

HESSに追加された新しい機能の紹介

2014年7月1日(火)
(独)製品評価技術基盤機構
化学物質管理センター

新しく実装された3つの機能

1. 代謝物の表示及び代謝物を対象とした毒性の評価機能
2. 実施した操作のUndo機能
3. HELP機能

今回の講習では、ケーススタディを交えて新機能の紹介を行う。

1. 代謝物の表示及び代謝物を 対象とした毒性の評価機能

Hazard Evaluation Support System

1-1. 予測対象物質の入力

Reset Options Help

Input
Profiling
RDT Data
Categories
Gap Filling
Report
Metabolism

Chemical name:
CAS No 103-88-8
SMILES c1(Br)ccc(NC(C)=O)cc1

to data matrix=> metabolism mode...

③ Set target ① Add to post-targets list ① CAS# Chemical name Drawing RDT tests Database User List Load DB Load Inventory

CAS # 103888 Search ②

Chemical name:

①CAS番号をクリック
↓
②CAS: 103-88-8を入力
↓
③「Set target」をクリック

Br

NH

O

CH₃

1 Single chemical 1/0/0 Developed by LMC, Bulgaria STOP

Hazard Evaluation Support System

1-2. 予測対象物質のProfiling

Reset Options Help

① Input

Profiling

RDT Data

Categories

Gap Filling

Report

Metabolism

Chemical name:

CAS No 103-88-8

SMILES c1(Br)ccc(NC(C)=O)cc1

to data matrix->

metabolism mode...

③

Show Boundaries Apply New Scheme

Profilers

Profiling methods

- ☐ in vivo mutagenicity (Micronucleus)
- ☐ Oncologic Primary Classification
- ☐ Skin irritation/corrosion Exclusion
- ☐ Skin irritation/corrosion Inclusion

Empiric

- ☐ Chemical elements
- ☐ Groups of elements
- ☐ Lipinski Rule Oasis
- ☐ Organic functional groups
- ☐ Organic functional groups (nest)
- ☐ Organic functional groups (US E)
- ☐ Organic functional groups, North
- ☒ Study No. (Link to SSRDT)
- ☒ Chemical No. (Link to HESS DB)
- ☒ RDT Report No.
- ☐ CSCL Class
- ☒ Rat Liver Metabolism Database

Toxicological

- ☒ Repeated dose (HESS)

Custom

- ☐ HESS Chemical Class

Metabolism

Documented

- ☐ Observed Rat Liver metabolism

Simulated

- ☐ Dissociation simulation
- ☐ Liver Metabolism Simulator
- ☐ NEDO In Vitro Rat Cellular Metabo
- ☐ NEDO In Vitro Rat Microsomal Met
- ☐ NEDO In Vivo Rat Metabolism Simu

Filter endpoint tree... 1 (Target)

Structure

Substance Identity

①「Profiling」の項目に移動

②「Study No.」、「Chemical No.」、「RDT Report No.」、「Rat Liver Metabolism」、「Repeated dose (HESS)」を選択

③「Apply」をクリック

5

1 Single chemical 17/07/0 Developed by LMC, Bulgaria STOP

1-3. Profiling結果の確認

Hazard Evaluation Support System

Reset Options Help

Input

Profiling

RDT Data

Categories

Gap Filling

Report

Metabolism

Chemical name:
 CAS No: 103-88-8
 SMILES: c1(Br)ccc(NC(C)=O)cc1

to data matrix-> metabolism mode...

Show Boundaries Apply New Scheme

Profilers

Profiling methods

- ☐ in vivo mutagenicity (Micronucleus test)
- ☐ Oncologic Primary Classification
- ☐ Skin irritation/corrosion Exclusion
- ☐ Skin irritation/corrosion Inclusion

Empiric

- ☐ Chemical elements
- ☐ Groups of elements
- ☐ Lipinski Rule Oasis
- ☐ Organic functional groups
- ☐ Organic functional groups (nested)
- ☐ Organic functional groups (US EPA)
- ☐ Organic functional groups, North America
- ☒ Study No. (Link to SSRDT)
- ☒ Chemical No. (Link to HESS DB)
- ☒ RDT Report No.
- ☐ CSCL Class
- ☒ Rat Liver Metabolism Database

Toxicological

- ☒ Repeated dose (HESS)

Custom

- ☐ HESS Chemical Classification

Metabolism

Documented

- ☐ Observed Rat Liver metabolism

Simulated

- ☐ Dissociation simulation
- ☐ Liver Metabolism Simulator
- ☐ NEDO In Vitro Rat Cellular Metabolism
- ☐ NEDO In Vitro Rat Microsomal Metabolism
- ☐ NEDO In Vivo Rat Metabolism Simulation

Filter endpoint tree... 1 (Target)

Structure

Substance Identity

Profile

- Study No. (Link to SSRDT)
- Chemical No. (Link to HESS DB)
- RDT Report No.
- Rat Liver Metabolism Database
- Repeated dose (HESS)

Root of map No. 181
Metabolite in map ...
Metabolite in map ...
Not categorized

反復投与毒性試験結果なし
代謝の実測データあり

(カテゴリー候補なし)

1 Single chemical 1/0/0 Developed by LMC, Bulgaria STOP

1-4. 反復投与毒性試験データの有無の確認

Hazard Evaluation Support System

Reset Options Help

Input
Profiling
RDT Data
Categories
Gap Filling
Report
Metabolism

Chemical name:
CAS No 103-88-8
SMILES c1(Br)ccc(NC(C)=O)cc1
to data matrix-> metabolism mode...

Structure

Filter endpoint tree... 1 (Target)

Databases

- ☐ Biomarker DB
- ☐ COSMOS DB
- ☒ HESS Repeated Dose Toxicity
- ☐ HESS Repeated Dose Toxicity (CSCL New Chemi...
- ☐ ToxRef DB

Substance Identity

Profile

- Study No. (Lin...
- Chemical No. ...
- RDT Report No.
- Rat Liver Meta...
- Repeated dos...

Root of map No. 181
Metabolite in map ...
Metabolite in map ...
Not categorized

1 Single chemical 17/07/0 Developed by LMC, Bulgaria STOP

①「RDT Data」の項目に移動
↓
②「HESS Repeat Dose Toxicity」を選択
↓
③「Gather」をクリック

1-5. 確認結果(今回の場合はNo data)

Hazard Evaluation Support System

Reset Options Help

Input
Profiling
RDT Data
Categories
Gap Filling
Report
Metabolism

Chemical name:
CAS No 103-88-8
SMILES c1(Br)ccc(NC(C)=O)cc1

to data matrix=> metabolism mode...

Gather

Databases

- ☐ Biomarker DB
- ☐ COSMOS DB
- ☒ HESS Repeated Dose Toxicity
- ☐ HESS Repeated Dose Toxicity (CSCL New Chemi
- ☐ ToxRef DB

Filter endpoint tree...

NITE HESS

No data found.

OK

(毒性データなし)

1 Single chemical Assigning to data matrix... 1/1/1 Developed by LMC, Bulgaria STOP

1-6. 予測対象物質の代謝物の表示(表示方法)

Chemical name: 4-bromoacetanilide
 CAS No: 103-88-8
 SMILES: c1(Br)ccc(NC(C)=O)cc1

① metabolism mode...

②

- metabolize...
- help
- Dissociation simulation
- Liver Metabolism Simulator
- NEDO In Vitro Rat Cellular Metabolism
- NEDO In Vitro Rat Microsomal Metabolism Simulator
- NEDO In Vivo Rat Metabolism Simulator
- Observed Rat Liver metabolism

Structure

Substance Identity

Profile

- Study No. (Lin...)
- Chemical No. ...
- RDT Report No.
- Rat Liver Meta...
- Repeated dos...

Root of map No. 181
 Metabolite in map ...
 Metabolite in map ...
 Not categorized

①「metabolism mode」をクリック

②「metabolite」→「Observed Rat Liver metabolism」を選択

Input
Profiling

RTD Data

Categories

Gap Filling

Report
Metabolism

Chemical name: 4-bromoacetanilide; 4'-bromoacetanil

CAS No 103-88-8

SMILES c1(Br)ccc(NC(C)=O)cc1

to data matrix ->

metabolism mode...

Gather

Databases

☐ Biomarker DB

☒ COSMOS DB

☒ HESS Repeated Dose Toxicity

☐ HESS Repeated Dose Toxicity (CSCL New Chemicals)

☒ ToxRef DB

Filter endpoint tree...

Structure

Substance Identity

Profile

Study No. (Link to ...)

Chemical No. (Link...

RTD Report No.

Rat Liver Metabolis...

Repeated dose (H...

1 (Target)

2 (Metabolite)

3 (Metabolite)

4 (Metabolite)

5 (Metabolite)

Root of map No. 181

Metabolite in map ...

Metabolite in map ...

Not categorized

10

Single chemical

Developed by LMC, Bulgaria

STOP

1-7. 予測対象物質の代謝物の表示(表示結果)

ResetOptionsHelp

Chemical name: 4-bromoacetanilide; 4'-bromoacetanil

CAS No 103-88-8

SMILES c1(Br)ccc(NC(C)=O)cc1

to data matrix ->

metabolism mode...

1 (Target)

2 (Metabolite)

3 (Metabolite)

4 (Metabolite)

5 (Metabolite)

Root of map No. 181

Metabolite in map ...

