 rows and 26 variables:

`Lab.Sample.Name` Sample description used in the laboratory

`Date` Date sample was acquired

`Compound.Name` Compound name

`DTXSID` DSSTox Substance Identifier (CompTox Chemicals Dashboard)

`Lab.Compound.Name` Compound as described in the laboratory

`Sample.Type` Type of RED sample

`Dilution.Factor` Number of times the sample was diluted

`Calibration` Identifier for mass spectrometry calibration - usually the date

`ISTD.Name` Name of compound used as internal standard (ISTD)

`ISTD.Conc` Concentration of ISTD (uM)

`ISTD.Area` Peak area internal standard (pixels)

`Area` Peak area of analyte (target compound)

`Analysis.Method` General description of chemical analysis method

`Analysis.Instrument` Instrument(s) used for chemical analysis

`Analysis.Parameters` Parameters for identifying analyte peak (for example, retention time)

`Note` Any laboratory notes about sample

`Level0.File` Name of data file from laboratory that was used to compile level-0 data.frame

`Level0.Sheet` Name of "sheet" (for Excel workbooks) from which the laboratory data were read

`Time` Time when sample was measured (h)

`Test.Compound.Conc` Measured concentration of analytic standard (for calibration curve) (uM)

`Test.Nominal.Conc` Expected initial concentration of chemical added to donor side (uM)

`Percent.Physiologic.Plasma` Percent of physiology plasma concentration in RED plate (in percent)

`Biological.Replicates` Identifier for measurements of multiple samples with the same analyte

`Technical.Replicates` Identifier for measurements of one sample of a compound

`Response` Response factor (calculated from analyte and ISTD peaks)

`Verified` If "Y", then sample is included in the analysis. (Any other value causes the data to be ignored.)

Source

Wambaugh et al. (2019)

References

Waters NJ, Jones R, Williams G, Sohal B (2008). "Validation of a rapid equilibrium dialysis approach for the measurement of plasma protein binding." *Journal of pharmaceutical sciences*, **97**(10), 4586–4595.

Wambaugh JF, Wetmore BA, Ring CL, Nicolas CI, Pearce RG, Honda GS, Dinallo R, Angus D, Gilbert J, Sierra T, others (2019). "Assessing toxicokinetic uncertainty and variability in risk prioritization." *Toxicological Sciences*, **172**(2), 235–251.

`wambaugh2019.red.L3` *Wambaugh et al. (2019) Rapid Equilibrium Dialysis Level-3 Data Set*

Description

Frequentist estimate of plasma protein binding using the rapid equilibrium dialysis (RED) assay method (Waters et al. 2008).

Usage

```
wambaugh2019.red.L3
```

Format

A data.frame 368 rows and 4 variables:

`Compound.Name` Compound name

`DTXSID` DSSTox Substance Identifier (CompTox Chemicals Dashboard)

`Calibration` Identifier for mass spectrometry calibration - usually the date

`Fup` Frequentist point estimate for fraction unbound in plasma (fup)

Source

Wambaugh et al. (2019)

References

Waters NJ, Jones R, Williams G, Sohal B (2008). "Validation of a rapid equilibrium dialysis approach for the measurement of plasma protein binding." *Journal of pharmaceutical sciences*, **97**(10), 4586–4595.

Wambaugh JF, Wetmore BA, Ring CL, Nicolas CI, Pearce RG, Honda GS, Dinallo R, Angus D, Gilbert J, Sierra T, others (2019). "Assessing toxicokinetic uncertainty and variability in risk prioritization." *Toxicological Sciences*, **172**(2), 235–251.

wambaugh2019.red.L4 *Wambaugh et al. (2019) Rapid Equilibrium Dialysis Level-4 Data Set*

Description

Bayesian estimate of plasma protein binding using the rapid equilibrium dialysis (RED) assay method (Waters et al. 2008).

Usage

```
wambaugh2019.red.L4
```

Format

A data.frame 301 rows and 7 variables:

`Compound.Name` Compound name

`Lab.Compound.Name` Compound as described in the laboratory

`DTXSID` DSSTox Substance Identifier (CompTox Chemical Dashboard)

`Fup.point` Point estimate of fraction unbound in plasma

`Fup.Med` Posterior median fraction unbound in plasma

`Fup.Low` Posterior 2.5th quantile of fraction unbound in plasma (lower credible interval bound)

`Fup.High` Posterior 97.5th quantile of fraction unbound in plasma (upper credible interval bound)

Source

Wambaugh et al. (2019)

References

Waters NJ, Jones R, Williams G, Sohal B (2008). "Validation of a rapid equilibrium dialysis approach for the measurement of plasma protein binding." *Journal of pharmaceutical sciences*, **97**(10), 4586–4595.

Wambaugh JF, Wetmore BA, Ring CL, Nicolas CI, Pearce RG, Honda GS, Dinallo R, Angus D, Gilbert J, Sierra T, others (2019). "Assessing toxicokinetic uncertainty and variability in risk prioritization." *Toxicological Sciences*, **172**(2), 235–251.

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