bayesian Weight of Evidence for REACH ITS generation

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and the Environment

EU FP6 project OSIRIS, Pillar 4

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Overall GOAL of OSIRIS:

- (generation of) **Integrated Testing Strategies** (ITS)

  - **Transparent** → document all choices
  - **Reproducible** → algorithm, choices
  - **Objective** → quantitative?
  - **Flexible** → allowing extension of methodology
  - **Practicle** → Implementation in a Webtool
    - Allowing user data entry
    - Allowing user test/model entry

ITS:

Most efficient strategy of fulfilling information requirement

Chemical Safety Assessment

REACH context (Annex VI)

4 steps are described:

1. Gather and share ALL available information
2. Consider information requirements *cf tonnage-bands*

   (Annexes VII-X)
3. Identify information gaps
4. Generate new testing data / propose testing strategy

In REACH (in vivo) testing is the last resort (art.13, 25 en Annex XI)

ITS:
Most efficient strategy of fulfilling information requirement

Step 1: Gather all available (Testing and Non-Testing) information

*Step 2+3: If **not** sufficient* ↓ *for **C&L** and **RA** cf REACH*

Step 4: Generate more information (non-Testing)

*Step 2+3: Still **not** sufficient* ↓ *for **C&L** and **RA** cf REACH*

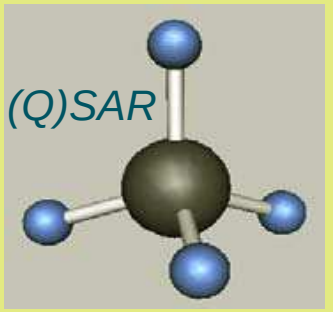
Step 4: Is Exposure-Based Waiving an option?

*Step 2+3: If **not** possible* ↓ ***and** information **not** sufficient*

Step 4: Perform / Propose (in vivo) Testing as last resort!!

Step 1: Available sources of information (Annex VII-X and Annex XI)

Human data



In vivo guideline test

In vitro

non guideline test

Grouping & read across

Exposure (-based waiving)

“Weight of Evidence”

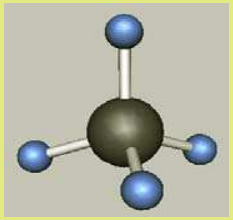
Step 2 and 3: Identify data gaps

Available information → REACH information requirements (for C&L, RC)

Non-guideline

\+

= sufficient ???



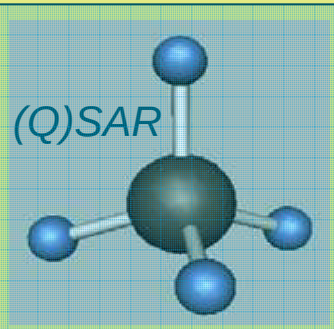
\+

= sufficient ???

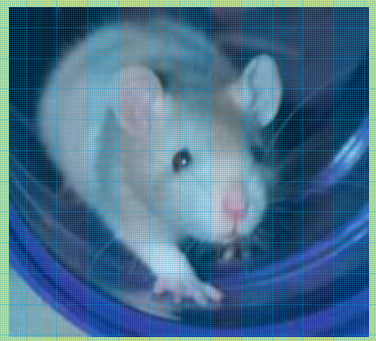
Step 2 and 3: Identify data gaps

Human data

(Q)SAR



In vivo guideline test



In vitro

non guideline tests

Grouping & read across

use
“Weight of Evidence”

Test Proposal ← Data Gap? ⇄ *Exposure (-based waiving)*

Step 2 and 3: Identify data gaps

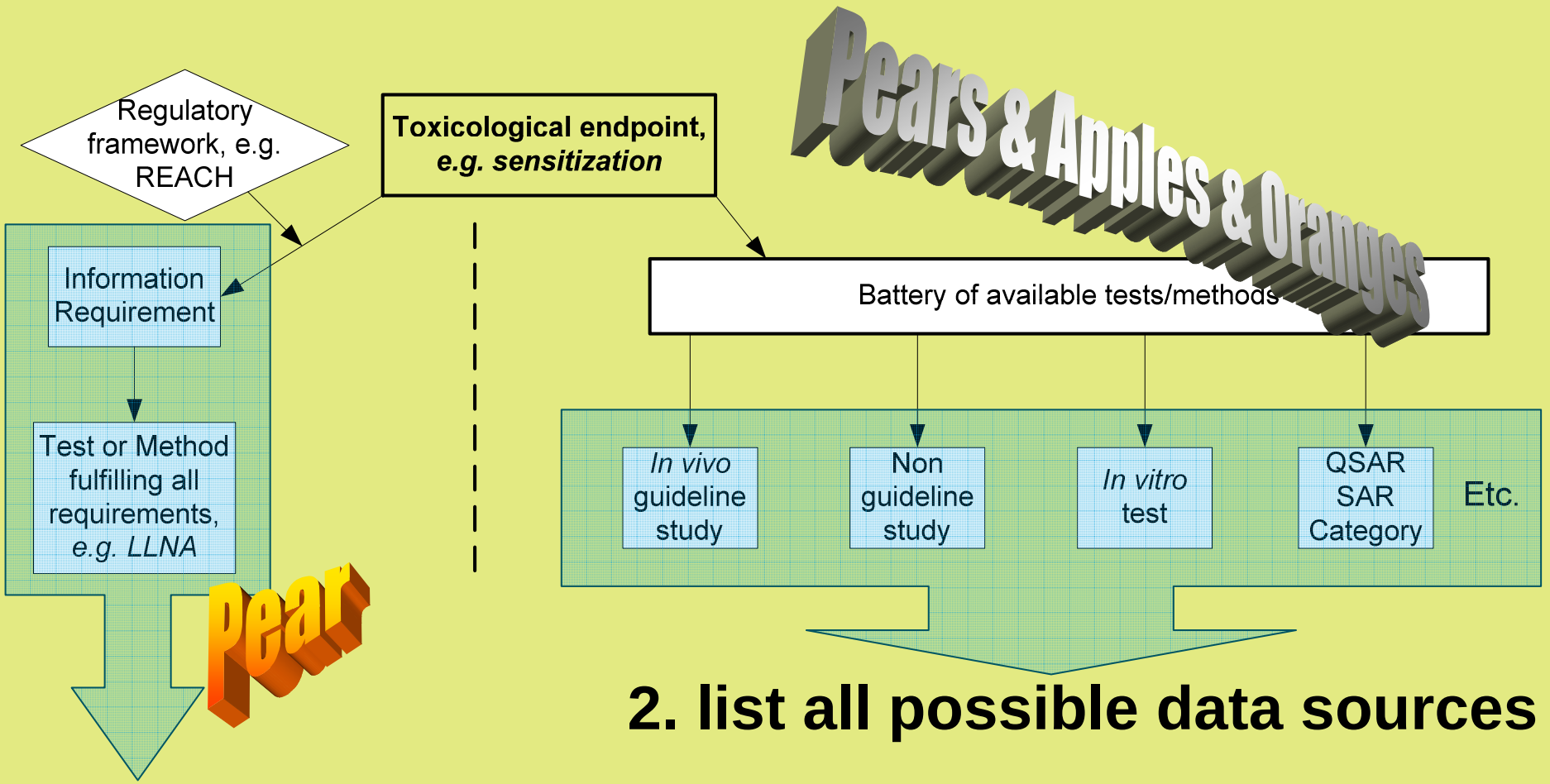
By applying “Weight of Evidence”

