

HESSを用いた有害性評価事例

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

内容

- ケーススタディ: エチレングリコールモノメチルエーテルと構造的に関連する化学物質の精巢毒性予測

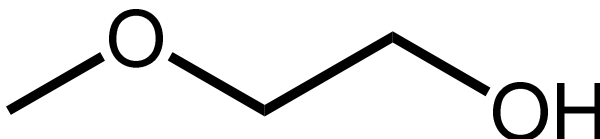
反復投与毒性試験で観察される精巣毒性所見

■ Testis (精巣)

- Atrophy (萎縮)
- Degeneration (変性)
 - Diffuse (びまん性)
 - Focal (限局性)
 - Germ cell (生殖細胞)
 - Seminiferous tubule (精細管)
 - Spermatocyte (primary/secondary) (精母細胞 (一次/二次))
 - Spermatid (精子細胞)
- Decrease in spermatozoa (精子数減少)
- Hyperplasia/Leydig cell (間質細胞過形成)
- Weight decrease (重量減)

■ Epididymis (精巣上体)

エチレングリコールモノメチルエーテル



Ethylene glycol monomethyl ether (EGME)
CAS: 109-86-4

分子量: 76.09

外観: 無色液体

用途:

洗浄用(積層板)、塗料、及び医薬用の溶剤として使用されている他、合成原料(アクリレート原料)、染料溶解剤等にも使用されている。

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ECHA
EUROPEAN CHEMICALS AGENCY

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ECHA > Addressing Chemicals of Concern > Authorisation > Substances of very high concern identification > Candidate List of Substances of Very High Concern for Authorisation > Candidate List table

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Candidate List of Substances of Very High Concern for Authorisation

(published in accordance with Article 59(10) of the REACH Regulation)

Notes:

- **Authentic version:** Only the Candidate List published on this website is deemed authentic. Companies may have immediate legal obligations following the inclusion of a substance in the Candidate List on this website.
- **EC number, CAS number:** The EC number includes both anhydrous and hydrated forms of a substance and consequently the entries cover both these forms. The CAS number included may be for the anhydrous form only, and therefore the CAS number shown does not always describe the entry accurately.
- **IUCLID 5 Substance Datasets:** These are partly pre-filled substance data sets in IUCLID 5 format. They are provided as a support for importers or producers of articles preparing notifications for substances in articles. The notifying company remains, however, solely responsible for the appropriateness and correctness of the information submitted in the notification.
- **Reason for Inclusion:** Superscript figures denote information on conditions applicable to the classification of the substance. This information can be accessed through the "Details" button and is available in the sub-menu "Substance Details" in field "Other remarks".

> [Candidate List introduction](#)

Number of substances on the Candidate List: 155 (last updated: 16 June 2014)

Showing 1 - 20 of 155 results. Items per Page 20 Page 1 of 8 First Previous Next Last

Substance Name	EC Number	CAS Number	Date of inclusion	Reason for inclusion	Decision number	IUCLID 5 Substance Dataset	
1,2-Benzenedicarboxylic acid, dihexyl ester, branched and linear	271-093-5	68515-50-4	2014/06/16	Toxic for reproduction (Article 57 c)	ED/49/2014		Details
Sodium perborate; perboric acid,	239-172-9;	-	2014/06/16	Toxic for reproduction	ED/49/2014		Details
2-Methoxyethanol	203-713-7	109-86-4	2010/12/15	Toxic for reproduction (article 57c)	ED/95/2010		Details

REACH 高懸念物質の候補としてリスト

Main [HessDB_Search]

Open View Save View Study_View Adme_View Mechanism_View Adme_List Option Help

All Clear Search

Search Results Search Conditions

Please set the search conditions.

Chemical Histopathology Measured Data

Add

☒ Cas_No. 109-86-4

☒ Chemical Name

☒ Chem_No.

☒ Study_No.

☒ MOL File

...

Search Conditions

No.	Type	Conditions
1	Cas_No.	109-86-4

Clear 1 Delete

①CAS No.を入力

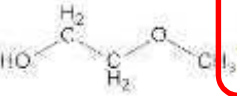
②クリック

③クリック

Main [HessDB_Search]
 Open View
Save View
Study_View
Adme_View
Mechanism_View
Adme_List
Option
Help
All Clear
Search

Search Results | Search Conditions

Results : 1
 Select All
Cancel All
Add to Study_View
Delete from Study_View

Chem...	Chemical Data	Structure	Study Lin...	Adme...	Mech...
<input type="checkbox"/> 288	[Cas_No.] 109-86-4 [Name] Ethanol, 2-methoxy-		298<91*>	288[5]	288[12]

試験報告書の情報
 毒性メカニズムの情報

No.	Type	Conditions
1	Cas_No.	109-86-4

Search Conditions

Study Link

Chem.No. 288

Chemical Data [Cas.No.] 109-86-4 [Name] Ethanol, 2-methoxy-

Test Result

Flag Summary

Test Method

Measured Data

298<91*>

Hematology

Blood Chemistry

Absolute organ weight

Relative organ weight

Necropsy (Survival)

Necropsy (Dead)

Histopathology (Survival)

