

評価事例2 ～腎毒性を対象とした 化学物質の毒性評価～

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(独)製品評価技術基盤機構
化学物質管理センター

腎毒性について

化審法試験でよく認められる腎毒性の分類と関連する主な毒性所見

1. 尿細管 (Renal tubule) 障害

病理組織学検査: 壊死(necrosis)・変性[好塩基性化 (Basophilic change)
再生像 (Regeneration)、拡張 (Dilatation)、円柱 (Cast) 他]

2. 乳頭 (Renal papilla) 障害

病理組織学検査: 壊死(necrosis)

3. 腎機能障害

血液生化学検査: BUN ↑、Creatinine ↑、電解質の変動

尿検査: 各所見

4. 腎重量増加

軽度な影響

5. α 2u-グロブリン腎症

雄ラット特有の病変でヒトに外挿されない

病理組織学検査: 近位尿細管 (Proximal Renal tubule) における硝子的変性
(Hyaline droplets)、好酸性小体 (Eosinophilic body).

HESSの腎毒性カテゴリー

カテゴリー	物質数	対象影響の LOELの平均 (mg/kg/day)	信頼性ランク
1. p-Aminophenols (尿細管障害)	2	63±476	A
2. Aliphatic/Alicyclic hydrocarbons (α 2u-グロブリン腎症)	6	76±100	C
3. Halobenzenes (尿細管障害)	9	101±79	A

A. 簡易予測

HESSが提示したカテゴリーの妥当性を大まかに確認し、特に問題がなければ、提示されたカテゴリーをそのまま用いて評価を行う。

1. 該当するカテゴリーレポートの確認（構造上の特徴、毒性の特徴の確認等）
2. 類似物質の構造類似性の確認
3. 類似物質の毒性の大まかな確認（フィルター機能の利用）
4. 類似物質の毒性強度の分布（logKowと対象毒性のLOELのプロット）の確認
5. 予測に使用する類似物質の選定→自動的に予測

Hazard Evaluation Support System

Reset Options

Input

Profiling

RDT Data

Categories

Gap Filling

Report

Metabolism

Chemical name:
CAS No
SMILES
to data matrix ->

NO SELECTED TARGET

評価対象物質の入力

①

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

Load Inventory

SMILES/InChi c1ccccc1

000000-00-0

Templates Work

②

③クリック

CH-CH
CH-CH
CH-CH

Document_1

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Hazard Evaluation Support System

Reset Options

Input

Chemical name:
CAS No
SMILES
to data matrix ->

NO SELECTED TARGET

評価対象物質の入力

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

Load Inventory

①ボタンが押されており、結合が"Single"となっていることを確認

SMILES/InChi c1(C)c(C)c(C)ccc1 Draw Mixture Edit names

000000-00-0

Templates Work

②それぞれクリック

CH₃ CH₃ CH₃

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Hazard Evaluation Support System

Reset Options

Input

Chemical name:
CAS No
SMILES
to data matrix ->

NO SELECTED TARGET

評価対象物質の入力

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

Load Inventory

SMILES/InChi: c1(C)c(C)c(C)ccc1

000000-00-0

Templates Work

Periodic Table

Selected element: Cl

Labeled Number:

Yes Cancel Help

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Hazard Evaluation Support System

Reset Options

Input

Chemical name: N/A
CAS No: N/A
SMILES: c1(Cl)c(Cl)c(C)ccc1
to data matrix ->

評価対象物質の入力

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

Load Inventory ①ボタンが押されており、元素が"Cl"となっていることを確認

SMILES/InChi: c1(Cl)c(Cl)c(C)ccc1
000000-00-0

Templates Work

②それぞれクリック

Single chemical

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Hazard Evaluation Support System

Reset Options

Input
Profiling

Chemical name:
CAS No: N/A
SMILES: c1(Cl)c(Cl)c(C)ccc1
to data matrix ->

プロファイリングの抽出

RDT Data
Categories
Gap Filling
Report
Metabolism

①

Profiling 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
- ☒ 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 Metaboli
- ☐ NEDO In Vitro Rat Microsomal Meta

②

Show Boundaries Apply New Scheme

Filter endpoint tree...

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)

1 (Target)

Structure

N/A

Halobenzenes (Hep...)

Halobenzenes (Ren...)