- Express all information sources (“Evidence”) in one unit (“Weight”)
  - *from tests*
  - *from models*
  - *from categories*
  - *etc.*
- Decide if *total* Weight of Evidence is sufficient
- If not → identify most efficient way of filling information gap

How to apply Weight of Evidence? Compare Apples and Pears

→OSIRIS: apply Bayesian statistics:

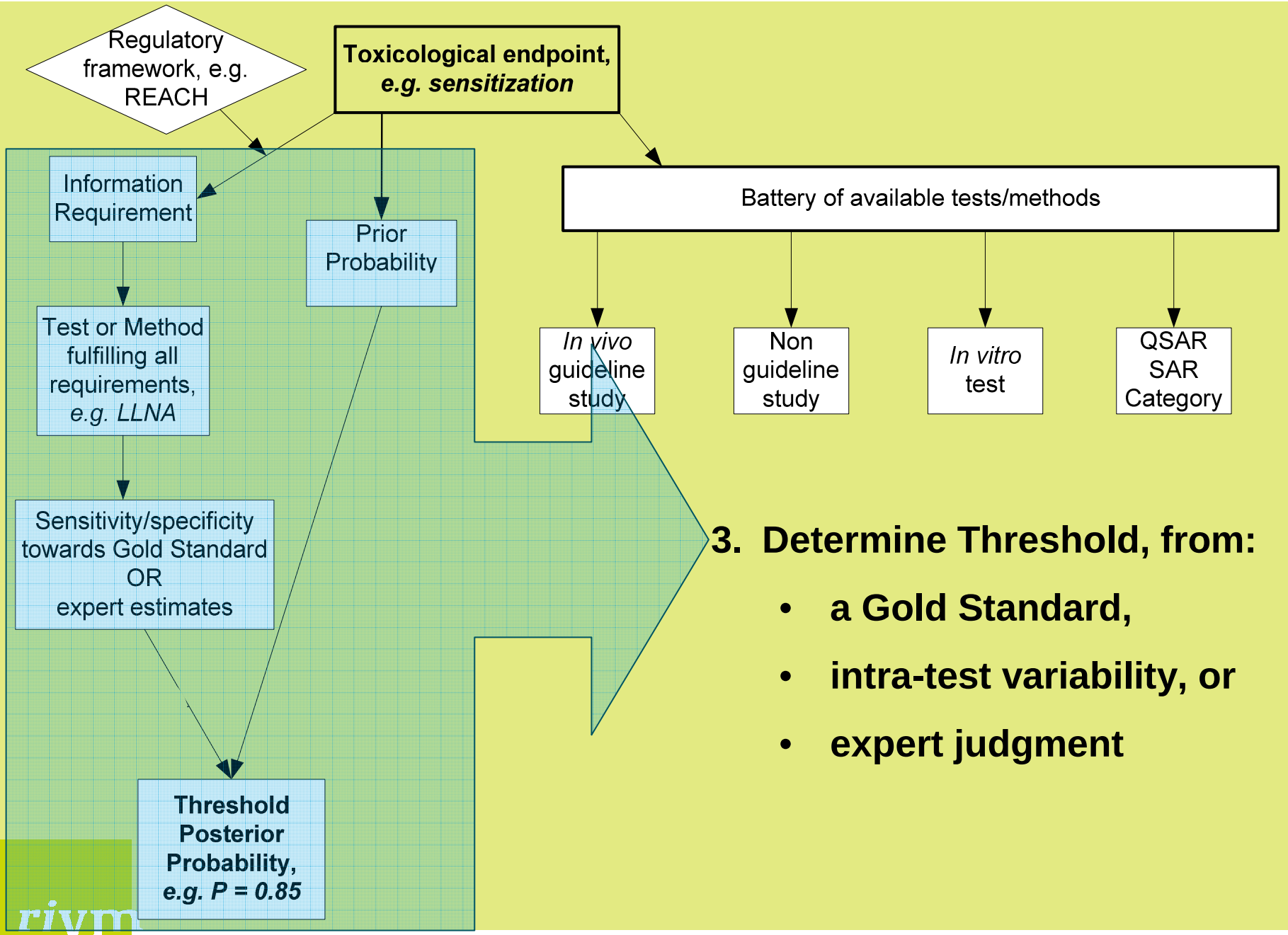
- calculate a *probability* that a result is true, given a specific test outcome
- add these probabilities (using Bayesian belief network)
- compare the combined probability to a threshold