Histopathology (Dead)

Male

HCT: ≥750

HGB: ≥750

Plt: ≥750

RBC: ≥750

RET: ≥750

WBC: ≥1500

LYMPH: ≥1500

SEG: ≥1500

TP: ≥750

ALB: ≥750

Bile acid: ≥750

Thymus: ≥750

Right testis: ≥1500

Thymus: ≥3000

Right testis: ≥1500

N/A

-

Spleen-Capsular fibrosis: ≥750

Testes-Atrophy: ≥750

Bone marrow-Cellular depletion: ≥4500

Spleen-Atrophy: ≥4500

Thymus-Atrophy: ≥1500

Prostate-Atrophy: ≥4500

Preputial gland-Atrophy: ≥3000

Seminal vesicle-Atrophy: ≥4500

Bone-metaphysis-Atrophy: ≥4500

Liver-Necrosis: ≥4500

Salivary glands-Atrophy: ≥4500

Stomach, glandular-Erosion: ≥4500

Forestomach, glandular-Mineralization: ≥4500

Adrenal gland, cortex-Hemorrhage: ≥4500

Lymph node, mandibular-Depletion lymphoid: ≥4500

Lymph node, mesenteric-Angiectasis: ≥4500

Lymph node, mesenteric-Depletion lymphoid: ≥3000

Bone-Metaphysis atrophy: ≥4500

-

Female

HCT: ≥1500

HGB: ≥750

Plt: ≥750

RBC: ≥3000

RET: ≥3000

WBC: ≥750

LYMPH: ≥750

SEG: ≥3000

TP: ≥750

ALB: ≥1500

Bile acid: ≥1500

Thymus: ≥750

Thymus: ≥750

N/A

-

Spleen-Capsular fibrosis: ≥1500

Bone marrow-Cellular depletion: ≥1500

Spleen-Atrophy: ≥1500

Thymus-Atrophy: ≥1500

Bone-metaphysis-Atrophy: ≥4500

Uterus-Atrophy: ≥3000

Ovary-Atrophy: ≥3000

Clitoral gland-Atrophy: ≥3000

Liver-Necrosis: 6000

Salivary glands-Atrophy: ≥4500

Stomach, glandular-Erosion: ≥4500

Forestomach, glandular-Mineralization: 6000

Adrenal gland, cortex-Hemorrhage: ≥4500

Lymph node, mandibular-Depletion lymphoid: ≥4500

Lymph node, mesenteric-Angiectasis: ≥4500

Lymph node, mesenteric-Depletion lymphoid: ≥4500

Bone-Metaphysis atrophy: ≥4500

-

Descriptive Data

Clinical sign

Male:Death: ≥4500

Tremors: ≥750

Diarrhea: ≥750

Emaciation: ≥750

Abnormal posture: ≥750

FOB

Male:-

Female:-

Urinalysis

Male:-

Female:-

Body weight

Male: ≥1500

Female: ≥1500

Food consumption

Male:-

Female:-

Water consumption

Male:N/A

Female: ≥1500

Toxicological index

	NOEL	NOAEL	LOEL	LOAEL
Male	<750 ppm		750 ppm	
Female	<750 ppm		750 ppm	

Comment

Evaluated by toxicology experts in the NEDO project

9

Study [HessDB_Search]