評価対象物質はハロベンゼンの肝毒性及び腎毒性カテゴリーに該当することを確認。
→クリックし、腎毒性のカテゴリーレポートを確認(付録)。

1 Single chemical

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Hazard Evaluation Support System

Reset Options

Input
Profiling
RDT Data
Categories
Gap Filling
Report
Metabolism

Chemical name: N/A
CAS No: N/A
SMILES: c1(Cl)c(Cl)c(C)ccc1
to data matrix ->

反復投与毒性試験データの抽出

② Gather

Databases
☐ Biomarker DB
☒ HESS Repeated Dose Toxicity ①
☐ HESS Repeated Dose Toxicity (CSCL New Chemicals)

使用するDBの選択

Filter endpoint tree... 1 (Target)

Structure

☒ Substance Identity
☐ Profile

Study No. (Link to ...)
 Chemical No. (Link ...)
 RDT Report No.
 Rat Liver Metabolism
 Repeated dose (HE...)

NEDO HESS
No data found.
OK ③

データがないことを確認

1 (Target)

N/A
 Halobenzenes (Hep...
 Halobenzenes (Ren...)

1 Single chemical

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Hazard Evaluation Support System

Input
Profiling
RDT Data
Categories
Gap Filling
Report
Metabolism

Chemical name:
CAS No N/A
SMILES c1(Cl)c(Cl)c(C)ccc1

to data matrix ->

Chemical structure: 1,2-dichloro-4-methylbenzene

Define
Subcategorize
Combine Categories

Grouping methods
Organic functional groups (US EPA)
Organic functional groups, Norbert Ha
Structure similarity
Effect similarity
Study No. (Link to SSRDT)
Chemical No. (Link to HESS DB)
RDT Report No.
CSCL Class
Rat Liver Metabolism Database

① Toxicological
Repeated dose (HESS)

Defined Categories
Document_1

Delete Delete All

Repeated dose (HESS) ④

Target(s) profiles
Halobenzenes (Renal toxicity) Rank A

カテゴリーの選択

All Profiles
4,4'-Methylenedianilines/benzidines (Hepatobiliary toxicity) Rank B
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
Anilines (Hemolytic anemia with methemoglobinemia) Rank A
Anilines (Hepatotoxicity) Rank C
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
Diphenyl disulphides (Hemolytic anemia with methemoglobinemia) Rank A
Ethyleneglycol alkylethers (Hemolytic anemia) Rank A
Ethyleneglycol alkylethers (Testicular toxicity) Rank B
Halobenzenes (Hepatotoxicity) Rank A

Combine profiles logically with
and or ⑤
☒ Strict ⑥

Invert result
OK
Cancel

類似物質の抽出

プロファイラーの選択

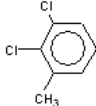

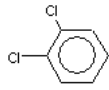


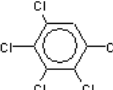
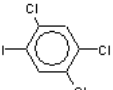
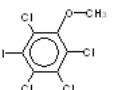
評価対象物質が属さないカテゴリーに属する類似物質を除外する