2. list all possible data sources

1. define (REACH) information requirement

for every combination of *purpose* and *endpoint*



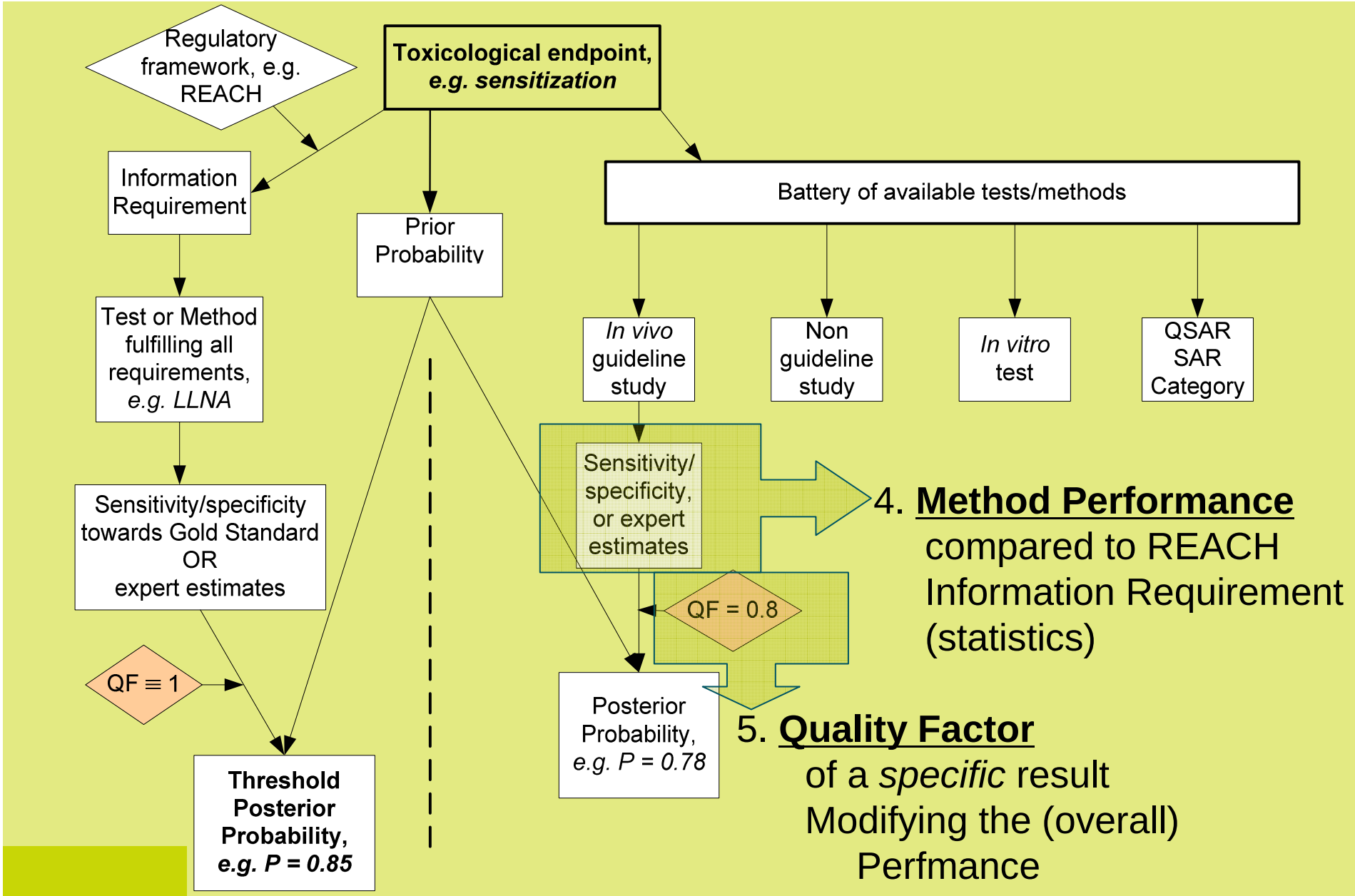
3. Determine Threshold, from:

- **a Gold Standard,**
- **intra-test variability, or**
- **expert judgment**

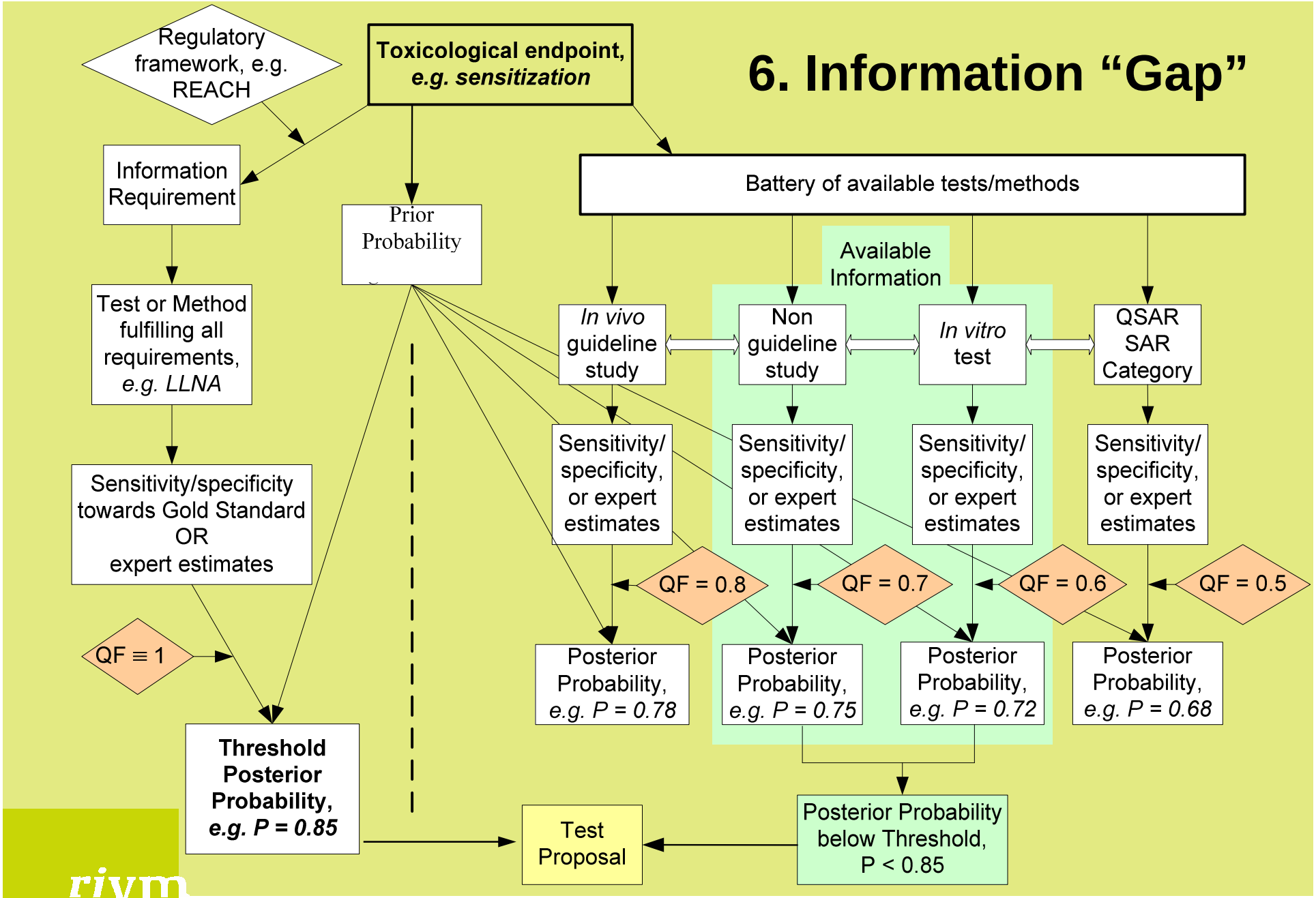
But: not all Apples are equal

→ the need for **Quality Factors (QF)**

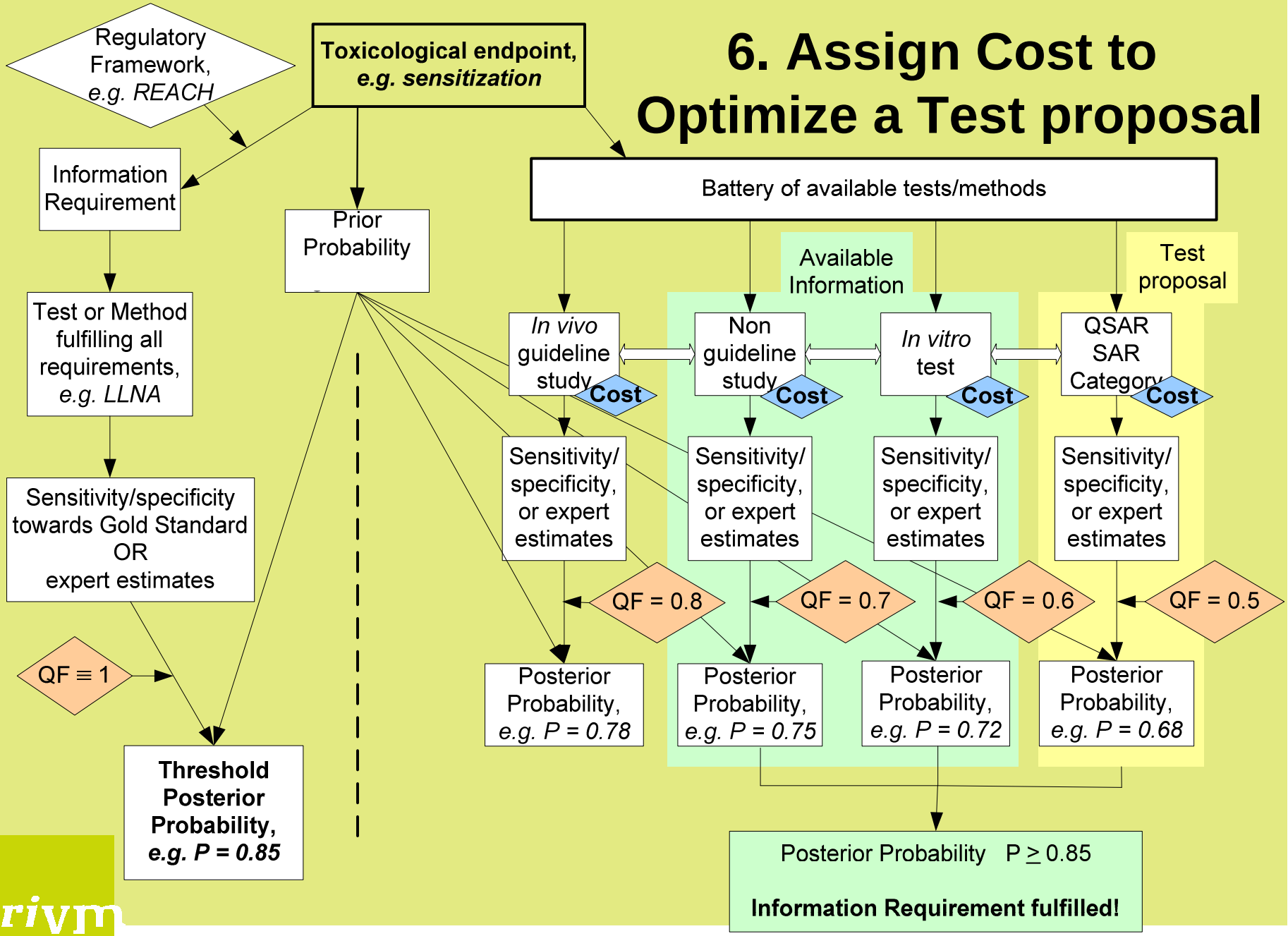
e.g. Klimisch(-like) codes for data quality