Chem_No. 288 Chemical Data [Cas_No.] 109-86-4 [Name] Ethanol, 2-methoxy-

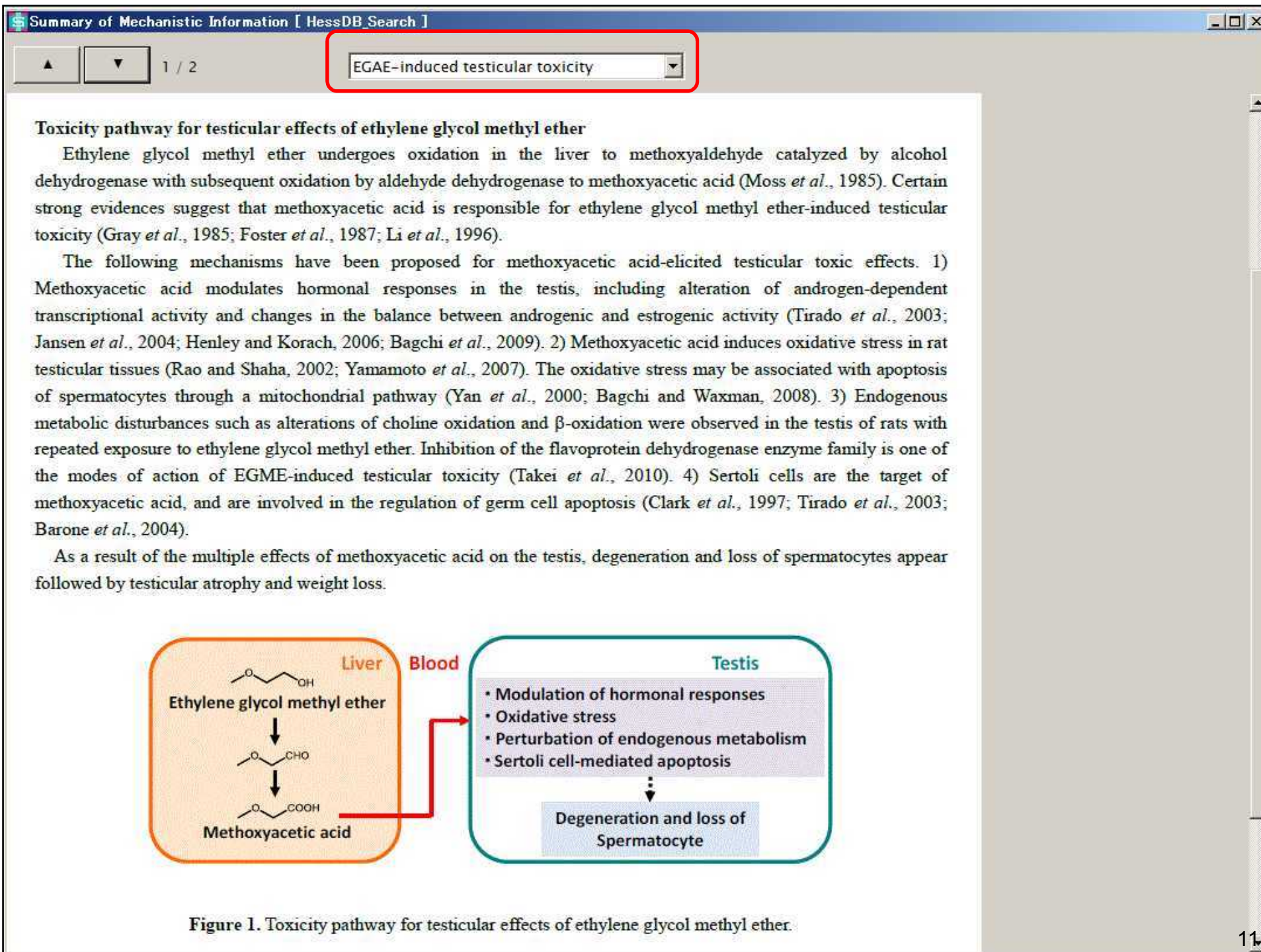
Study Link ID 298<91*>

Test Result | Flag Summary | Test Method Measured Data

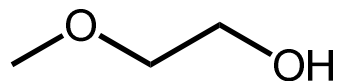
Test Item Histo(Survival)_Male Actual

Comment Data includes animals (8/10 at 4500 ppm, 10/10 at 6000 ppm) which died before the end of the scheduled sacrifice.

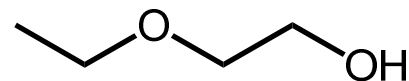
DOSE		ppm	0		750		1500		3000		4500		6000				
Organ	Finding		count	sig...	F1	F2	F3	count	sig...	F1	F2	F3	count	sig...	F1	F2	F3
Prostate	Metaplasia, squamous	Total	0/10					0/10					0/10				
		±															
		+															
		++															
		+++															
		++++															
		T or P															
Seminal vesicle	Atrophy	Total	0/10					0/10					0/10			8/10 (...)	9/10 (...)
		±															
		+															
		++															
		+++															
		++++															
		T or P															
Testes	Atrophy (Degeneration)	Total	0/10					7/10 (...)					10/10...			9/10 (...)	10/10...
		±															
		+															
		++															
		+++															
		++++															
		T or P															
Bone marrow	Depletion cellular	Total	0/10					0/10					0/10			8/10 (...)	10/10...
		±															
		+															
		++															
		+++															
		++++															
		T or P															
Lymph node	Mediastinal, angiectasis	Total	0/10					0/10					1/10 (...)			1/9 (1...	0/9
		±															
		+															
		++															
		+++															
		++++															
		T or P															
Lymph node	Mediastinal, depletion...	Total	0/10					0/10					0/10			1/9 (1...	1/9 (1...
		±															
		+															
		++															



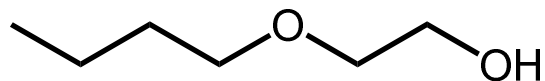
エチレングリコールモノメチルエーテル 関連物質の精巢毒性を予測する



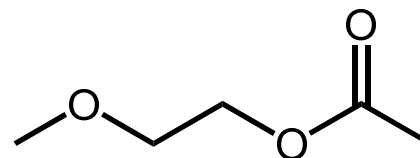
109-86-4
ethylene glycol monomethyl ether



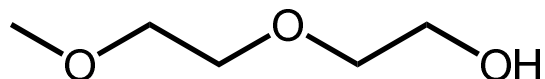
110-80-5
ethylene glycol monoethyl ether



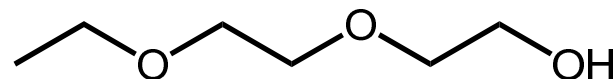
111-76-2
ethylene glycol (mono) n-butyl ether



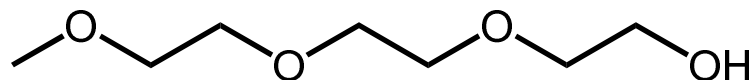
110-49-6
ethylene glycol monomethyl ether acetate