Single chemical Grouping Developed by LMC, Bulgaria 11

簡易予測おけるカテゴリーの確認

①構造類似性を
目視により確認

シクロトルエンの異性体がいっつかあるため、カテゴリーに該当すると考えられる

Filter ei	1 (Target)	2	3	4	5	6	7	8
Substance Identity								
Repeated Dose Toxicity								
LOEL	Min	M: 250 mg/kg/day	M: 100 mg/kg/day	M: 300 mg/kg/day	M: 300 mg/kg/day	M: 7.69 mg/kg/day	M: 7.69 mg/kg/day	M: 40 mg/kg/day
Blood Chemical Examination								
Blood Serum (Electrolyte)	(3/6)							
Blood Serum (Nitrogen Compound)								
Undefined Tissue								
BUN↑	(4/4)		M: 500 mg/kg/day	M: 1.2E3 mg/kg/day	M: 300 mg/kg/day			
Creatinine↑	(2/3)				M: 300 mg/kg/day	M: 76.9 mg/kg/day, ...		
Histopathological Findings								
Kidney								
Glomerulus	(1/1)							
Renal Tubule (Distal/Collecting Duct)								
Mineralization	(1/1)					M: 25.4 mg/kg/day		
Renal Tubule (Other)								
Necrosis	(2/3)			M: 300 mg/kg/day, ...				
Atrophy	(1/1)							
Casts	(3/5)					M: 154 mg/kg/day, ...	M: 76.9 mg/kg/day, ...	
Mineralization	(1/1)						M: 7.69 mg/kg/day	
Basophilic Change/Regeneration/Dege...	(8/12)		M: 500 mg/kg/day	M: 300 mg/kg/day, ...	M: 300 mg/kg/day	M: 7.69 mg/kg/day, ...	M: 7.69 mg/kg/day, ...	
Dilatation	(6/8)				M: 300 mg/kg/day	M: 7.69 mg/kg/day	M: 7.69 mg/kg/day	
Renal Tubule (Proximal)								
Basophilic Change/Regeneration/Degen...	(1/1)							
Undefined Tissue	(3/4)	M: 250 mg/kg/day, ...				M: 25.4 mg/kg/day		
Organ Weights								
Kidney								
Undefined Tissue								
Absolute Organ Weight↑	(7/11)					M: 25.4 mg/kg/day, ...	M: 23.1 mg/kg/day, ...	M: 80 mg/kg/day
Relative Organ Weight↑	(10/16)	M: 500 mg/kg/day	M: 100 mg/kg/day, ...			M: 7.69 mg/kg/day, ...	M: 7.69 mg/kg/day, ...	M: 40 mg/kg/day, 8
Urinalysis								
Urine	(4/13)	M: 750 mg/kg/day				M: 25.4 mg/kg/day, ...	M: 23.1 mg/kg/day, ...	

②カテゴリーに関連する毒性所見が類似物質全体に認められていることを確認

Input

Profiling

RDT Data

Categories

Report

Metabolism

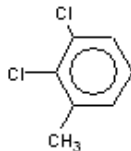
Chemical name:

CAS No N/A

SMILES c1(Cl)c(Cl)c(C)ccc1

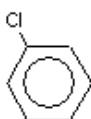
to data matrix ->

1 (Target)



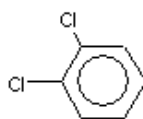
M: 250 mg/kg/day

2



M: 100 mg/kg/day

3



M: 100 mg/kg/day

Read-across

Trend analysis

(Q)SAR models

Target Endpoint

Repeated Dose Toxicity LOEL

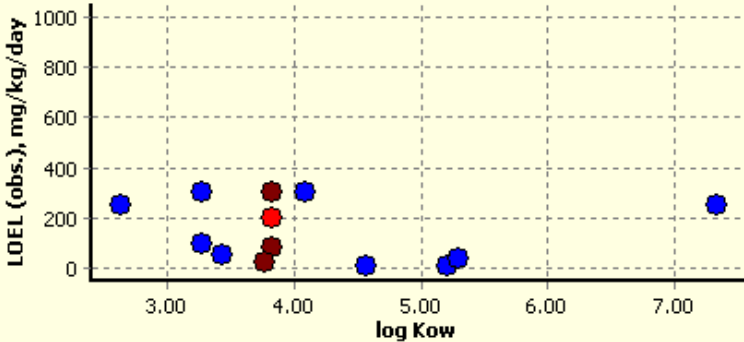
LOEL

(14/95) Min

Descriptors

Prediction

Read across prediction of LOEL,
taking the average from the nearest 5 neighbours,
based on 5 data points from 5 neighbour chemicals,
Observed target value: N/A, Predicted target value: 200 mg/kg/day



Descriptor X:

log Kow

Accept prediction

Return to matrix

Select/filter data

Selection navigation

Gap filling approach

Descriptors/data

Model/(Q)SAR

Calculation options

Visual options

Information

Miscellaneous

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Halobenzenes (Renal toxicity) Rank A Strict (Re)