Metabolite in map ...

Not categorized

実測試験で得られている
代謝物の構造が表示される
(今回の場合は9物質)

実測試験で得られている
代謝物の構造が表示される
(今回の場合は9物質)

1-9. 代謝物のProfiling結果

Hazard Evaluation Support System

Reset Options Help

Input
Profiling
RDT Data
Categories
Gap Filling
Report
Metabolism

Chemical name:
CAS No 103-88-8
SMILES c1(Br)ccc(NC(C)=O)cc1

to data matrix-> metabolism mode...

Show Boundaries Apply New Scheme

Profiling methods
☐ in vivo mutagenicity (Micronucleus)
☐ Oncologic Primary Classification
☐ Skin irritation/corrosion Exclusion
☐ Skin irritation/corrosion Inclusion

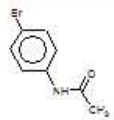
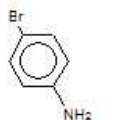
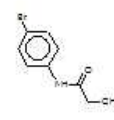
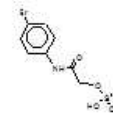
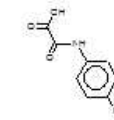
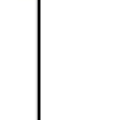
Empiric
☐ Chemical elements
☐ Groups of elements
☐ Lipinski Rule Oasis
☐ Organic functional groups
☐ Organic functional groups (nested)
☐ Organic functional groups (US EPA)
☐ Organic functional groups, North America
☒ Study No. (Link to SSRDT)
☒ Chemical No. (Link to HESS DB)
☒ RDT Report No.
☐ CSCL Class
☒ Rat Liver Metabolism Database

Toxicological
☒ Repeated dose (HESS)

Custom
☐ HESS Chemical Classification

Metabolism
Documented
☐ Observed Rat Liver metabolism
Simulated
☐ Dissociation simulation
☐ Liver Metabolism Simulator
☐ NEDO In Vitro Rat Cellular Metabolism
☐ NEDO In Vitro Rat Microsomal Metabolism
☐ NEDO In Vivo Rat Metabolism Simulation

Filter endpoint tree...

	1 (Target)	2 (Metabolite)	3 (Metabolite)	4 (Metabolite)	5 (Metabolite)	6 (Metabolite)
Structure						
Substance Identity						
Profile						
Study No. (Link to SSRDT)						
Chemical No. (Link to HESS DB)						
RDT Report No.						
Root of map No. 181	Root of map No. 181	Root of map No. 509	Metabolite in map ...	Metabolite in map ...	Metabolite in map ...	Metabolite in map ...
Metabolite in map ...	Metabolite in map ...	Metabolite in map ...	Metabolite in map ...	Metabolite in map ...	Metabolite in map ...	Metabolite in map ...
Metabolite in map ...	Metabolite in map ...	Metabolite in map ...	Metabolite in map ...	Metabolite in map ...	Metabolite in map ...	Metabolite in map ...
Repeated dos...	Not categorized	Anilines (Hemolytic... Anilines (Hepatotox...	Not categorized	Not categorized	Not categorized	Not categorized

①アニリンカテゴリーに属する代謝物がある

↓

②評価対象物質ではなく、代謝物の影響で、毒性が発現する可能性がある

↓

③この代謝物を評価対象にして、毒性の評価を行う

10 Single chemical 17/0/0 Developed by LMC, Bulgaria STOP

1-10. 代謝物を評価対象(Target)に設定する

Reset

Options

Help

Input

Profiling

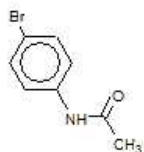
RDT Data

Categories

Gap Filling

Report

Metabolism



Chemical name:

CAS No 103-88-8

SMILES c1(Br)ccc(NC(C)=O)cc1

to data matrix ->

metabolism mode...

Show Boundaries Apply New Scheme

Filter endpoint tree...	1 (Target)	2 (Metabolite)	3 (Metabolite)	4 (Metabolite)	5 (Metabolite)	6 (Metabolite)
Structure						
Substance Identity						
Profile						
Study No. (Lin...						
Chemical No.						
RDT Report No.						
Rat Liver Meta...	Root of map No. 181	Root of map No. 509				
Repeated dos...	Metabolite in map ...	Metabolite in map ...				
	Metabolite in map ...	Metabolite in map ...				
	Not categorized	Anilines (Hemolytic)				
		Anilines (Hepatotoxic)				

① 評価対象(Target)に設定したい代謝物の分子構造の上で右クリック

② 表示されたメニューバーから、「Focus metabolite」を選択

1-11. 評価対象に設定した代謝物の反復投与毒性の実測の有無を確認する

Hazard Evaluation Support System

Reset Options Help

Input
Profiling
RDT Data
Categories
Gap Filling
Report
Metabolism

Chemical structure: CC(=O)Nc1ccc(Br)cc1
CAS No: 103-88-8
SMILES: c1(Br)ccc(NC(C)=O)cc1
to data matrix-> metabolism mode...

①

Gather **③**

Databases
☐ Biomarker DB
☐ COSMOS DB
☒ HESS Repeated Dose Toxicity **②**
☐ HESS Repeated Dose Toxicity (CSCL New Chemi...
☐ ToxRef DB

Filter endpoint tree... 1 (Target) (Metabolite)

Structure

Substance Identity

Profile

Study No. (Lin...
Chemical No. ...
RDT Report No.
Rat Liver Meta...
Repeated dos...

Root of map No. 509
Metabolite in map ...
Metabolite in map ...
Anilines (Hemolytic...
Anilines (Hepatotox...

①「RDT Data」の項目に移動
↓
②「HESS Repeat Dose Toxicity」を選択
↓
③「Gather」をクリック

1 Single chemical 17/07/0 Developed by LMC, Bulgaria STOP

1-12. 評価対象に設定した代謝物の反復投与毒性の実測データの検索結果

Hazard Evaluation Support System

Reset Options Help

Input
Profiling
RDT Data
Categories
Gap Filling
Report
Metabolism

Chemical structure: CC(=O)Nc1ccc(Br)cc1
CAS No: 103-88-8
SMILES: c1(Br)ccc(NC(C)=O)cc1
to data matrix-> metabolism mode...

Gather

Databases
☐ Biomarker DB
☐ COSMOS DB
☒ HESS Repeated Dose Toxicity
☐ HESS Repeated Dose Toxicity (CSCL New Chemi...
☐ ToxRef DB

Filter endpoint tree... 1 (Target) (Metabolite)

Structure

Substance Identity

Profile

Study No. (Lin...
Chemical No. ...
RDT Report No.
Rat Liver Meta...
Repeated dos...

Root of map No. 509
Metabolite in map ...
Metabolite in map ...
Anilines (Hemolytic...
Anilines (Hepatotox...

NITE HESS
No data found.
OK

(反復投与毒性の実測データなし)

1 Single chemical Assigning to data matrix... 1/1/1 Developed by LMC, Bulgaria STOP

1-13. 評価対象に設定した代謝物の類似物質の検索① (反復投与毒性試験が実施済みのもの)

Hazard Evaluation Support System

Input
Profiling
① RDT Data
Categories
Gap Filling
Report
Metabolism

CAS No 103-88-8
SMILES c1(Br)ccc(NC(C)=O)cc1
to data matrix-> metabolism mode...

Define
Subcategorize
Combine Categories

Grouping methods
Empiric
Chemical elements
Groups of elements
Lipinski Rule Oasis
Organic functional groups
Organic functional groups (nested)
Organic functional groups (US EPA)
Organic functional groups, Norbert
Structure similarity
Effect similarity
Study No. (Link to SSRDT)
Chemical No. (Link to HESS DB)
RDT Report No.
CSCL Class
Rat Liver Metabolism Database
Toxicological
Repeated dose (HESS)
Custom
HESS Chemical Class

Defined Categories
Document_1

Filter endpoint tree... 1 (Target) (Metabolite)

Structure
Substance Identity
Profile
Study No. (Lin...
Chemical No. ...
RDT Report No.
Rat Liver Meta...
Repeated dos...

Root of map No. 509
Metabolite in map ...
Metabolite in map ...
Anilines (Hemolytic...
Anilines (Hepatotox...

①「Categories」の項目に移動
↓
②「Repeated dose(HESS)」を選択
↓
③「Define」をクリック

1 Single chemical 17/07/0 Developed by LMC, Bulgaria STOP

1-14. 評価対象に設定した代謝物の類似物質の検索② (反復投与毒性試験が実施済みのもの)

Hazard Evaluation Support System

Input
Profiling
RDT Data
Categories
Gap Filling
Report
Metabolism

CAS No 103-88-8
SMILES c1(Br)ccc(NC(C)=O)cc1
to data matrix-> metabolism mode...