111-77-3
diethylene glycol monomethyl ether

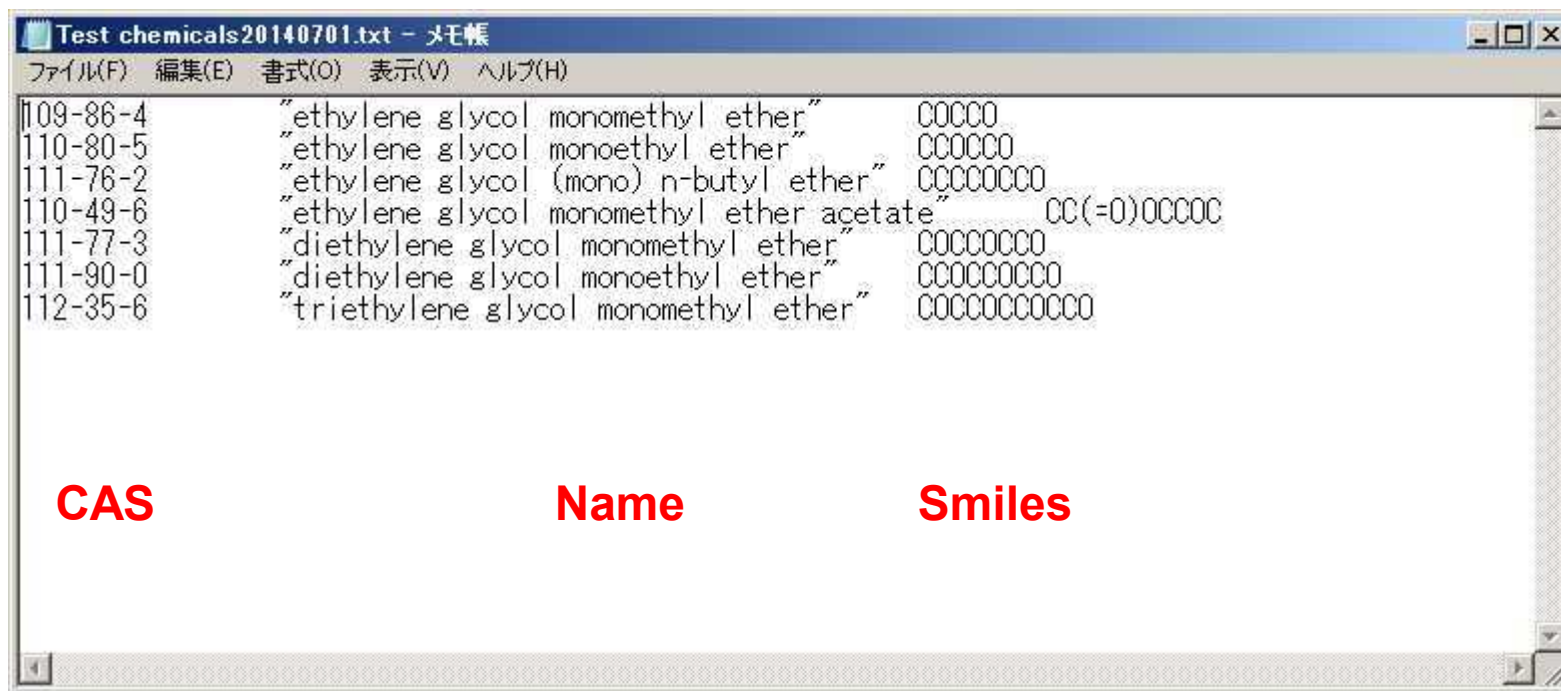


111-90-0
diethylene glycol monoethyl ether



112-35-6
triethylene glycol monomethyl ether

準備するファイル



CAS	Name	Smiles
109-86-4	"ethylene glycol monomethyl ether"	<chem>COCOC</chem>
110-80-5	"ethylene glycol monoethyl ether"	<chem>CCOCCO</chem>
111-76-2	"ethylene glycol (mono) n-butyl ether"	<chem>CCCCOCCO</chem>
110-49-6	"ethylene glycol monomethyl ether acetate"	<chem>CC(=O)OCCOC</chem>
111-77-3	"diethylene glycol monomethyl ether"	<chem>COCOCOCO</chem>
111-90-0	"diethylene glycol monoethyl ether"	<chem>CCOCCOCCO</chem>
112-35-6	"triethylene glycol monomethyl ether"	<chem>COCOCOCOCO</chem>

Hazard Evaluation Support System

Reset Options Help

Input
Profiling
RDT Data
Categories
Gap Filling
Report
Metabolism

Chemical name:
CAS No
SMILES

NO SELECTED TARGET

to data matrix -> metabolism mode...

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

準備したファイル
“Test chemicals 20140701.txt”を選択

Test20140701_3 name.txt 1/20/00 Developed by LMC, Bulgaria STOP

Metabolism

metabolism mode...

 **N**

☐ NEDO In Vivo Rat Metabolism Simulation

STOP

Input

Profiling

RDT Data

Categories

Gap Filling

Report

Metabolism

Chemical name:

CAS No

SMILES

to data matrix <->

metabolism mode...