Data gap filling

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データギャップ
補完の結果

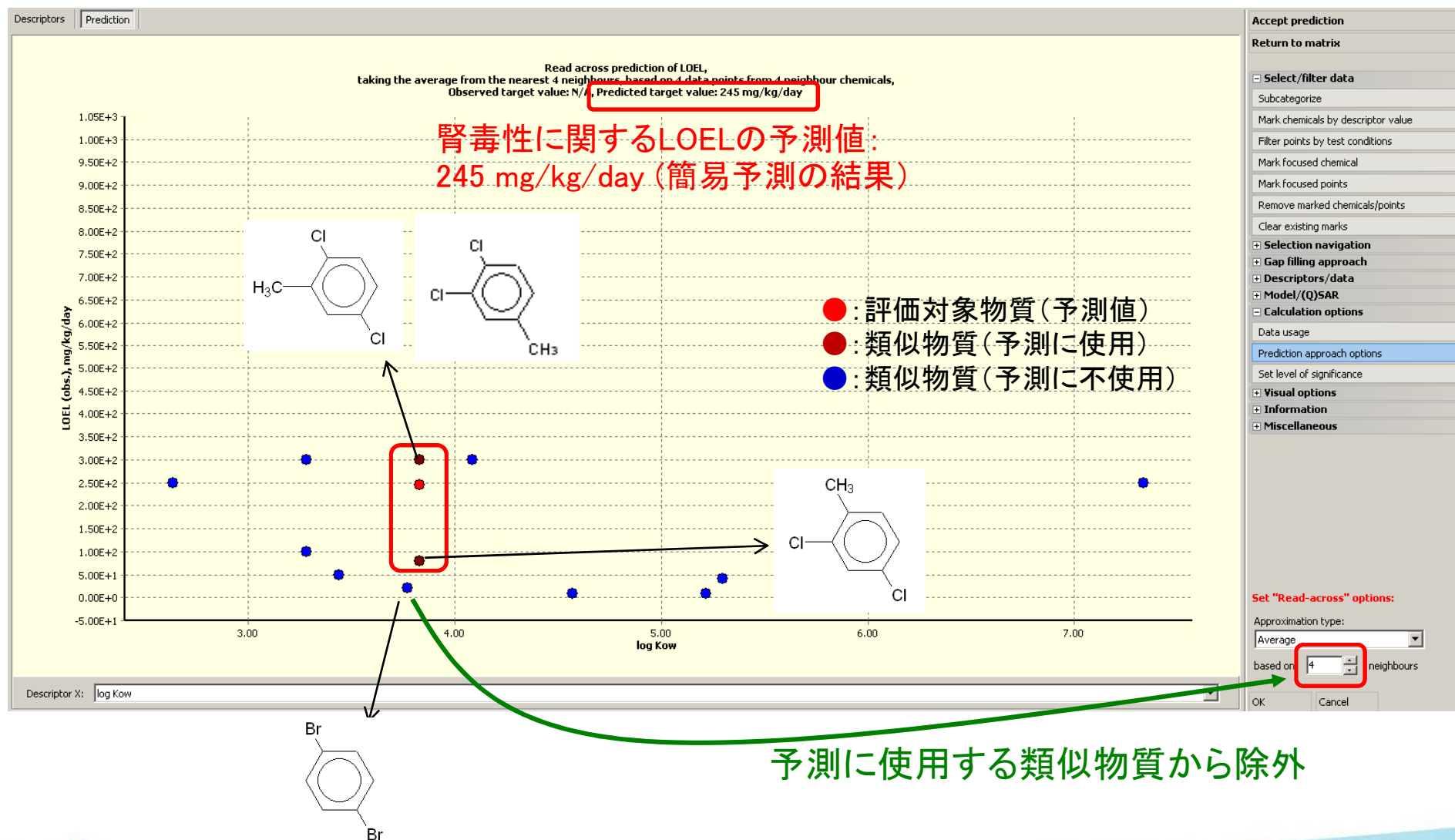
Read across prediction of LOEL,
taking the average from the nearest 5 neighbours,
based on 5 data points from 5 neighbour chemicals,
Observed target value: N/A, Predicted target value: 200 mg/kg/day

log Kow	LOEL (obs.) (mg/kg/day)
2.8	250
3.2	100
3.3	300
3.4	150
3.5	100
3.6	200
3.7	100
3.8	200
3.9	100
4.0	300
4.1	100
4.2	300
4.5	100
4.8	100
5.0	100
5.2	100
7.2	250

Descriptor X: log Kow

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予測に使用する類似物質の確定と予測結果



B. 詳細予測

専門家の知見や、HESS が提示する様々な関連情報を吟味することにより、HESSが提示したカテゴリーの妥当性を詳細に確認し、必要に応じて、カテゴリーの修正や組み直しを行った上で評価する。

1. 各試験データの毒性の内容の吟味
2. 試験条件の絞り込み
3. 代謝・メカニズムの情報の吟味
2. データギャップ補完に使用する所見の選定

Hazard Evaluation Support System

Reset Options

Input
Profiling
RDT Data
Categories
Gap Filling
Report
Metabolism

Chemical name:
CAS No N/A
SMILES c1(Cl)c(Cl)c(C)ccc1
to data matrix ->

Cl
Cl
CH₃

類似物質の絞り込み
(logKowの範囲による)