Define
Subcategorize
Combine Categories

Grouping methods
Empiric
Chemical elements
Groups of elements
Lipinski Rule Oasis
Organic functional groups
Organic functional groups (nested)
Organic functional groups (US EPA)
Organic functional groups, Norbert
Structure similarity
Effect similarity
Study No. (Link to SSRDT)
Chemical No. (Link to HESS DB)
RDT Report No.
CSCL Class
Rat Liver Metabolism Database
Toxicological
Repeated dose (HESS)
Custom
HESS Chemical Class

Defined Categories
Document_1
Delete Delete All

Repeated dose (HESS)
Target(s) profiles
Anilines (Hemolytic anemia with methemoglobinemia) Rank A
Anilines (Hepatotoxicity) Rank C
All Profiles
3-Methylcholantrene (Hepatotoxicity) Alert
4,4'-Diethylaminoethoxyhexestrol (Hepatotoxicity) Alert
4,4'-Methylenedianilines/benzidines (Hepatobiliary toxicity) Rank B
4-Aminopyrazolopyrimidine (Hepatotoxicity) Alert
Acrylamides (Neurotoxicity) Rank C
Aliphatic amines (Mucous membrane irritation) Rank C
Aliphatic nitriles (Hepatotoxicity) Rank B
Aliphatic/Alicyclic hydrocarbons (Alpha 2u-globulin nephropathy) Rank A
Allyl esters (Hepatotoxicity) Rank A
Amineptine (Hepatotoxicity) Alert
Amiodarone (Hepatotoxicity) Alert
Aromatic hydrocarbons (Liver enzyme induction) Rank C
Azobenzenes (Hemolytic anemia with methemoglobinemia) Rank B
Benzene/ Naphthalene sulfonic acids (Less susceptible) Rank C
Benzenesulfonamides (Toxicity to urinary system) Rank B

Combine profiles logically with
☒ and ☐ or
☐ Invert result
☐ Strict
OK Cancel

①「Aniline (Hepatotoxicity)」を選択
②「下矢印」をクリック
③「OK」をクリック

17
Single chemical Grouping 17/170 Developed by LMC, Bulgaria STOP

1-15. 評価対象に設定した代謝物の類似物質の検索結果 (アニリンの溶血性貧血のカテゴリーに該当する20物質)

Hazard Evaluation Support System

Reset Options Help

Input
Profiling
RDT Data
Categories
Gap Filling
Report
Metabolism

CAS No 103-88-8
SMILES c1(Br)ccc(NC(C)=O)cc1
to data matrix=> metabolism mode...

Structure

Substance Identity
Repea... (20/12613)
Profile
Study No. (Lin...
Chemical No. ...
RDT Report No.
Rat Liver Meta...
Repeated dos...

Grouping methods
Empiric
Chemical elements
Groups of elements
Lipinski Rule Oasis
Organic functional groups
Organic functional groups (nested)
Organic functional groups (US EPA
Organic functional groups, Norbert
Effect similarity
Study No. (Link to SSRDT)
Chemical No. (Link to HESS DB)
RDT Report No.
CSCL Class
Rat Liver Metabolism Database
Toxicological
Repeated dose (HESS)
Custom
HESS Chemical Class

Defined Categories
Document_1
[21] Anilines (Hemolytic anemia with methemoglobinemia)

Delete Delete All

1 (Target) (Metabolite)	2	3	4	5	6
	M: 10 mg/kg/day, 1...	M: 10 mg/kg/day, 1...	M: 15 mg/kg/day, 1...	M: 100 mg/kg/day, ...	M: 3

Root of map No. 509
Metabolite in map ...
Metabolite in map ...
Anilines (Hemolytic...
Anilines (Hepatotox...

アニリンの溶血性貧血のカテゴリーに該当する20物質

21 Anilines (Hemolytic anemia with methemoglobinemia) Ran

17/0/0

Developed by LMC, Bulgaria

STOP

18

1-16. 評価対象に設定した代謝物の類似物質のProfiling結果 (アニリンの溶血性貧血のカテゴリーに該当する20物質)

Input

Profiling

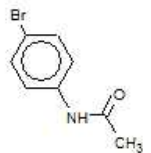
RDT Data

Categories

Gap Filling

Report

Metabolism



CAS No **103-88-8**

SMILES **c1(Br)ccc(NC(=O)C)cc1**

to data matrix-> metabolism mode...

Show Boundaries Apply New Scheme

Profiling methods

- ☐ in vivo mutagenicity (Micronucleus)
- ☐ Oncologic Primary Classification
- ☐ Skin irritation/corrosion Exclusion
- ☐ Skin irritation/corrosion Inclusion

Empiric

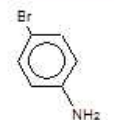
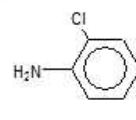
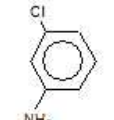
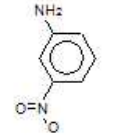
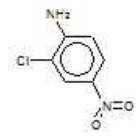
- ☐ Chemical elements
- ☐ Groups of elements
- ☐ Lipinski Rule Oasis
- ☐ Organic functional groups
- ☐ Organic functional groups (nested)
- ☐ Organic functional groups (US EPA)
- ☐ Organic functional groups, Normalized
- ☒ Study No. (Link to SSRDT)
- ☒ Chemical No. (Link to HESS DB)
- ☒ RDT Report No.
- ☐ CSCL Class
- ☒ Rat Liver Metabolism Database

Toxicological

- ☒ Repeated dose (HESS)

Custom

- ☐ HESS Chemical Classification

Filter endpoint tree...	1 (Target) (Metabolite)	2	3	4	5	6
Structure						
Substance Identity						
Repeated dose (20/12613)		M: 10 mg/kg/day, 1...	M: 10 mg/kg/day, 1...	M: 15 mg/kg/day, 1...	M: 100 mg/kg/day, ...	M: 3
Profile						
Study No. (Lin...		312	313	5	701	201
Chemical No. ...		301	302	5	564	196
RDT Report No.		301	301	5	591	199
Root of map No. 509 Metabolite in map ...	Root of map No. 509 Metabolite in map ...	Root of map No. 248 Metabolite in map ...	Root of map No. 249 Metabolite in map ...	Root of map No. 6 Metabolite in map ...	N/A	Root
Rat Liver Meta...						
Repeated dos...	Anilines (Hemolytic... Anilines (Hepatotox...	Anilines (Hemolytic... Anilines (Hepatotox...	Anilines (Hemolytic... Anilines (Hepatotox...	Anilines (Hemolytic... Anilines (Hepatotox... Nitrobenzenes (He... Nitrobenzenes (Hep...	Anilines (Hemolytic... Anilines (Hepatotox... Nitrobenzenes (He... Nitrobenzenes (Hep...	Anilin... Anilin...

Reset Options Help

21 Anilines (Hemolytic anemia with methemoglobinemia) Ran

17/0/0

Developed by LMC, Bulgaria

STOP

※Profilingの方法は1-2参照(スライド5)

1-17. NOELの最小値の表示① (全所見に対するNOELの最小値)

Input

Profiling

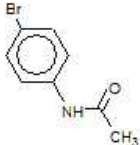
RDT Data

Categories

Gap Filling

Report

Metabolism



CAS No **103-88-8**

SMILES **c1(Br)ccc(NC(C)=O)cc1**

to data matrix--> metabolism mode...

Show Boundaries Apply New Scheme

Profilers

Profiling methods

- ☐ in vivo mutagenicity (Micronucleus test)
- ☐ Oncologic Primary Classification
- ☐ Skin irritation/corrosion Exclusion
- ☐ Skin irritation/corrosion Inclusion

Empiric

- ☐ Chemical elements
- ☐ Groups of elements
- ☐ Lipinski Rule Oasis
- ☐ Organic functional groups
- ☐ Organic functional groups (nested)
- ☐ Organic functional groups (US EPA)
- ☐ Organic functional groups, North America
- ☒ Study No. (Link to SSRDT)
- ☒ Chemical No. (Link to HESS DB)
- ☒ RDT Report No.
- ☐ CSCL Class
- ☒ Rat Liver Metabolism Database

Toxicological

- ☒ Repeated dose (HESS)

Custom

- ☐ HESS Chemical Class

Metabolism

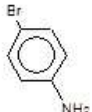
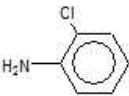
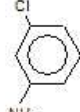
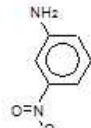
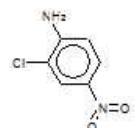
Documented

- ☐ Observed Rat Liver metabolism

Simulated

- ☐ Dissociation simulation
- ☐ Liver Metabolism Simulator
- ☐ NEDO In Vitro Rat Cellular Metabolism
- ☐ NEDO In Vitro Rat Microsomal Metabolism
- ☐ NEDO In Vivo Rat Metabolism Simulation

Filter endpoint tree...

	1 (Target) (Metabolite)	2	3	4	5	6
Structure						
Substance Identity						
Repeated Dose ...						
LOEL (19/825)		M: 10 mg/kg/day, 1...	M: 10 mg/kg/day, 1...	M: 15 mg/kg/day, 1...		M: 3
NOEL (20/11788)		M: 10 mg/kg/day, 1...	M: 10 mg/kg/day, 1...	M: 15 mg/kg/day, 1...	M: 100 mg/kg/day, ...	M: 3
Prof						
SI		312	313	5	701	201
CI		301	302	5	564	196
RI		301	301	5	591	199
Function...		map No. 248	Root of map No. 249	Root of map No. 6	N/A	Root
Filter effects		Metabolite in map ...	Metabolite in map ...	Metabolite in map ...		
Set tree hierarchy...						
Export CAS list						
Export		Anilines (Hemolytic...	Anilines (Hemolytic...	Anilines (Hemolytic...	Anilines (Hemolytic...	Anilines (Hemolytic...
Copy path		Anilines (Hepatotox...	Anilines (Hepatotox...	Anilines (Hepatotox...	Anilines (Hepatotox...	Anilines (Hepatotox...
		Nitrobenzenes (He...	Nitrobenzenes (He...	Nitrobenzenes (He...	Nitrobenzenes (He...	Nitrobenzenes (He...