NO SELECTED TARGET

プロファイリング

Reset

Options

Help

Profiling methods

☐ Bioaccumulation – metabolism half

☐ 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

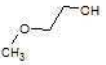
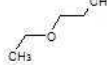
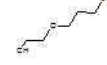
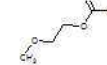
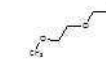
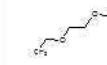

☐ Liver Metabolism Simulator

☐ NEDO In Vitro Rat Cellular Metabolism

☐ NEDO In Vitro Rat Microsomal Metab

☐ NEDO In Vivo Rat Metabolism Simulat

Filter endpoint tree...

	1	2	3	4	5	6	7
Structure							
Substance Identity							
Profile							
Study No. (Link ...	298	299	300				
Chemical No. (Li...	288	289	290				
RDT Report No.	290	290	290				
Root of map No. 235	Root of map No. 235	Root of map No. 237	Root of map No. 238	Root of map No. 773	Metabolite in map ...	N/A	N/A
Root of map No. 233	Root of map No. 233	Root of map No. 236	Root of map No. 239				
Root of map No. 234	Root of map No. 234	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 dose (...	Ethyleneglycol alky...	Ethyleneglycol alky...	Ethyleneglycol alky...	Not categorized	Not categorized	Not categorized	Not categorized

(カテゴリー候補が表示される。)

7 Test20140701_3 name.txt

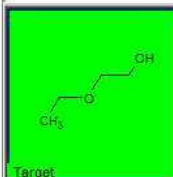
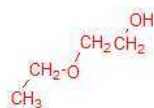
17/07/01

Developed by LMC, Bulgaria

15

Ethyleneglycol alkylethers (Testicular toxicity) Rank B

Target



Target

Boundaries Training set Options

Boundary Options Metabolism

Fragment

C(H2)(O(H))C(H2)O**Exh16"



Common Fragments

Definition	1	2
1	[Exh ₁₆]	

Profile Description

2. Observed Effects in the RDT DB

In repeated-dose toxicity studies, some EGAEs show a variety of toxic effects. However, the most severe adverse effects of EGAEs with short alkyl chain lengths C1 and C2 are the effects on the testes. EGAE (C1) is more testicular toxic than EGAE (C2). EGAEs (C3 and C4) caused no toxic effects in testis.

	Chemical/Descriptor			RDT Test data			Category Boundary
	Name (CAS)	Structure	MW logP	Test Method	NOEL LOEL*1 (mg/kg/day)	Observed effects related to the target endpoint*2	
1	2-Methoxyethanol (109-86-4)	C=1	78.1 -0.907	NTP_S water S,298	♂: <58.58 ♀: <58.58	Testis- abs wt 1: >115 d [†] , relat wt 1: >115 d [†] Atrophy: >58 d [†]	In
2	2-Ethoxyethanol (110-80-5)	C=2	90.1 -0.416	NTP_S water S,298	♂: <98.98 ♀: <98.98	Testis- abs wt 1: >789 d [†] , relat wt 1: >789 d [†] Atrophy: 3846 d [†] Epididymis- Aspermia: >789 d [†]	In
3	Ethanol, 2-(1-methylethoxy)- (108-59-1)	C=3	104 0.002	TG407 gavage S,108	♂: <30.30 ♀: <30.30	-	Out
4	2-Butoxyethanol (111-76-2)	C=4	118 0.567	NTP_S water S,300	♂: <58.58 ♀: <58.58	-	Out
5	2-tert-Butoxyethanol (7880-85-0)	C=4	118 0.455	TG422 gavage S,286	♂: 4.20	-	Out

*1 For the dose of feed test was calculated by the following equation: mg/kg/day=13/ppm.

*2 **Bold red:** Differential diagnosis for the target endpoint.

Ordinary font: Supporting evidence for the target endpoint.

(in parentheses): Reference information related to the target endpoint.

EGME EGMEの方が
EGEE 精巣毒性は強い

アルキル基炭素数3以上では精巣毒性は発現しない。

Hazard Evaluation Support System

Input

Profiling

RDT Data

Categories

Gap Filling

Report

Metabolism

Chemical name:

CAS No

SMILES

NO SELECTED TARGET

to data matrix ->

metabolism mode...

Reset

Options

Help

Show Boundaries

Apply

New Scheme

Profiling methods

☐ Bioaccumulation – metabolism half
 ☐ 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

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	2	3	4	5	6	7
298	299	300				
288	289	290				
290	290	290				
Root of map No. 235	Root of map No. 237	Root of map No. 238	Root of map No. 773	Metabolite in map ...	N/A	N/A
Root of map No. 233	Root of map No. 236	Root of map No. 239				
Root of map No. 234	Metabolite in map ...	Metabolite in map ...				
Metabolite in map ...						
Metabolite in map ...						
Ethyleneglycol alkyl ether	Ethyleneglycol alkyl ether	Ethyleneglycol alkyl ether	Not categorized	Not categorized	Not categorized	Not categorized
Ethyleneglycol alkyl ether	Ethyleneglycol alkyl ether	Ethyleneglycol alkyl ether				

In

In

Out

EGAE (精巢毒性) カテゴリーに入る: In

EGAE (精巢毒性) カテゴリーに入らない: Out

7 Test chemicals20140701.txt

17/0/0

Developed by LMC, Bulgaria

STOP

18

Hazard Evaluation Support System

Reset

Options

Help

Input

Profiling

RDT Data

Categories

Gap Filling

Report

Metabolism

NO SELECTED TARGET

Chemical name:

CAS No

SMILES

to data matrix ->

metabolism mode...