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

Target Endpoint
Repeated Dose Toxicity LOEL

Filter endpoint tree... 1 (Target) 2 3

Structure

Cl
Cl
CH₃

Cl

Descriptors Prediction

Read across prediction of LOEL,
taking the average from the nearest 4 neighbours,
based on 4 data points from 4 neighbour chemicals,
Observed target value: N/A, Predicted target value: 245 mg/kg/day

LOEL (obs.), mg/kg/day

log Kow

Descriptor X: log Kow

Accept prediction
Return to matrix

Select/filter data

Subcategorize

Mark chemicals by descriptor value

Filter points by test conditions

Select a descriptor boundary values:

Name Uni

Log Koa (Air-water partition coefficient...)

Log Koa (Henry's law constant model)

log Kow

logP Multicase

LLMO Energy eV

>= 4

<= 3.8

OK Cancel

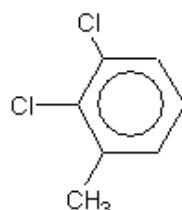
logKow>=4又は
3.8>=logKowの物質
を選択

15 Halobenzenes (Renal toxicity) Rank A Strict (Re Data gap filling

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Metabolism




to data matrix ->

類似物質の絞り込み
(logKowの範囲による)

Repeated Dose Toxicity LOEL

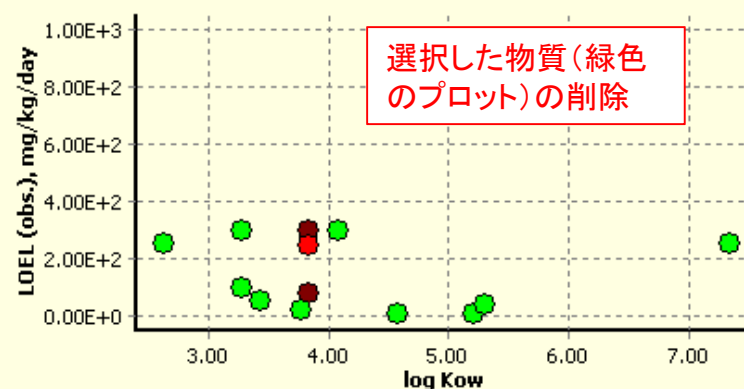
Structure

CC1=CC=C(Cl)C(Cl)=C1

a.

Prediction

Read across prediction of LOEL,
taking the average from the nearest 4 neighbours,
based on 4 data points from 4 neighbour chemicals,
Observed target value: N/A, Predicted target value: 245 mg/kg/day



Descriptor X: log K_{ow}

Data usage

Hazard Evaluation Support System

Subcategorization [Close] ⑤

Reset Options

Grouping methods

- 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 EP
- Organic functional groups, Norber
- Structure similarity
- Effect similarity
- Study No. (Link to SSRDT) ②
- Chemical No. (Link to HESS DB) ③
- RDT Report No.
- CSCL Class
- Rat Liver Metabolism Database ④

Toxicological

- Repeated dose (HESS)

Custom

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 Metab
- NEDO In Vivo Rat Metabolism Simula

Adjust options

Target

Differ from target by:

- At least one category
- All categories

Analogue

- (1) 181
- (1) 208
- (1) 524
- (1) 528

1 (Target) 5 9

Cl

CH₃

Cl

CH₃

Cl

Read across prediction of LOEL, the average from the nearest 4 neighbours, on 4 data points from 4 neighbour chemicals, et value: N/A, Predicted target value: 245 mg/kg/day ①

log Kow

1.00 2.00 3.00 4.00 5.00 6.00 7.00

15 Halobenzenes (Renal toxicity) Rank A Strict (Re Data gap filling

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SSRDT及びHESS DBへのリンクの作成

順次選択することにより、それぞれのリンクが作成される

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

Data usage

Hazard Evaluation Support System

Reset Options

Input
Profiling
RDT Data
Categories
Gap Filling
Report
Metabolism

Chemical name:
CAS No: N/A
SMILES: c1(Cl)c(Cl)c(C)ccc1
to data matrix ->

類似物質の絞り込み
とDB等へのリンクの作成結果

Filter endpoint tree...
Structure
Repeated Dose Toxicity
LOEL
NOEL
Profile
Study No. (Link to SSRDT)