①「NOEL」の文字の上で右クリック

↓

②「Function」→「Min」を選択

20

21 Anilines (Hemolytic anemia with methemoglobinemia) Ran

17/0/0

Developed by LMC, Bulgaria

STOP

1-18. NOELの最小値の表示② (全所見に対するNOELの最小値)

Input

Profiling

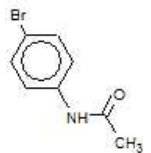
RDT Data

Categories

Gap Filling

Report

Metabolism

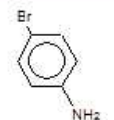
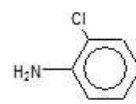
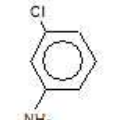
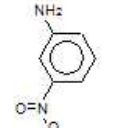
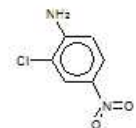


CAS No **103-88-8**

SMILES **c1(Br)ccc(NC(C)=O)cc1**

to data matrix-> metabolism mode...

Show Boundaries Apply
New Scheme

Filter endpoint tree...	1 (Target) (Metabolite)	2	3	4	5	6
Structure						
Substance Identity						
Repeated Dose ...						
LOEL (19/825)		M: 10 mg/kg/day, 1...	M: 10 mg/kg/day, 1...	M: 15 mg/kg/day, 1...		M: 3
(20/11788) Min		M: <10 mg/kg/day	M: <10 mg/kg/day	M: <15 mg/kg/day	M: 100 mg/kg/day	M: <
Profile						
Study No. (Lin...		312	313	5	701	201
Chemical No. ...		301	302	5	564	196
RDT Report No.		301	301	5	591	199
Rat Liver Meta...	Root of map No. 509 Metabolite in map ...	Root of map No. 248 Metabolite in map ...	Root of map No. 249 Metabolite in map ...	Root of map No. 6 Metabolite in map ...	N/A	Root
Repeated dos...	Anilines (Hemolytic... Anilines (Hepatotox...	Anilines (Hemolytic... Anilines (Hepatotox...	Anilines (Hemolytic... Anilines (Hepatotox...	Anilines (Hemolytic... Anilines (Hepatotox... Nitrobenzenes (He... Nitrobenzenes (Hep...	Anilines (Hemolytic... Anilines (Hepatotox... Nitrobenzenes (He... Nitrobenzenes (Hep...	Anili... Anili...

Profiling methods

- ☐ in vivo mutagenicity (Micronucle...
- ☐ Oncologic Primary Classification
- ☐ Skin irritation/corrosion Exclusion
- ☐ Skin irritation/corrosion Inclusion

Empiric

- ☐ Chemical elements
- ☐ Groups of elements
- ☐ Lipinski Rule Oasis
- ☐ Organic functional groups
- ☐ Organic functional groups (nest...
- ☐ Organic functional groups (US I...
- ☐ Organic functional groups, Nort...
- ☒ Study No. (Link to SSRDT)
- ☒ Chemical No. (Link to HESS DB)
- ☒ RDT Report No.
- ☐ CSCL Class
- ☒ Rat Liver Metabolism Database

Toxicological

- ☒ Repeated dose (HESS)

Custom

- ☐ HESS Chemical Char...

Metabolism

Documented

- ☐ Observed Rat Liver metabolism

Simulated

- ☐ Dissociation simulation
- ☐ Liver Metabolism Simulator
- ☐ NEDO In Vitro Rat Cellular Metabo...
- ☐ NEDO In Vitro Rat Microsomal Met...
- ☐ NEDO In Vivo Rat Metabolism Simu...

全所見に対するNOELの最小値が表示される

21

21 Anilines (Hemolytic anemia with methemoglobinemia) Rat

1/0/0

Developed by LMC, Bulgaria

STOP

1-19. NOELの最小値の表示① (溶血性貧血に対するNOELの最小値)

Hazard Evaluation Support System

Reset Options Help

Input
Profiling
RDT Data
Categories
Gap Filling
Report
Metabolism

SMILES: c1(Br)ccc(NC(C)=O)cc1

to data matrix -> metabolism mode...

Show Boundaries Apply New Scheme

Profiling methods

- ☐ Biodegradation fragments (BioWIN)
- ☐ Carcinogenicity (genotox and non)
- ☐ Eye irritation/corrosion Exclusion r
- ☐ Eye irritation/corrosion Inclusion r
- ☐ in vitro mutagenicity (Ames test)
- ☐ in vivo mutagenicity (Micronucleus)
- ☐ Oncologic Primary Classification
- ☐ Skin irritation/corrosion Exclusion r
- ☐ Skin irritation/corrosion Inclusion r

Empiric

- ☐ Chemical elements
- ☐ Groups of elements
- ☐ Lipinski Rule Oasis
- ☐ Organic functional groups
- ☐ Organic functional groups (nested)
- ☐ Organic functional groups (US EPA)
- ☐ Organic functional groups, Norbert
- ☒ Study No. (Link to SSRDT)
- ☒ Chemical No. (Link to HESS DB)
- ☒ RDT Report No.
- ☐ CSCL Class
- ☒ Rat Liver Metabolism Database

Toxicological

- ☒ Repeated dose (HESS)

Metabolism

Documented

- ☐ Observed Rat Liver metabolism

Simulated

- ☐ Dissociation simulation
- ☐ Liver Metabolism Simulator
- ☐ NEDO In Vitro Rat Cellular Metabolism
- ☐ NEDO In Vitro Rat Microsomal Metabolism
- ☐ NEDO In Vivo Rat Metabolism Simulation

Filter endpoint tree...

Structure

Substance Identity

Repeated Dose Toxicity

NOEL (19/825) Min

NOEL (20/11788) Min

Hide

Show hidden

Collapse all

Sort (targets priority)

Sort

Function...

Filter effects

Edit filters...

Set tree hierarchy...

Remove filter

Export CAS list

Export

Copy path

1 (Target) (Metabolite)	2	3	4	5	6
M: 10 mg/kg/day	M: 10 mg/kg/day	M: 10 mg/kg/day	M: 15 mg/kg/day	M: 100 mg/kg/day	M: 30 mg/kg/day
M: <10 mg/kg/day	M: <10 mg/kg/day	M: <10 mg/kg/day	M: <15 mg/kg/day	M: 100 mg/kg/day	M: <30 mg/kg/day
2	1	313	5	701	201
1	302	5	5	564	196
1	301	5	5	591	199
Root of map No. 248	Root of map No. 249	Root of map No. 6	N/A	Root of map No. 6	Root of map No. 6
Metabolite in map ...	Metabolite in map ...	Metabolite in map ...			
Anilines (Hemolytic...)	Anilines (Hemolytic...)	Anilines (Hemolytic...)	Anilines (Hemolytic...)	Anilines (Hemolytic...)	Anilines (Hemolytic...)
Anilines (Hepatotox...)	Anilines (Hepatotox...)	Anilines (Hepatotox...)	Anilines (Hepatotox...)	Anilines (Hepatotox...)	Anilines (Hepatotox...)
Nitrobenzenes (He...)	Nitrobenzenes (He...)	Nitrobenzenes (He...)	Nitrobenzenes (He...)	Nitrobenzenes (He...)	Nitrobenzenes (He...)
Nitrobenzenes (Hep...)	Nitrobenzenes (Hep...)	Nitrobenzenes (Hep...)	Nitrobenzenes (Hep...)	Nitrobenzenes (Hep...)	Nitrobenzenes (Hep...)

21 Anilines (Hemolytic anemia with methemoglobinemia) Rank A (R)

1/0/0

Developed by LMC, Bulgaria

STOP

①「NOEL」の文字の上で右クリック

②「Filter effects」→「Edit filters」を選択

1-20. NOELの最小値の表示② (溶血性貧血に対するNOELの最小値)

Hazard Evaluation Support System

Input
Profiling
RDT Data
Categories
Gap Filling
Report
Metabolism

CAS No 103-88-8
SMILES c1(Br)ccc(NC(C)=O)cc1
to data matrix -> metabolism mode...

Structure
Substance Identity
Repeated Dose ...
Profile name...
Enter profile name: Anemia
OK Cancel

Effects...
Profiles...
Save current settings to profile...
Delete profile
Predefined list...
Alpha 2u-globulin nephropathy
Energy metabolism dysfunction
Hemolytic anemia
Hemolytic anemia with methemoglobinemia
Hepatotoxicities/Liver effects
Less susceptible
Lipodosis of Adrenocortical
Liver_enzyme induction
Mucous membrane irritation
Neurotoxicity
Renal Toxicity/Kidney Effects
Testis
Thyroid toxicity
Urinary bladder

1 (Target) (Metabolite) 2 3 4 5 6

Root of map No. 509
Metabolite in map ...
Root of map No. ...
Metabolite in map ...

Anilines (Hemolytic...
Anilines (Hepatotox...
Anilines (Hemolytic...
Anilines (Hepatotox...
Anilines (Hemolytic...
Anilines (Hepatotox...
Anilines (Hemolytic...
Anilines (Hepatotox...
Nitrobenzenes (He...
Nitrobenzenes (He...
Nitrobenzenes (Hep...
Nitrobenzenes (Hep...