Show Boundaries Apply New Scheme

Profilers

Profiling methods

- ☐ Bioaccumulation - metabolism half
- ☐ Biodegradation fragments (BioWIN)
- ☐ Carcinogenicity (genotox and non)
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- ☐ Eye irritation/corrosion Inclusion r
- ☐ in vitro mutagenicity (Ames test)
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- ☐ Skin irritation/corrosion Exclusion r
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Empiric

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- ☐ Groups of elements
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- ☐ Organic functional groups
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- ☐ Organic functional groups, Norbert
- ☒ Study No. (Link to SSRDT)
- ☒ Chemical No. (Link to HESS DB)
- ☒ RDT Report No.
- ☐ CSDL Class
- ☒ Rat Liver Metabolism Database

Toxicological

- ☒ Repeated dose (HESS)

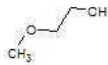
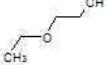
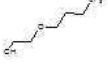
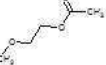
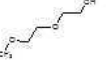
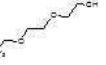
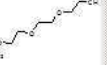
Metabolism

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

	1	2	3	4	5	6	7
Structure							
Repeated dos...	Ethyleneglycol alky...	Ethyleneglycol alky...	Ethyleneglycol alky...	Not categorized	Not categorized	Not categorized	Not categorized
Metabolism	Ethyleneglycol alky...	Ethyleneglycol alky...	Ethyleneglycol alky...				
Observed R...	8 metabolites	2 metabolites	2 metabolites	2 metabolites			
Study No...							
Chemical...							
RDT Rep...							
Rat Liver ...	1 x Metabolite in m... 1 x Metabolite in m... 1 x Metabolite in m... 1 x Metabolite in m... 1 x Metabolite in m... 1 x Metabolite in m... 5 x Metabolite in m... 8 x Metabolite in m... 1 x Metabolite in m... 1 x Metabolite in m... 1 x Metabolite in m... 1 x Metabolite in m... 1 x Metabolite in m...	1 x Metabolite in m... 2 x Metabolite in m...	2 x Metabolite in m... 2 x Metabolite in m... 2 x Metabolite in m... 1 x Metabolite in m... 1 x Metabolite in m...	1 x Metabolite in m... 1 x Metabolite in m... 2 x Metabolite in m... 1 x Metabolite in m... 1 x Metabolite in m... 1 x Metabolite in m... 1 x Metabolite in m... 1 x Metabolite in m... 1 x Metabolite in m... 1 x Metabolite in m... 1 x Metabolite in m... 1 x Metabolite in m... 1 x Metabolite in m...			
Repeated...	8 x Not categorized	2 x Not categorized	2 x Not categorized	1 x Carboxylic acid... 1 x Ethyleneglycol ... 1 x Ethyleneglycol ...			

In

In

Out

In

の可能性

Profiling

Metabolism

Close

METABOLISM DATABASE

Trans flex search...

(1)

(2)

(3)

(4)

(5)

(6)

(7)

(8)

(9)

対象物質

(EGME, EGEEなど)

対象物質

(EGME, EGEEなし)

[illegible]

Hazard Evaluation Support System

Reset Options Help

Input
Profiling
RDT Data
Categories
Gap Filling
Report
Metabolism

Chemical name:
CAS No
SMILES

NO SELECTED TARGET

to data matrix-> metabolism mode...

Show Boundaries Apply New Scheme

Profiling methods

- ☐ Bioaccumulation – metabolism half
- ☐ Biodegradation fragments (BioWIT)
- ☐ Carcinogenicity (genotox and non)
- ☐ Eye irritation/corrosion Exclusion rule
- ☐ Eye irritation/corrosion Inclusion rule
- ☐ in vitro mutagenicity (Ames test)
- ☐ in vivo mutagenicity (Micronucleus)
- ☐ Oncologic Primary Classification
- ☐ Skin irritation/corrosion Exclusion rule
- ☐ Skin irritation/corrosion Inclusion rule

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

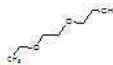
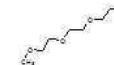
Documented

- ☐ Observed Rat Liver metabolism

Simulated

- ☐ Degradation 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	2
Structure		
Substance Identity		
Profile		
Study No. (Li...)		
Chemical No....		
RDT Report No.		
Rat Liver Met...	N/A	N/A
Repeated dos...	Not categorized	Not categorized
Metabolism		

2 Test chemicals20140701.txt

17/07/0

Developed by LMC, Bulgaria

STOP

代謝シミュレータを用いて推定代謝物をつくる。
推定代謝物に対してプロファイリングする。

Profiling

Metabolism

metabolism mode...