1 (Target)	5	9	11	15
	M: 300 mg/kg/day M: 100 mg/kg/day, ...	M: 79 mg/kg/day M: 12.5 mg/kg/day, ...	M: 300 mg/kg/day M: 100 mg/kg/day, ...	M: 300 mg/kg/day M: 30 mg/kg/day, 3...
	665	186	213	661
	528	181	208	524
	N/A	N/A	N/A	N/A

試験データの要約
(SSRDT)へリンク

HESS DB (試験報告書DB、
毒性作用機序DB、ADME DB)
へリンク

ラット代謝マップDBへリンク
(この例の場合、情報なし)

Read across prediction of LOEL,
taking the average from the nearest 4 neighbours, based on 4 data points from 4 neighbour chemicals,
Observed target value: N/A, Predicted target value: 245 mg/kg/day

LOEL (obs.), mg/kg/day

log Kow

5, 11, 15

9

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

15 Halobenzenes (Renal toxicity) Rank A Strict (Repeated) Data gap filling

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腎毒性の内容の吟味

簡易評価:

腎毒性に関連する所見が認められているかをフィルター機能を利用して確認。

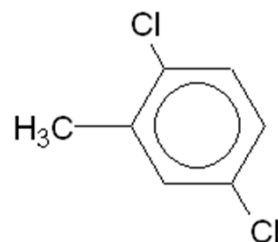
詳細評価

- ①**標的臓器としての確度**: 病理組織検査における腎臓の部位の壊死や変性の所見は、腎臓が標的であることを示す明確なエビデンスとなり得る。これに、血液生化学検査におけるBUNやクレアチニンの増加を伴っていれば、さらに確度が増す。
- ②**毒性の強さ(用量を考慮しつつ)**
 - ・壊死＞変性(尿細管再生像、好塩基性尿細管等)＞腎重量増
 - ・検査値の変動の大きさ
- ③**標的部位**

糸球体、尿細管(近位尿細管、遠位尿細管、集合管)、乳頭。

試験報告書において分類されていないケースも多い

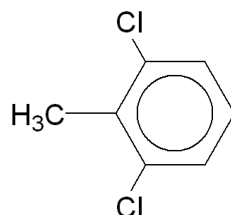
SSRDTの確認(1)



腎臓に対する軽微な影響
が示唆される

S661 R551 C524	
Cas No.	19398-61-9
Study type	TG422/OECD: Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test
Species	Rat(SD)
Route	Oral (gavage)
Solvent	Olive oil
Dose level	3doses(3,30,300mg/kg/day)
Death	None
NOEL	30mg/kg/day
Clinical observation	White turbid urine:300♂ ⁷ Salivation:300♂ ⁷
FOB	N/A
Body weight	N/A
Food consumption	N/A
Urinalysis	—
Hematology	N/A
Blood chemistry	N/A
Absolute organ weight	Kidney ↑ :300♂ ⁷
Relative organ weight	Kidney ↑ :300♂ ⁷ ,300R♂ ⁷
Necropsy	—
Histopathology	N/A

SSRDTの確認(2)



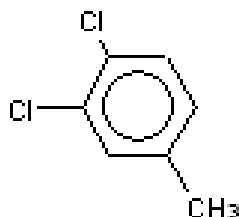
腎臓に対する軽微な影響
が示唆される

α2uグロブリン腎
症に関連する所見
のため除外

精巣への明確な影響
が認められる

S213	R211	C208
Cas No.	118-69-4	
Study type	TG 422/OECD: Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test	
Species	Rat(SD)	
Route	Gavage	
Solvent	Corn oil	
Dose level	4 doses (30, 100, 300, 1000 mg/kg/day)	
Death	None	
NOEL	30 mg/kg/day	
(male data were adopted as repeated toxicity)		
Clinical observation	locomotor activity↓: 1000♂ prone position: 1000♂ salivation : 1000♂	
Body weight	↓ : >300♂	
Blood Chemistry	Glu↓: >300♂ P↑: 1000♂	
Relative organ weight	kidney↑: >300♂ liver↑: 1000♂	
Histopathology	kidney-eosinophilic body: >100♂ liver/centrilobular-hypertrophy hepatocellular: >300♂ liver/centrilobular-ground glass appearance hepatocyte: 1000♂ spleen-deposit, pigment: 1000♂ testis-atrophy, seminiferous tubule: >300♂	