Regulatory framework, e.g. REACH
Toxicological endpoint, e.g. sensitization
Information Requirement
Prior Probability
Battery of available tests/methods
Test or Method fulfilling all requirements, e.g. LLNA
In vivo guideline study
Non guideline study
In vitro test
QSAR SAR Category
Sensitivity/specificity towards Gold Standard OR expert estimates
Sensitivity/ specificity, or expert estimates
4. Method Performance compared to REACH Information Requirement (statistics)
QF = 0.8
QF ≡ 1
Posterior Probability, e.g. P = 0.78
5. Quality Factor of a specific result Modifying the (overall) Perfmance
Threshold Posterior Probability, e.g. P = 0.85

6. Information "Gap"



6. Assign Cost to Optimize a Test proposal



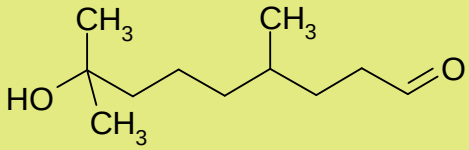
Optimization function for Test Proposal

- If the cost function is “correct” (politically) then “Non-testing” is exhausted before (in vivo) Testing
- If Non-Testing is exhausted, and a REACH required test is performed, this effectively ignores all previously gathered WoE information.
- Do we need options to *adapt* testing protocols?

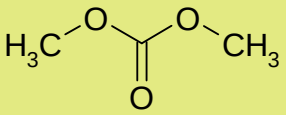
Case (proof-of-principle) of qWoE ITS: Skin Sensitization

- Excel implementation
- Hugin® implementation
- OSIRIS webtool implementation

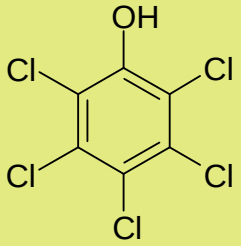
- hydroxycitronellal 107-75-5



- dimethyl carbonate 616-38-6



- pentachlorophenol 87-86-5



Fill in by user	Regulatory choice
Calculated	Calculated

Endpoint: **Sensitization**

Framework: **REACH A.VII**

Gold Standard: OECD 429 LLNA

Information Requirement: OECD 429 LLNA

Prior Probability

Positive	50%	Pr(C=1)
Negative	50%	Pr(C=0)

Threshold level: 80%

Battery of Available Tests

testnr.	1	2	3	4	5
test type	-	-	-	-	-
Sensitivity:	0.959	0.500	0.500	0.500	0.500	0.500
Specificity:	0.993	0.500	0.500	0.500	0.500	0.500
Test Result:						
Weight Factors:	1	Quality Factors:	0.00	0.00	0.00	0.00	0.00
		adapted sensitivity	0.500	0.500	0.500	0.500	0.500
		adapted specificity	0.500	0.500	0.500	0.500	0.500
		Pr(C=1)	50%	50%	50%	50%	50%
		Pr(C=0)	50%	50%	50%	50%	50%

Posterior Probabilities

Pr(C=1 | T=1)	99%
Pr(C=0 | T=0)	96%

Posterior Probabilities

Pr(C=1 | T)	50.00%	50.00%	50.00%	50.00%	50.00%
Pr(C=0 | T)	50.00%	50.00%	50.00%	50.00%	50.00%

Threshold Probabilities (reproducability):

for a positive conclusion	**79%**
for a negative conclusion	**77%**

Posterior Probability of the qWoE conclusion

for a positive conclusion	**50%**
for a negative conclusion	**50%**

Information Gap:

for a positive conclusion	**29%**	**TEST PROPOSAL needed**
for a negative conclusion	**27%**	**TEST PROPOSAL needed**

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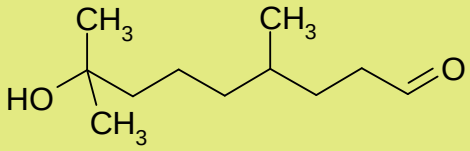
Case (proof-of-principle) of qWoE ITS: Skin Sensitization

- Excel implementation

  - hydroxycitronellal 107-75-5



  - DEREK alert found positive
  - SMARTs alert found positive
  - TOPKAT probability>0.7 positive
  - TIMES-SS alert found positive
  - MultiCASE alert found positive

  - LLNA test (2 results) positive

Endpoint: **Sensitization**

Framework: **REACH A.VII**

Gold Standard: OECD 429 LLNA

Information Requirement: OECD 429 LLNA

Prior Probability

Positive	50%	Pr(C=1)
Negative	50%	Pr(C=0)

Threshold level: 80%

Battery of Available Tests

testnr.	1	2	3	4	5
	429				
test type	**LLNA**	-	-	-	-
Sensitivity:	0.959	0.500	0.500	0.500	0.500
Specificity:	0.993	0.500	0.500	0.500	0.500
Test Result:	**1**				
Weight Factors:	1				
Quality Factors:	**1.00**	0.00	0.00	0.00	0.00
adapted sensitivity	0.959	0.500	0.500	0.500	0.500
adapted specificity	0.993	0.500	0.500	0.500	0.500
Pr(C=1)	50%	99%	99%	99%	99%
Pr(C=0)	50%	1%	1%	1%	1%

Posterior Probabilities

Pr(C=1 | T=1)	99%
Pr(C=0 | T=0)	96%

Posterior Probabilities

Pr(C=1 | T)	99.31%	99.31%	99.31%	99.31%	99.31%
Pr(C=0 | T)	0.69%	0.69%	0.69%	0.69%	0.69%

Threshold Probabilities (reproducability):

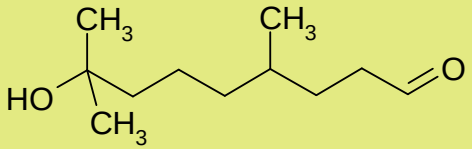
for a positive conclusion	**79%**
for a negative conclusion	**77%**

Posterior Probability of the qWoE conclusion

for a positive conclusion	**99%**
for a negative conclusion	**1%**

Information Gap:

for a positive conclusion	**-20%**	**WoE satisfied**
for a negative conclusion	**76%**	**TEST PROPOSAL needed**