NO SELECTED TARGET

 Show Boundaries **Apply** **New Scheme**

1

—Repeated

☐ NEDO In Vivo Rat Metabolism Simulation

カテゴリー

1代謝物:カルボン酸(肝毒性)

カテゴリー

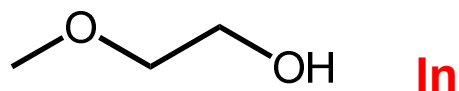
1 代謝物:カルボン酸(肝毒性)

1 代謝物: EGAE (溶血性貧血)

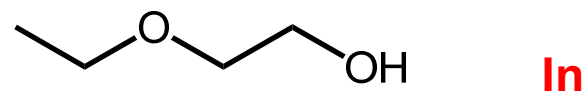
1 代謝物: EGAE (精巢毒性)

簡易予測例

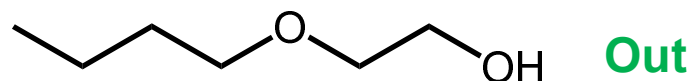
EGAE精巢毒性カテゴリーに 入る → **In** 入らない → **Out**



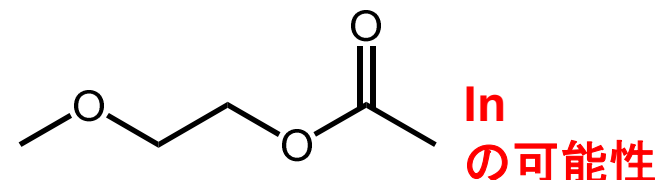
109-86-4
ethylene glycol monomethyl ether



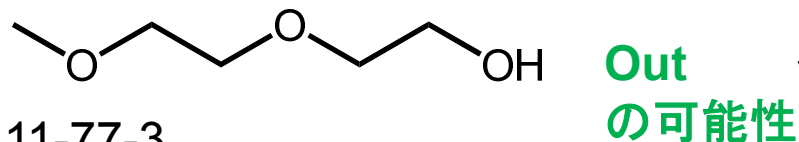
110-80-5
ethylene glycol monoethyl ether



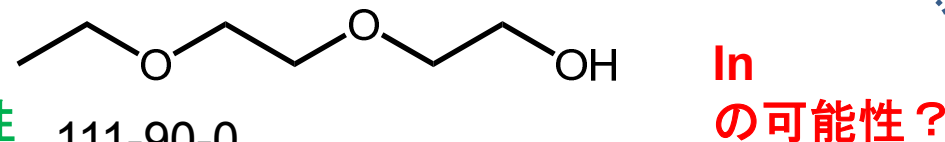
111-76-2
ethylene glycol (mono) n-butyl ether



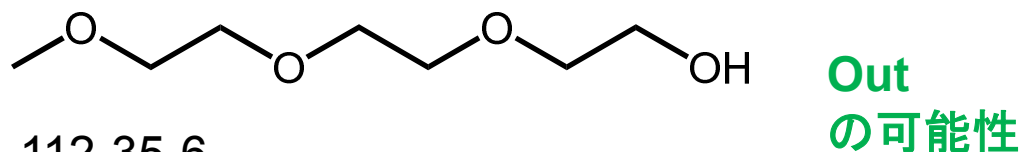
110-49-6
ethylene glycol monomethyl ether acetate



111-77-3
diethylene glycol monomethyl ether

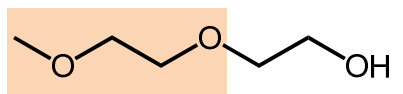
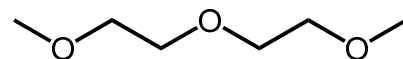


111-90-0
diethylene glycol monoethyl ether

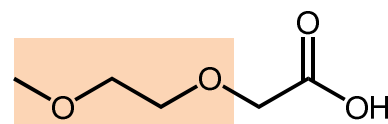
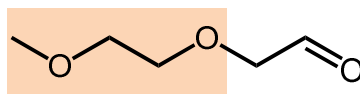


112-35-6
triethylene glycol monomethyl ether

代謝経路に関する考察



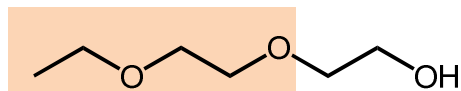
111-77-3



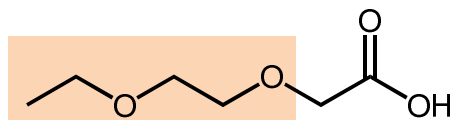
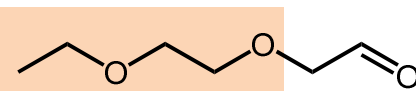
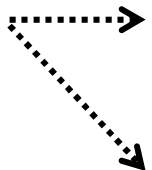
(*in vitro/in vivo*)

(実測でEGMEは検出されず)

<Richards *et al.*, 1993>



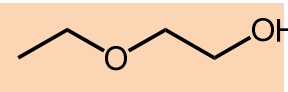
111-90-0



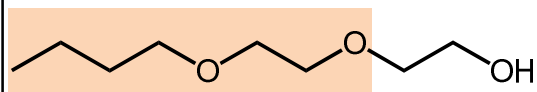
両経路を予測。定量性なし。

(*in vitro/in vivo*)