①「Predefined list」を選択
②「Hemolytic anemia～」を選択
③「Profilers」→「Save current setting～」を選択
④「Anemia」を入力

21 Anilines (Hemolytic anemia with methemoglobinemia) Rar 17/07/00 Developed by LMC, Bulgaria STOP

1-21. NOELの最小値の表示③ (溶血性貧血に対するNOELの最小値)

Input

Profiling

RDT Data

Categories

Gap Filling

Report

Metabolism

Chemical Name:

CAS No: 103-88-8

SMILES: c1(Br)ccc(NC(C)=O)cc1

to data matrix--> metabolism mode...

Show Boundaries Apply New Scheme

Profilers

Profiling methods

- ☐ in vivo mutagenicity (Micronucle...
- ☐ Oncologic Primary Classification
- ☐ Skin irritation/corrosion Exclusion
- ☐ Skin irritation/corrosion Inclusion

Empiric

- ☐ Chemical elements
- ☐ Groups of elements
- ☐ Lipinski Rule Oasis
- ☐ Organic functional groups
- ☐ Organic functional groups (nest...
- ☐ Organic functional groups (US E...
- ☐ Organic functional groups, Norb...
- ☒ Study No. (Link to SSRDT)
- ☒ Chemical No. (Link to HESS DB)
- ☒ RDT Report No.
- ☐ CSCL Class
- ☒ Rat Liver Metabolism Database

Toxicological

- ☒ Repeated dose (HESS)

Custom

- ☐ HESS Chemical Class

Structure

Substance Identity

Repeated Dose ...

LOEL (19/825)

NOEL (20/11788) Min

Profile

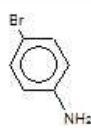
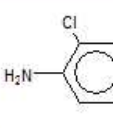
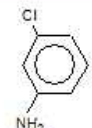
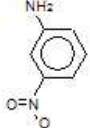
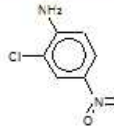
Study No. (Lin...

Chemical No. (...)

RDT Report No.

Rat Liver Meta...

Repeated dos...

1 (Target) (Metabolite)	2	3	4	5	6
					
M: 10 mg/kg/day, 1...	M: 10 mg/kg/day, 1...	M: 10 mg/kg/day, 1...	M: 15 mg/kg/day, 1...	M: 100 mg/kg/day	M: 3...
M: <10 mg/kg/day	M: <10 mg/kg/day	M: <15 mg/kg/day	M: <15 mg/kg/day	M: 100 mg/kg/day	M: <...
		313	5	701	201
		302	5	564	196
		301	5	591	199
		Root of map No. 248	Root of map No. 249	Root of map No. 6	Root
		Metabolite in map ...	Metabolite in map ...	Metabolite in map ...	
		Metabolite in map ...	Metabolite in map ...	Metabolite in map ...	
		Anilines (Hemolytic...	Anilines (Hemolytic...	Anilines (Hemolytic...	Anili...
		Anilines (Hepatotox...	Anilines (Hepatotox...	Anilines (Hepatotox...	Anili...
		Nitrobenzenes (He...	Nitrobenzenes (He...	Nitrobenzenes (He...	
		Nitrobenzenes (Hep...	Nitrobenzenes (Hep...	Nitrobenzenes (Hep...	

①「NOEL(20/11788)Min」の文字の上で右クリック

②「Filter effects」→「Anemia」を選択

↓

溶血性貧血に関連する所見のNOELの最小値が表示される

24

21 Anilines (Hemolytic anemia with methemoglobinemia) Rar

1/0/0

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STOP

1-22. NOELの最小値の表示④ (溶血性貧血に対するNOELの最小値)

Reset

Options

Help

Input

Profiling

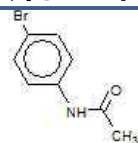
RDT Data

Categories

Gap Filling

Report

Metabolism



CAS No 103-88-8

SMILES c1(Br)ccc(NC(C)=O)cc1

to data matrix->

metabolism mode...

Data Gap Filling Method

☒ Read-across☐ Trend analysis☐ (Q)SAR models

Apply

Target Endpoint

Repeated Dose Toxicity NOEL

Filter endpoint tree...

Structure

Substance Identity

Repeated Dose Toxicity

LOEL (19/312) Min

NOEL Min

Blood Chem (17/28)

Hematological Ex...

Blood Cell (Eryt...

Undefined Tis...

RBC↓ (20/34)

HGB↓ (20/34)

Reti... (17/28)

Met... (11/20)

HCT↓ (20/34)

Histopath... (20/237)

Organ Wei... (19/59)

Profile

Study No. (Link to ...)

Chemical No. (Link ...)

RDT Report No.

Rat Liver Metabolis...

Metabolite in map ...

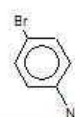
Metabolite in map ...

Anilines (Hemolytic...

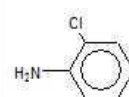
Anilines (Hepatotox...

Repeated dose (HE...

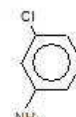
1 (Target) (Metabolite)



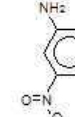
2



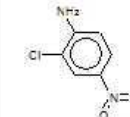
3



4



5



6



M: 10 mg/kg/day

M: <10 mg/kg/day

M: 100 mg/kg/day

M: 100 mg/kg/day

M: 100 mg/kg/day

M: 100 mg/kg/day

M: 100 mg/kg/day

M: 100 mg/kg/day

M: 100 mg/kg/day

M: 100 mg/kg/day

M: 100 mg/kg/day

M: 100 mg/kg/day

M: 100 mg/kg/day

M: 100 mg/kg/day

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M: 100 mg/kg/day

M: 100 mg/kg/day

M: 100 mg/kg/day

M: 100 mg/kg/day

M: 100 mg/kg/day

M: 100 mg/kg/day

M: 100 mg/kg/day

M: 100 mg/kg/day

溶血性貧血に関連する
所見のみが表示される

1-23. 評価対象に設定した代謝物のRead-acrossによる毒性評価① (溶血性貧血を対象とした評価)

Input

Profiling

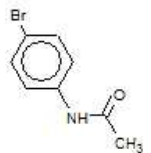
RDT Data

Categories

Gap Filling

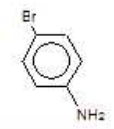
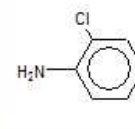
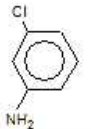
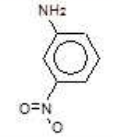
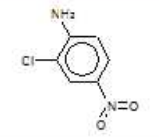
Report

Metabolism



CAS No **103-88-8**
SMILES **c1(Br)ccc(NC(C)=O)cc1**

to data matrix >> metabolism mode...

Filter endpoint tree...	1 (Target) (Metabolite)	2	3	4	5	6
Structure						
Substance Identity						
Repeated Dose ...						
LOEL (19/825)		M: 10 mg/kg/day, 1...	M: 10 mg/kg/day, 1...	M: 15 mg/kg/day, 1...		
NOEL Mit		M: <10 mg/kg/day	M: <10 mg/kg/day	M: <15 mg/kg/day	M: 100 mg/kg/day	
Blo... (19/1058)		M: 20 mg/kg/day, 8...	M: 80 mg/kg/day, 8...	M: 15 mg/kg/day, 1...	M: 100 mg/kg/day, ...	
FOB (6/192)					M: 100 mg/kg/day, ...	
Ge... (20/1154)		M: 10 mg/kg/day, 2...	M: 40 mg/kg/day, 4...	M: 170 mg/kg/day, ...	M: 100 mg/kg/day, ...	
He... (20/1003)		M: 10 mg/kg/day, 1...	M: 10 mg/kg/day, 1...	M: 15 mg/kg/day, 1...	M: 100 mg/kg/day, ...	
His... (20/5311)		M: 20 mg/kg/day, 4...	M: 10 mg/kg/day, 2...	M: 15 mg/kg/day, 1...	M: 100 mg/kg/day, ...	
Ne... (20/1535)		M: 160 mg/kg/day, ...	M: 160 mg/kg/day, ...	M: 170 mg/kg/day, ...	M: 100 mg/kg/day, ...	
NOAEL... (1/1)						
NOE... (20/36)		M: <10 mg/kg/day, ...	M: <10 mg/kg/day, ...	M: <15 mg/kg/day, ...	M: 100 mg/kg/day	
Or... (20/1056)		M: 10 mg/kg/day, 2...	M: 10 mg/kg/day, 1...	M: 15 mg/kg/day, 1...	M: 100 mg/kg/day, ...	
Other E... (1/1)			M: 80 mg/kg/day			
Urin... (16/441)				M: 170 mg/kg/day, ...	M: 100 mg/kg/day, ...	
Profile						
Study No. (Lin...		312	313	5	701	20
Chemical No. (...)		301	302	5	564	19
RDT Report No.		301	301	5	591	19
Rat Liver Meta...	Root of map No. 509 Metabolite in map ... Metabolite in map ...	Root of map No. 248 Metabolite in map ... Metabolite in map ...	Root of map No. 249 Metabolite in map ... Metabolite in map ...	Root of map No. 6 Metabolite in map ...	N/A	R
Repeated dos...	Anilines (Hemolytic... Anilines (Hepatotox...	Anilines (Hemolytic... Anilines (Hepatotox...	Anilines (Hemolytic... Anilines (Hepatotox...	Anilines (Hemolytic... Anilines (Hepatotox... Nitrobenzenes (He... Nitrobenzenes (Hep...	Anilines (Hemolytic... Anilines (Hepatotox... Nitrobenzenes (He... Nitrobenzenes (Hep...	A A