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Quality Factors

	test nr.	1
	test type	OECD 429 LLNA

General Questions

	Klimisch code of test quality (1,2,3 or 4)	1
1	Performed under GLP (Y/N)	Y
2	Documentation OK (Y/N)	Y
3	Within Domain of Applicability (Y/N)	Y
4	etc…	

Test specific Questions

1	Coverage of all Mechanisms of Action (0..1)	1
2	Experimental issues (vehicle, test duration, etc)	1
3	etc…	1

OVERALL QUALITY FACTOR **1**

Quality Factors

	test nr.	1
		OECD 429
General Questions	test type	LLNA
Klimisch code of test quality (1,2,3 or 4)		2
1 Performed under GLP (Y/N)		Y
2 Documentation OK (Y/N)		Y
3 Within Domain of Applicability (Y/N)		Y
4 etc…		
Test specific Questions		
1 Coverage of all Mechanisms of Action (0..1)		1
2 Experimental issues (vehicle, test duration, etc)		1
3 etc…		1
OVERALL QUALITY FACTOR		**0.8**

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Quality Factors

	test nr.	1
		OECD 429
General Questions	test type	LLNA
Klimisch code of test quality (1,2,3 or 4)		1
1 Performed under GLP (Y/N)		Y
2 Documentation OK (Y/N)		Y
3 Within Domain of Applicability (Y/N)		Y
4 etc…		
Test specific Questions		
1 Coverage of all Mechanisms of Action (0..1)		1
2 Experimental issues (vehicle, test duration, etc)		0.8
3 etc…		0.8
OVERALL QUALITY FACTOR		**0.64**

Endpoint: **Sensitization**

Framework: **REACH A.VII**

Gold Standard: OECD 429 LLNA

Information Requirement: OECD 429 LLNA

Prior Probability			Threshold level:
Positive	50%	Pr(C=1)	80%
Negative	50%	Pr(C=0)	

Battery of Available Tests

testnr.	1	2	3	4	5
	429				
test type	**LLNA**	-	-	-	-
Sensitivity:	0.959	0.500	0.500	0.500	0.500
Specificity:	0.993	0.500	0.500	0.500	0.500
Test Result:	**1**				
Weight Factors:	1				
Quality Factors:	**0.64**	0.00	0.00	0.00	0.00
adapted sensitivity	0.794	0.500	0.500	0.500	0.500
adapted specificity	0.816	0.500	0.500	0.500	0.500
Pr(C=1)	50%	81%	81%	81%	81%
Pr(C=0)	50%	19%	19%	19%	19%

Posterior Probabilities

Pr(C=1 | T=1)	99%
Pr(C=0 | T=0)	96%

Posterior Probabilities

Pr(C=1 | T)	81.16%	81.16%	81.16%	81.16%	81.16%
Pr(C=0 | T)	18.84%	18.84%	18.84%	18.84%	18.84%

Threshold Probabilities (reproducability):

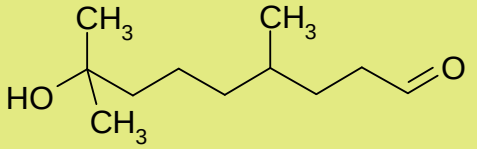
for a positive conclusion	**79%**
for a negative conclusion	**77%**

Posterior Probability of the qWoE conclusion

for a positive conclusion	**81%**
for a negative conclusion	**19%**

Information Gap:

for a positive conclusion	**-2%**	**WoE satisfied**
for a negative conclusion	**58%**	**TEST PROPOSAL needed**



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Endpoint: **Sensitization**

Framework: **REACH A.VII**

Gold Standard: OECD 429 LLNA

Information Requirement: OECD 429 LLNA

Prior Probability — Threshold level: 80%

Positive 50% Pr(C=1)

Negative 50% Pr(C=0)

Battery of Available Tests

testnr.	1	2	3	4	5
test type	**DEREK**	-	-	-	-
Sensitivity:	0.788	0.500	0.500	0.500	0.500
Specificity:	0.506	0.500	0.500	0.500	0.500
Test Result:	**1**				
Quality Factors:	**1.00**	0.00	0.00	0.00	0.00
adapted sensitivity	0.788	0.500	0.500	0.500	0.500
adapted specificity	0.506	0.500	0.500	0.500	0.500
Pr(C=1)	50%	61%	61%	61%	61%
Pr(C=0)	50%	39%	39%	39%	39%

Sensitivity: 0.959

Specificity: 0.993

Weight Factors: 1

Posterior Probabilities

Pr(C=1 | T=1) 99%

Pr(C=0 | T=0) 96%

Posterior Probabilities

Pr(C=1 | T)	61.44%	61.44%	61.44%	61.44%	61.44%
Pr(C=0 | T)	38.56%	38.56%	38.56%	38.56%	38.56%

Threshold Probabilities (reproducability):

for a positive conclusion **79%**

for a negative conclusion **77%**

Posterior Probability of the qWoE conclusion

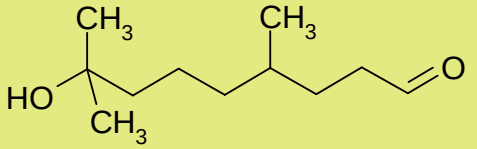
for a positive conclusion **61%**

for a negative conclusion **39%**

Information Gap:

for a positive conclusion **18%** **TEST PROPOSAL needed**

for a negative conclusion **38%** **TEST PROPOSAL needed**



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Endpoint: **Sensitization**

Framework: **REACH A.VII**

Gold Standard: OECD 429 LLNA

Information Requirement: OECD 429 LLNA

Prior Probability — Threshold level: 80%

Positive	50%	Pr(C=1)
Negative	50%	Pr(C=0)