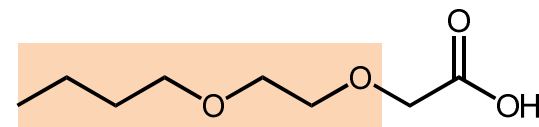
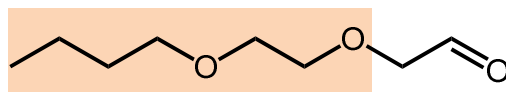
<代謝シミュレータ>



EGEE



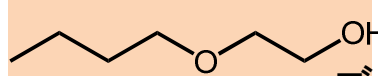
112-34-5



主要な代謝経路

(*in vivo*)

<Boatman *et al.*, 1993>



ごくわずかに検出

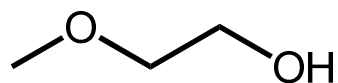
nite



挟み込みによる類推からCAS 111-90-0は代謝を介してEGEEをほとんど生成しないと予測される。

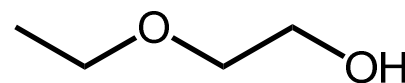
詳細予測例

EGAE精巢毒性カテゴリーに入る → **In** 入らない → **Out**



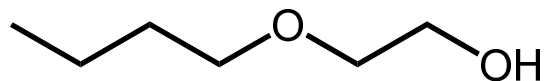
In

109-86-4
ethylene glycol monomethyl ether



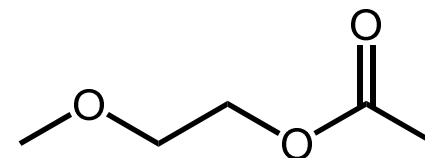
In

110-80-5
ethylene glycol monoethyl ether



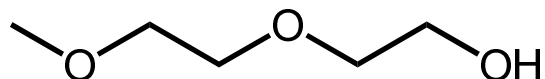
Out

111-76-2
ethylene glycol (mono) n-butyl ether



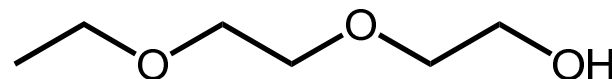
In
の可能性

110-49-6
ethylene glycol monomethyl ether acetate



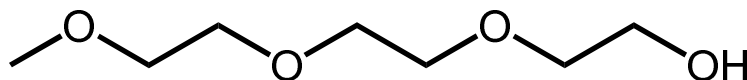
Out
の可能性

111-77-3
diethylene glycol monomethyl ether



Out
の可能性

111-90-0
diethylene glycol monoethyl ether

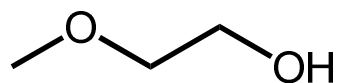


Out
の可能性

112-35-6
triethylene glycol monomethyl ether

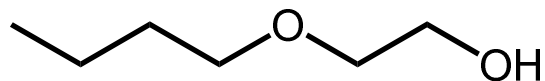
検証

EGAE精巣毒性カテゴリーに入る → **In** 入らない → **Out**



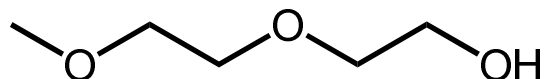
In

109-86-4
精巣萎縮 70 mg/kg/d 以上
(HESS)



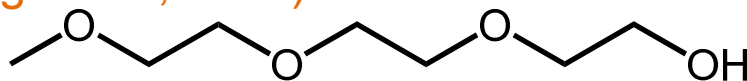
Out

111-76-2
精巣毒性なし 6000 ppm (HESS)

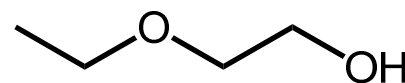


**Out
の可能性**

111-77-3
精巣萎縮 3600 mg/kg/d, NOAEL 900
mg/kg/d (Krasavage et al, 1982)

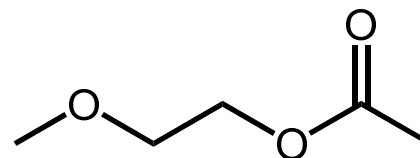


112-35-6
公開試験データなし



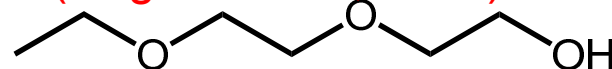
In

110-80-5
精巣萎縮 400 mg/kg/d 以上
(HESS)



**In
の可能性**

110-49-6
精巣萎縮 500 mg/kg/d (ICR mice)
(Nagano et al., 1984)



**Out
の可能性**

111-90-0
公開試験データなし

ポイント

- 評価対象物質がHESSのどの反復投与毒性カテゴリーにも属さない場合：
 - 代謝物がHESSカテゴリーに属する場合がある。
 - 実測の代謝データが利用できる場合には有効に活用し、それがない場合には代謝シミュレータを用いる。
 - 代謝シミュレータは想定される代謝物を定性的に表示する。
- 予測の信頼性の向上へ向けて：
 - 試験済みの類似物質を用いた予測性の検証を実施する。
 - 必要に応じて関連情報を収集し、予測結果を支援する証拠を追加。