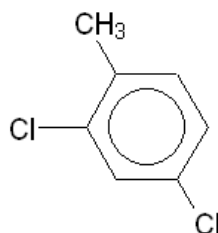
SSRDTの確認(3)



尿細管に対する明確な影響が認められる

S665 R555 C528	
Cas No.	95-75-0
Study type	TG422/OECD:Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test
Species	Rat(SD)
Route	Oral(Gavage)
Solvent	Corn oil
Dose level	3 doses(30,100,300mg/kg/day)
Death	1/6 (300R 15th day after administration)
NOEL	100mg/kg/day
Clinical observation	Death-1/6 on treatment day 15:300R
FOB	N/A
Body weight	↓ (tendency):300♂ Body weight gain ↓ (tendency):300♂
Food consumption	↓ :300♂
Urinalysis	—
Hematology	Plt ↓ :300♂,300R♂ EOSN ↓ :300♂
Blood chemistry	ALT ↑ :300♂ Cr ↑ :300♂ BUN ↑ (tendency):300♂
Absolute organ weight	N/A
Relative organ weight	Liver ↑ :300♂
Necropsy	—
Histopathology	Kidney-Regenerative tubule :300♂,300R♂ Kidney-Tubule dilatation:300♂,300R♂ Stomach/Glandular stomach-Ulcer:300♂,300R♂ Stomach/Glandular stomach-Erosion + Hemorrhage:300♂

SSRDTの確認(4)



尿細管に対する明確な影響が認められる

α2uグロブリン腎症に関連する所見のため除外 ←

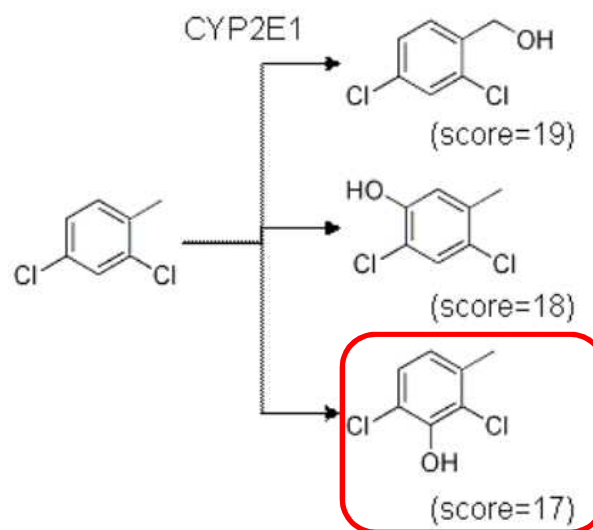
S186	R184	C181
Cas No.	95-73-8	
Study type	TG 422/OECD: Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test	
Species	Rat(SD)	
Route	Gavage	
Solvent	Purified water	
Dose level	3 doses (12.5, 79, 500 mg/kg/day)	
Death	None	
NOEL	<12.5mg/kg/day	
(male data were adopted as repeated toxicity)		
Clinical observation	salivation: >12.5♂	
Blood Chemistry	ChE↑: 500♂	
Absolute organ weight	liver ↑: 500♂ kidney↑: 500♂	
Relative organ weight	liver ↑: 500♂ kidney↑: 500♂	
Histopathology	liver/centrilobular-hypertrophy hepatocellular : >79♂ kidney-hyaline droplet, deposition tubular epithelium: >79♂ kidney-eosinophilic body deposition in tubular epithelium: >79♂ kidney-dilatation of tubules: >79♂ kidney-atrophy of tubular epithelium: >79♂ kidney-regeneration of tubular epithelium: 500♂	

代謝及び作用機序情報

ラット代謝マップDB: 情報なし

作用機序DB: 情報なし

ADME DB: 1物質において毒性に関連する代謝の可能性を確認



評価例（詳細予測の結果）

試験方法は全てOECD TG422による。

類似4物質全てにおいて腎臓が主要標的であり、NOELの根拠となっていることを確認。

標的部位は2物質は尿細管。2物質は不明であり、毒性の強度にばらつきがある。

評価事例1と比較し、カテゴリーのメカニズム的根拠は弱い。

→ 評価対象物質は、25mg/kg/day～250mg/kg/dayの範囲で、尿細管を標的とした腎毒性が発現する可能性がある。
（定性的な評価）