Battery of Available Tests

testnr.	1	2	3	4	5
test type	**DEREK**	**SMARTs**	-	-	-
Sensitivity:	0.788	0.776	0.500	0.500	0.500
Specificity:	0.506	0.522	0.500	0.500	0.500
Test Result:	**1**	**1**			
Quality Factors:	**1.00**	**1.00**	0.00	0.00	0.00
adapted sensitivity	0.788	0.776	0.500	0.500	0.500
adapted specificity	0.506	0.522	0.500	0.500	0.500
Pr(C=1)	50%	61%	72%	72%	72%
Pr(C=0)	50%	39%	28%	28%	28%

	Sensitivity:	Specificity:
	0.959	0.993

Weight Factors: 1

Posterior Probabilities

Pr(C=1 | T=1)	99%
Pr(C=0 | T=0)	96%

Posterior Probabilities

Pr(C=1 | T)	61.44%	72.12%	72.12%	72.12%	72.12%
Pr(C=0 | T)	38.56%	27.88%	27.88%	27.88%	27.88%

Threshold Probabilities (reproducability):

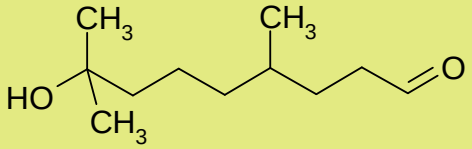
for a positive conclusion	**79%**
for a negative conclusion	**77%**

Posterior Probability of the qWoE conclusion

for a positive conclusion	**72%**
for a negative conclusion	**28%**

Information Gap:

for a positive conclusion	**7%**	**TEST PROPOSAL needed**
for a negative conclusion	**49%**	**TEST PROPOSAL needed**



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Endpoint: **Sensitization**

Framework: **REACH A.VII**

Gold Standard: OECD 429 LLNA

Information Requirement: OECD 429 LLNA

Prior Probability: Positive 50% Pr(C=1); Negative 50% Pr(C=0)

Threshold level: 80%

Battery of Available Tests

testnr.	1	2	3	4	5
test type	**DEREK**	**SMARTs**	**TIMES-SS**	**TOPKAT**	**Multi CASE**
Sensitivity:	0.788	0.776	0.562	0.670	0.877
Specificity:	0.506	0.522	0.761	0.444	0.106
Test Result:	**1**	**1**	**1**	**1**	**1**
Quality Factors:	**1.00**	**1.00**	**1.00**	**1.00**	**1.00**
adapted sensitivity	0.788	0.776	0.562	0.670	0.877
adapted specificity	0.506	0.522	0.761	0.444	0.106
Pr(C=1)	50%	61%	72%	86%	88%
Pr(C=0)	50%	39%	28%	14%	12%

Sensitivity: 0.959

Specificity: 0.993

Weight Factors: 1

Posterior Probabilities

Pr(C=1 | T=1) 99%

Pr(C=0 | T=0) 96%

Posterior Probabilities

Pr(C=1 | T)	61.4%	72.1%	85.9%	88.0%	87.8%
Pr(C=0 | T)	38.6%	27.9%	14.1%	12.0%	12.2%

Threshold Probabilities (reproducability):

for a positive conclusion **79%**

for a negative conclusion **77%**

Posterior Probability of the qWoE conclusion

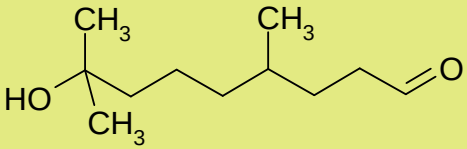
for a positive conclusion **88%**

for a negative conclusion **12%**

Information Gap:

for a positive conclusion **-8%** **WoE satisfied**

for a negative conclusion **65%** **TEST PROPOSAL needed**



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Endpoint: Sensitization

Framework: REACH A.VII

Gold Standard: OECD 429 LLNA

Information Requirement: OECD 429 LLNA

Prior Probability

Positive	50%	Pr(C=1)
Negative	50%	Pr(C=0)

Threshold level: 80%

Battery of Available Tests

testnr.	1	2	3	4	5
test type	**DEREK**	**SMARTs**	**TIMES-SS**	**TOPKAT**	**Multi CASE**
Sensitivity:	0.788	0.776	0.562	0.670	0.877
Specificity:	0.506	0.522	0.761	0.444	0.106
Test Result:	**1**	**1**	**1**	**1**	**1**
Quality Factors:	**0.80**	**0.80**	**0.80**	**0.80**	**0.80**
adapted sensitivity	0.730	0.721	0.549	0.636	0.802
adapted specificity	0.504	0.518	0.709	0.456	0.184
Pr(C=1)	50%	60%	69%	81%	83%
Pr(C=0)	50%	40%	31%	19%	17%

Sensitivity: 0.959

Specificity: 0.993

Weight Factors: 1

Posterior Probabilities

Pr(C=1 | T=1)	99%
Pr(C=0 | T=0)	96%

Posterior Probabilities

Pr(C=1 | T)	59.6%	68.8%	80.6%	82.9%	82.7%
Pr(C=0 | T)	40.4%	31.2%	19.4%	17.1%	17.3%

Threshold Probabilities (reproducability):

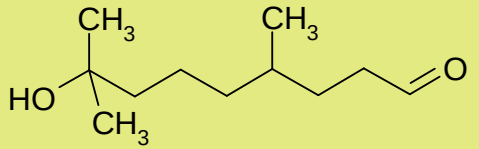
for a positive conclusion	**79%**
for a negative conclusion	**77%**

Posterior Probability of the qWoE conclusion

for a positive conclusion	**83%**
for a negative conclusion	**17%**

Information Gap:

for a positive conclusion	**-3%**	**WoE satisfied**
for a negative conclusion	**60%**	**TEST PROPOSAL needed**



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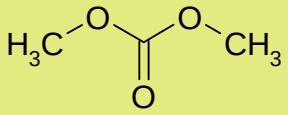
Case (proof-of-principle) of qWoE ITS: Skin Sensitization

- Excel implementation



- dimethyl carbonate 616-38-6

- DEREK	no alert found	negative
- SMARTs	no alert found	negative
- TOPKAT	probability<0.7	negative
- TIMES-SS	no alert found	negative
- MultiCASE	no alert found	negative