①「Gap Filling」の項目に移動

↓

②「Read-across」を選択

↓

③評価対象に設定した代謝物のNOELのセルを選択

↓

④「Apply」をクリック

26

21 Anilines (Hemolytic anemia with methemoglobinemia) Rar

1/0/0

Developed by LMC, Bulgaria

STOP

1-24. 評価対象に設定した代謝物のRead-acrossによる毒性評価② (NOELの表示単位の変更)

NOELの単位をmol/kg/d
に変換する

①「Option」をクリック

②「Unit」を選択

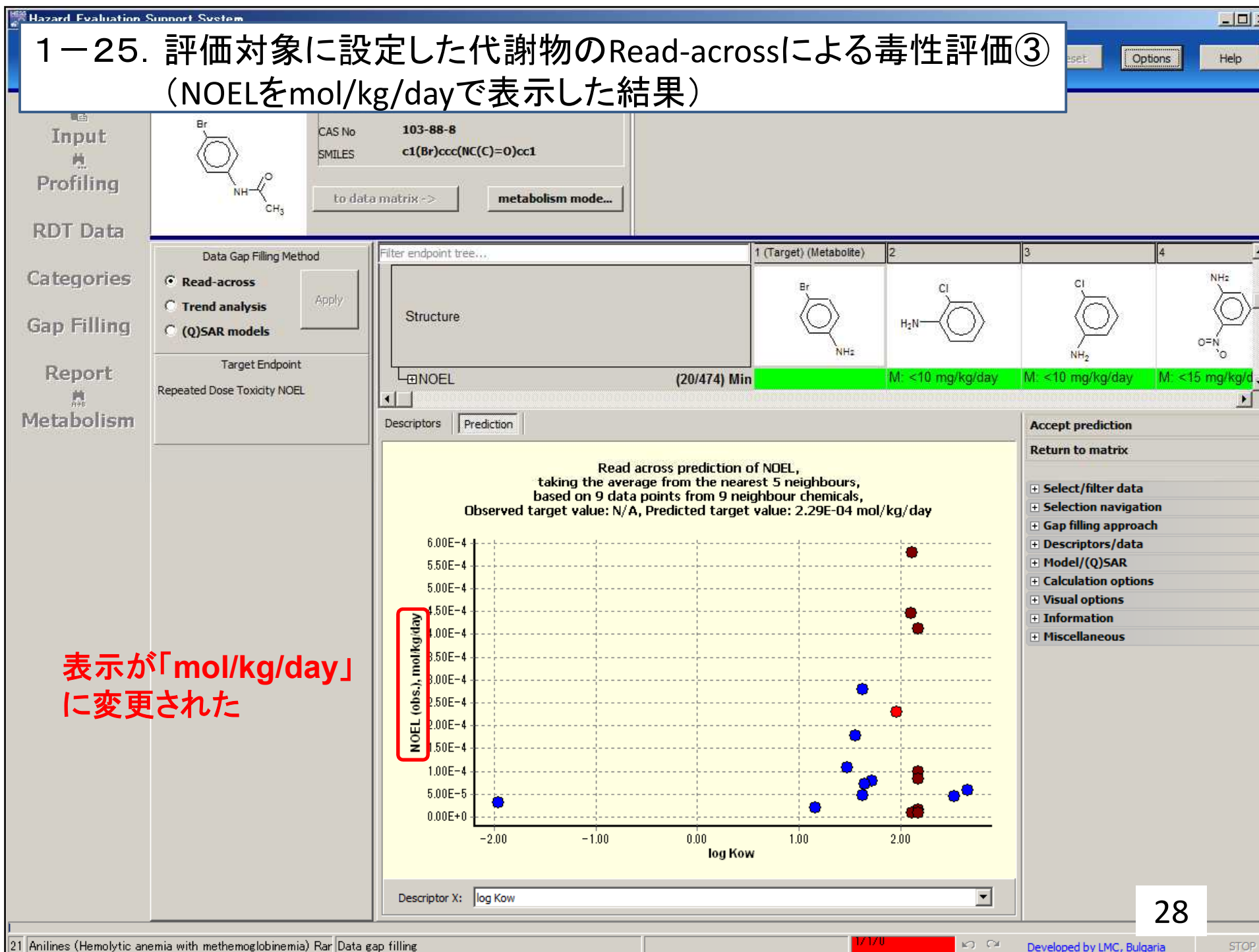
③「Administrated
dose」を選択

④「mol/kg/day」を選択

⑤「OK」をクリック

The screenshot shows the HESS software interface. The 'Options' dialog box is open, with the 'Unit' tab selected. The 'Data matrix' dropdown is set to 'Administrated dose'. In the 'Preferred units' section, 'mol/kg/day' is selected. The 'Conversion' section has 'As it is' selected. The 'OK' button is highlighted with a red box and a circled 5. A scatter plot at the bottom shows NOEL on the y-axis (0 to 300) and log Kow on the x-axis (-2.00 to 2.00). The plot contains several data points, mostly clustered between log Kow 1.00 and 2.00. The status bar at the bottom indicates '21 Anilines (Hemolytic anemia with methemoglobinemia) Rat Data gap filling'.

1-25. 評価対象に設定した代謝物のRead-acrossによる毒性評価③ (NOELをmol/kg/dayで表示した結果)



1-26. 評価対象に設定した代謝物のRead-acrossによる毒性評価④ (毒性と構造が類似な物質の抽出)

Input

Profiling

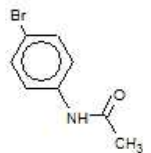
RDT Data

Categories

Gap Filling

Report

Metabolism



CAS No **103-88-8**

SMILES **c1(Br)ccc(NC(C)=O)cc1**

to data matrix -> metabolism mode...

Data Gap Filling Method

☒ Read-across

☐ Trend analysis

☐ (Q)SAR models

Apply

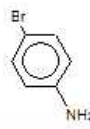
Target Endpoint

Repeated Dose Toxicity NOEL

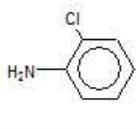
Filter endpoint tree...

Structure

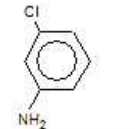
1 (Target) (Metabolite)



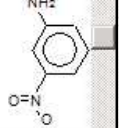
2



3



4



NOEL (20/474) Min

M: <10 mg/kg/day M: <10 mg/kg/day M: <15 mg/kg/d

Accept prediction

Return to matrix

Select/filter data

Subcategorize

Mark chemicals by descriptor value

Filter points by test conditions

Mark focused chemical

Mark focused points

Remove marked chemicals/points

Clear existing marks

+ Selection navigation

+ Gap filling approach

+ Descriptors/data

+ Model/(Q)SAR

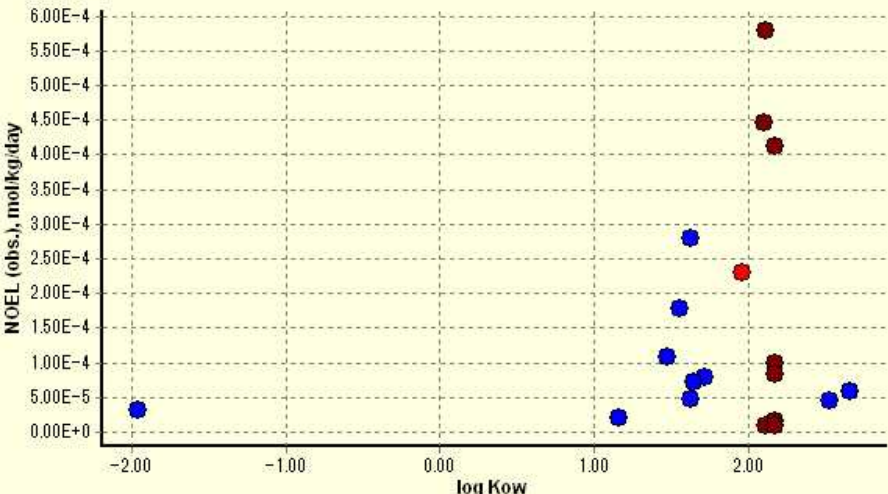
+ Calculation options

+ Visual options

+ Information

+ Miscellaneous

Read across prediction of NOEL, taking the average from the nearest 5 neighbours, based on 9 data points from 9 neighbour chemicals, Observed target value: N/A, Predicted target value: 2.29E-04 mol/kg/day



Descriptor X: log Kow

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- ①「Select/filter data」を選択
- ②「Subcategories」をクリック

1-27. 評価対象に設定した代謝物のRead-acrossによる毒性評価⑤ (Repeated dose (HESS)を用いた類似な物質の抽出)

①「Repeated dose (HESS)」を選択

②「Aniline」以外のカテゴリーを選択

③「Remove」をクリック

Subcategorization

Grouping methods

- Carcinogenicity (genotox)
- Eye irritation/corrosion
- Eye irritation/corrosion
- in vitro mutagenicity (Ames)
- in vivo mutagenicity (MutaScreen)
- Oncologic Primary Class
- Skin irritation/corrosion
- Skin irritation/corrosion

Empiric

- Chemical elements
- Groups of elements
- Lipinski Rule Oasis
- Organic functional groups
- Organic functional groups
- Organic functional groups
- Organic functional groups
- Structure similarity
- Effect similarity
- Study No. (Link to SSR)
- Chemical No. (Link to HPLC)
- RDT Report No.
- CSCL Class
- Rat Liver Metabolism Data

Toxicological

- ① Repeated dose (HESS)**
- Custom
- HESS Chemical Class

Metabolism

Do not account metabolism

Documented

- Observed Rat Liver metabolism

Simulated

- Dissociation simulation
- Liver Metabolism Simulator
- NEDO In Vitro Rat Cellular Metabolism
- NEDO In Vitro Rat Microsomal Metabolism
- NEDO In Vivo Rat Metabolism

③ **Remove**

03-88-8

Nc1ccc(NC(C)=O)cc1

metabolism mode...

endpoint tree...

structure

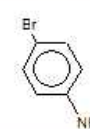
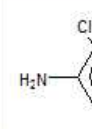


NOEL

(20/474) Min

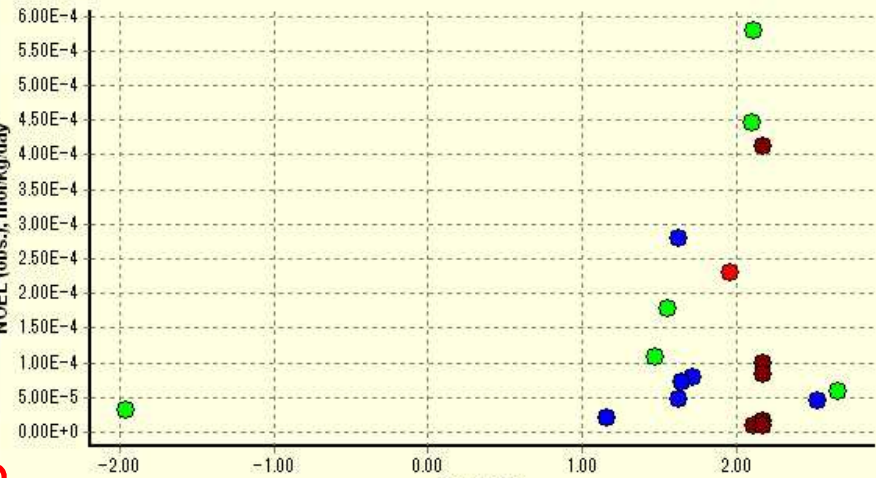
M: <10 mg/kg/day

M: <10 mg/kg/day

M: <15 mg/kg/day

1 (Target) (Metabolite)	2	3	4
			

Read across prediction of NOEL,
taking the average from the nearest 5 neighbours,
based on 9 data points from 9 neighbour chemicals,
Observed target value: N/A, Predicted target value: 2.29E-04 mol/kg/day



log Kow

Accept prediction

Return to matrix

☐ **Select/filter data**

- Subcategorize
- Mark chemicals by descriptor value
- Filter points by test conditions
- Mark focused chemical
- Mark focused points
- Remove marked chemicals/points
- Clear existing marks

+ Selection navigation

+ Gap filling approach

+ Descriptors/data

+ Model/(Q)SAR

+ Calculation options

+ Visual options

+ Information

+ Miscellaneous

1-28. 評価対象に設定した代謝物のRead-acrossによる毒性評価⑥ (類似物質5物質を用いたRead-acrossの予測値の確定)

Input

Profiling

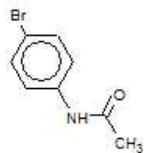
RDT Data

Categories

Gap Filling

Report

Metabolism



CAS No **103-88-8**

SMILES **c1(Br)ccc(NC(C)=O)cc1**

to data matrix ->
metabolism mode...

Data Gap Filling Method

☒ Read-across

☐ Trend analysis

☐ (Q)SAR models

Apply

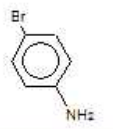
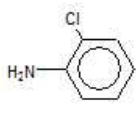
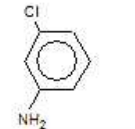
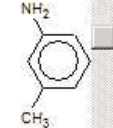
Target Endpoint

Repeated Dose Toxicity NOEL

Filter endpoint tree...

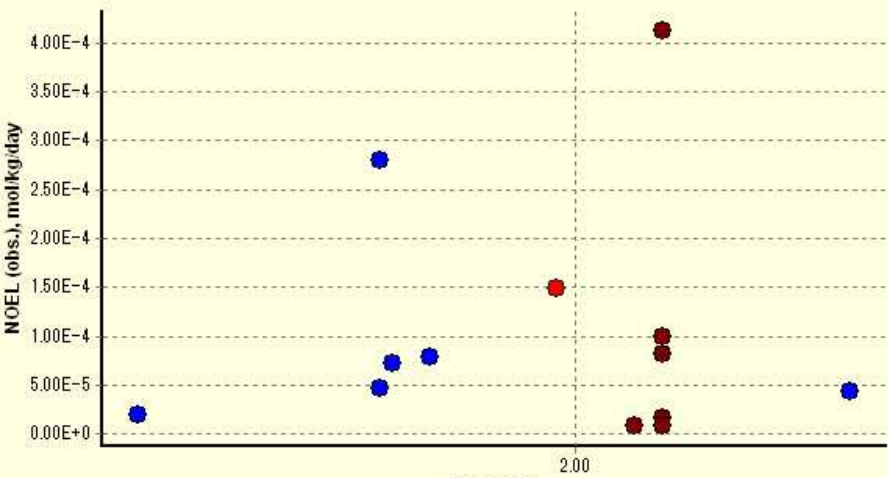
Structure

NOEL (21/475) Min

1 (Target) (Metabolite)	2	3	6
			
R: 25.6 mg/kg/day	M: <10 mg/kg/day	M: <10 mg/kg/day	M: <30 mg/kg/day

Descriptors
Prediction

Read across prediction of NOEL,
taking the average from the nearest 5 neighbours,
based on 7 data points from 7 neighbour chemicals,
Observed target value: N/A, Predicted target value: 1.49E-04 mol/kg/day



log Kow

Descriptor X: log Kow

Select/filter data

Subcategorize

Mark chemicals by descriptor value

Filter points by test conditions

Mark focused chemical

Mark focused points

Remove marked chemicals/points

Clear existing marks

+ Selection navigation

+ Gap filling approach

+ Descriptors/data

+ Model/(Q)SAR

+ Calculation options

+ Visual options

+ Information

+ Miscellaneous

①

Accept prediction

Return to matrix

①「Accept prediction」をクリック

②Read-acrossによる予測値R:25.6mg/kg/dayが表示される

③「Return to matrix」をクリック

1-29. 代謝物の予測値を用いた評価対象物質の毒性評価① (評価対象を代謝物から評価対象物質に変更する)

Reset Options Help

 Input
Profiling

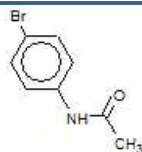
RDT Data

Categories

Gap Filling

Report

Metabolism


 CAS No 103-88-8
 SMILES c1(Br)ccc(NC(C)=O)cc1

to data matrix ->

metabolism mode...

Data Gap Filling Method

☒ Read-across
☐ Trend analysis
☐ (Q)SAR models

Apply

Target Endpoint

Repeated Dose Toxicity

Filter endpoint tree...

Structure

Substance Identity

Repeated Dose ...

LOEL (19/312)

N... (21/475) Min R: 25.6 mg/kg/day

Profile

Study No. (Lin...

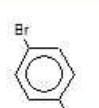
Chemical No. ...

RDT Report No.

Rat Liver Meta...

Repeated dos...

1 (Target) (Metabolite)



2

Defocus metabolite

Remove this target

Select all as targets

Remove all as targets

Add target

Add in category

Delete chemical

Delete all except current

Save to SMI file (DayLight format)

Save to SMI file

Print structures

Export data for targets

Export CAS list

Search

Ctrl+F

Root of map No. 50

Metabolite in map ...

Metabolite in map ...

Anilines (Hemolytic...

Anilines (Hepatotox...

Anilines (Hemolytic...

Anilines (Hepatotox...

Anilines (Hepatotox...

Anilines (Hemolytic...

Anilines (Hepatotox...

Anilines (Hemolytic...

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Anilines (Hepatotox...

Anilines (Hemolytic...

Anilines (Hepatotox...

Anilines (Hepatotox...

Anilines (Hemolytic...

Anilines (Hepatotox...

①「分子構造」の上で右クリック

②「Defocus metabolite」を選択

1-30. 代謝物の予測値を用いた評価対象物質の毒性評価② (代謝物の予測値を用いた評価対象物質のRead-across)

Hazard Evaluation Support System

Input
Profiling
RDT Data
Categories
Gap Filling
Report
Metabolism

CAS No 103-88-8
SMILES c1(Br)ccc(NC(C)=O)cc1
to data matrix-> metabolism mode...

② Data Gap Filling Method
☒ Read-across ③ Apply
☐ Trend analysis
☐ (Q)SAR models

Target Endpoint
Repeated Dose Toxicity NOEL

①「評価対象物質のNOEL」のセルを選択
②「Read-across」を選択
③「Apply」をクリック

Filter endpoint tree...	1 (Target)	2 (Metabolite)	3 (Metabolite)	4 (Metabolite)	5 (Metabolite)	6 (Metabolite)
Structure						
Substance Identity						
Repeated Dose ...						
NOEL (1/1) Mir		R: 25.6 mg/kg/day				
Profile						
Study No. (Lin...						
Chemical No. ...						
RDT Report No.						
Rat Liver Meta...	Root of map No. 181	Root of map No. 509	Metabolite in map ...	Metabolite in map ...	Metabolite in map ...	Metabolite in map ...
Repeated dos...	Metabolite in map ...	Metabolite in map ...	Metabolite in map ...	Metabolite in map ...	Metabolite in map ...	Metabolite in map ...
	Metabolite in map ...	Metabolite in map ...	Metabolite in map ...	Metabolite in map ...	Metabolite in map ...	Metabolite in map ...
	Not categorized	Anilines (Hemolytic... Anilines (Hepatotox...	Not categorized	Not categorized	Not categorized	Not categorized

10 Single chemical 1/0/0 Developed by LMC, Bulgaria STOP

Options

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2. 実施した操作のUNDO機能

2. Undo機能の利用 (例. Read-acrossをやり直す場合)

Hazard Evaluation Support System

Reset Options Help

Input
Profiling
RDT Data
Categories
Gap Filling
Report
Metabolism

CAS No 103-88-8
 SMILES c1(Br)ccc(NC(C)=O)cc1
 to data matrix-> metabolism mode...

Chemical structure: CC(=O)Nc1ccc(Br)cc1

Data Gap Filling Method
☒ Read-across
☐ Trend analysis
☐ (Q)SAR models
 Apply

Target Endpoint
 Repeated Dose Toxicity

Filter endpoint tree...

Structure

Substance Identity
☐ Repeated Dose Toxicity
 LOEL (19/312)
 NOEL (21/475) M: 25.6 mg/kg/day
☐ Profile
 Study No. (Link to SSRDT)
 Chemical No. (Link to HESS DB)
 RDT Report No.
 Rat Liver Metabolism Database
 Repeated dose (HESS)

1 (Target) (Metabolite)	2	3	4
<chem>Nc1ccc(Br)cc1</chem>	<chem>Nc1ccc(Cl)cc1</chem>	<chem>Nc1ccc(Cl)cc1</chem>	<chem>Nc1ccc([N+](=O)[O-])cc1</chem>
M: 10 mg/kg/day, 1...	M: 10 mg/kg/day, 1...	M: 10 mg/kg/day, 1...	M: 15 mg/kg/day, 1...
M: <10 mg/kg/day	M: <10 mg/kg/day	M: <10 mg/kg/day	M: <15 mg/kg/day
312	313	5	
301	302	5	
301	301	5	
Root of map No. 509 Metabolite in map ... Metabolite in map ... Anilines (Hemolytic... Anilines (Hepatotox...	Root of map No. 248 Metabolite in map ... Metabolite in map ... Anilines (Hemolytic... Anilines (Hepatotox...	Root of map No. 249 Metabolite in map ... Metabolite in map ... Anilines (Hemolytic... Anilines (Hepatotox...	Root of map No. 6 Metabolite in map ... Metabolite in map ... Anilines (Hemolytic... Anilines (Hepatotox... Nitrobenzenes (He...

①「左向きの矢印」のアイコンをクリック
 ②1つ前の動作(予測値の表示前)に戻る

※Undo機能は様々なところで操作可能ですが、Data Gap Filling 中(「Data Gap Filling Method」の「Apply」をクリックした後の画面)の操作には使用できません。

①

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21 Anilines (Hemolytic anemia with methemoglobinemia) Rar 1/0/0 Developed by LMC, Bulgaria STOP

3. HELP機能

3. HELP機能の参照

The screenshot displays the HESS (Hazard Evaluation Support System) interface. The main window has a blue header bar with the title 'Hazard Evaluation Support System' and buttons for 'Reset', 'Options', and 'Help'. The 'Help' button is highlighted with a red box. A red arrow points from the 'Help' button to the 'HESS User Manual' window. The 'HESS User Manual' window is open, showing a 'Table of contents' on the left and the 'HESS User Manual' title page on the right. The title page lists various sections: HESS Overview, Data-matrix, Input, Profiling, Data gathering, Categories, Data gap filling, Data Gap filling handling of metabolic activation, Metabolism, and Report. The main window also features a sidebar with icons for 'Input', 'Profiling', 'RDT Data', 'Categories', 'Gap Filling', 'Report', and 'Metabolism'. The chemical name '103-88-8' is entered in the 'CAS #' field, and the chemical structure of 4-bromo-N-(4-chlorophenyl)acetanilide is shown. The 'metabolism mode...' button is also visible.

「HELP」をクリックすると、HELP機能を参照することができる

HESS User Manual

- [HESS Overview](#)
- [Data-matrix](#)
- [Input](#)
- [Profiling](#)
- [Data gathering](#)
- [Categories](#)
- [Data gap filling](#)
- [Data Gap filling handling of metabolic activation](#)
- [Metabolism](#)
- [Report](#)

10 Single chemical 1/0/0 Developed by LMC, Bulgaria STOP

(参考)

参考. 評価対象に設定した代謝物のRead-acrossによる毒性評価① (Read-acrossの予測値を算出する際の類似物質数を変更する場合)

Hazard Evaluation Support System

Input
Profiling
RDT Data
Categories
Gap Filling
Report
Metabolism

CAS No: 103-88-8
 SMILES: c1(Br)ccc(NC(C)=O)cc1

to data matrix >> metabolism mode...

Data Gap Filling Method
☒ Read-across
☐ Trend analysis
☐ (Q)SAR models

Target Endpoint
 Repeated Dose Toxicity NOEL

Filter endpoint tree...

1 (Target) (Metabolite)	2	3	4	5	6
Structure					
Substance Identity					
Repeated Dose ...					
LOEL (19/825)	M: 10 mg/kg/day, 1...	M: 10 mg/kg/day, 1...	M: 15 mg/kg/day, 1...		
NOEL Mit	M: <10 mg/kg/day	M: <10 mg/kg/day	M: <15 mg/kg/day	M: 100 mg/kg/day	
Blo... (19/1058)	M: 20 mg/kg/day, 8...	M: 80 mg/kg/day, 8...	M: 15 mg/kg/day, 1...	M: 100 mg/kg/day, ...	
FOB (6/192)				M: 100 mg/kg/day, ...	
Ge... (20/1154)	M: 10 mg/kg/day, 2...	M: 40 mg/kg/day, 4...	M: 170 mg/kg/day, ...	M: 100 mg/kg/day, ...	
He... (20/1003)	M: 10 mg/kg/day, 1...	M: 10 mg/kg/day, 1...	M: 15 mg/kg/day, 1...	M: 100 mg/kg/day, ...	
His... (20/5311)	M: 20 mg/kg/day, 4...	M: 10 mg/kg/day, 2...	M: 15 mg/kg/day, 1...	M: 100 mg/kg/day, ...	
Ne... (20/1535)	M: 160 mg/kg/day, ...	M: 160 mg/kg/day, ...	M: 170 mg/kg/day, ...	M: 100 mg/kg/day, ...	
NOAEL... (1/1)					
NOE... (20/36)	M: <10 mg/kg/day, ...	M: <10 mg/kg/day, ...	M: <15 mg/kg/day, ...	M: 100 mg/kg/day	
Or... (20/1056)	M: 10 mg/kg/day, 2...	M: 10 mg/kg/day, 1...	M: 15 mg/kg/day, 1...	M: 100 mg/kg/day, ...	
Other E... (1/1)		M: 80 mg/kg/day			
Urin... (16/441)			M: 170 mg/kg/day, ...	M: 100 mg/kg/day, ...	
Profile					
Study No. (Lin...	312	313	5	701	20
Chemical No. (...)	301	302	5	564	19
RDT Report No.	301	301	5	591	19
Root of map No. 509	Root of map No. 248	Root of map No. 249	Root of map No. 6	N/A	
Metabolite in map ...	Metabolite in map ...	Metabolite in map ...	Metabolite in map ...		
Anilines (Hemolytic...	Anilines (Hemolytic...	Anilines (Hemolytic...	Anilines (Hemolytic...	Anilines (Hemolytic...	
Anilines (Hepatotox...	Anilines (Hepatotox...	Anilines (Hepatotox...	Anilines (Hepatotox...	Anilines (Hepatotox...	
			Nitrobenzenes (He...	Nitrobenzenes (He...	
			Nitrobenzenes (Hep...	Nitrobenzenes (Hep...	

①「Gap Filling」の項目に移動
②「Read-across」を選択
③評価対象に設定した代謝物のNOELのセルを選択
④「Apply」をクリック

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17/0/0

Developed by LMC, Bulgaria

STOP

参考. 評価対象に設定した代謝物のRead-acrossによる毒性評価②
(Read-acrossの予測値を算出する際の類似物質数の変更)

- ①「Calculation option」をクリック
- ②「Prediction approach options」をクリック
- ③予測値の算出に使う類似物質数を「5」→「14」に変更
（14物質を用いて予測値を算出する）
- ④「OK」→「Accept prediction」をクリック