- LLNA test (1 results) negative

Endpoint: Sensitization

Framework: REACH A.VII

Gold Standard: OECD 429 LLNA

Information Requirement: OECD 429 LLNA

Prior Probability

Positive	50%	Pr(C=1)
Negative	50%	Pr(C=0)

Threshold level: 80%

Battery of Available Tests

testnr.	1	2	3	4	5
test type	**DEREK**	**SMARTs**	**TIMES-SS**	**TOPKAT**	**Multi CASE**
Sensitivity:	0.788	0.776	0.562	0.670	0.877
Specificity:	0.506	0.522	0.761	0.444	0.106
Test Result:	**0**	**0**	**0**	**0**	**0**
Quality Factors:	**1.00**	**1.00**	**1.00**	**1.00**	**1.00**
adapted sensitivity	0.788	0.776	0.562	0.670	0.877
adapted specificity	0.506	0.522	0.761	0.444	0.106
Pr(C=1)	50%	30%	15%	9%	7%
Pr(C=0)	50%	70%	85%	91%	93%
Posterior Probabilities					
Pr(C=1 | T)	29.6%	15.3%	9.4%	7.2%	8.2%
Pr(C=0 | T)	70.4%	84.7%	90.6%	92.8%	91.8%

Sensitivity: 0.959

Specificity: 0.993

Weight Factors: 1

Posterior Probabilities

Pr(C=1 | T=1) 99%

Pr(C=0 | T=0) 96%

Threshold Probabilities (reproducability):

for a positive conclusion **79%**

for a negative conclusion **77%**

Posterior Probability of the qWoE conclusion

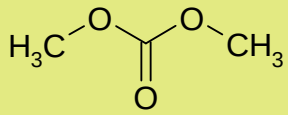
for a positive conclusion **8%**

for a negative conclusion **92%**

Information Gap:

for a positive conclusion **71%** **TEST PROPOSAL needed**

for a negative conclusion **-15%** **WoE satisfied**



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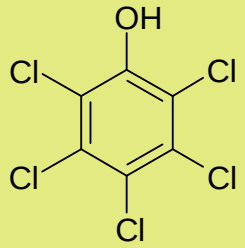
Case (proof-of-principle) of qWoE ITS: Skin Sensitization

- Excel implementation



- Pentachlorophenol 87-86-5

- DEREK	no alert found	negative
- SMARTs	alert found	positive
- TIMES-SS	no alert found	negative
- TOPKAT	probability<0.7	negative
- MultiCASE	alert found	positive

- LLNA test (2 results) ?

Endpoint: Sensitization

Framework: REACH A.VII

Gold Standard: OECD 429 LLNA

Information Requirement: OECD 429 LLNA

Prior Probability

Positive	50%	Pr(C=1)
Negative	50%	Pr(C=0)

Threshold level: 80%

Battery of Available Tests

testnr.	1	2	3	4	5
test type	**DEREK**	**SMARTs**	**TIMES-SS**	**TOPKAT**	**Multi CASE**
Sensitivity:	0.788	0.776	0.562	0.670	0.877
Specificity:	0.506	0.522	0.761	0.444	0.106
Test Result:	**0**	**1**	**0**	**0**	**1**
Quality Factors:	**1.00**	**1.00**	**1.00**	**1.00**	**1.00**
adapted sensitivity	0.788	0.776	0.562	0.670	0.877
adapted specificity	0.506	0.522	0.761	0.444	0.106
Pr(C=1)	50%	30%	41%	28%	23%
Pr(C=0)	50%	70%	59%	72%	77%

Sensitivity: 0.959

Specificity: 0.993

Weight Factors: 1

Posterior Probabilities

Pr(C=1 | T=1)	99%
Pr(C=0 | T=0)	96%

Posterior Probabilities

Pr(C=1 | T)	29.6%	40.5%	28.2%	22.6%	22.2%
Pr(C=0 | T)	70.4%	59.5%	71.8%	77.4%	77.8%

Threshold Probabilities (reproducability):

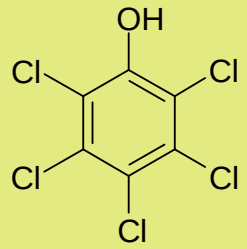
for a positive conclusion	**79%**
for a negative conclusion	**77%**

Posterior Probability of the qWoE conclusion

for a positive conclusion	**22%**
for a negative conclusion	**78%**

Information Gap:

for a positive conclusion	**57%**	**TEST PROPOSAL needed**
for a negative conclusion	**-1%**	**WoE satisfied**



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Endpoint:

Sensitization

Framework:

REACH A.VII

Gold Standard: OECD 429 LLNA

Information Requirement: OECD 429 LLNA

Prior Probability

Positive	50%	Pr(C=1)
Negative	50%	Pr(C=0)

Threshold level: 80%

Battery of Available Tests

testnr.	1	2	3	4	5
test type	**DEREK**	**SMARTs**	**TIMES-SS**	**TOPKAT**	**Multi CASE**
Sensitivity:	0.788	0.776	0.562	0.670	0.877
Specificity:	0.506	0.522	0.761	0.444	0.106
Test Result:	**0**	**1**	**0**	**0**	**1**
Quality Factors:	**0.80**	**1.00**	**1.00**	**1.00**	**1.00**
adapted sensitivity	0.730	0.776	0.562	0.670	0.877
adapted specificity	0.504	0.522	0.761	0.444	0.106
Pr(C=1)	50%	35%	46%	33%	27%
Pr(C=0)	50%	65%	54%	67%	73%

Weight Factors: 1

Posterior Probabilities

Pr(C=1 | T=1)	99%
Pr(C=0 | T=0)	96%

Posterior Probabilities

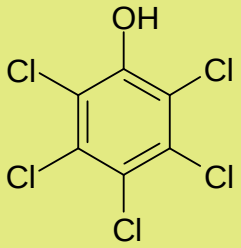
Pr(C=1 | T)	34.8%	46.5%	33.3%	27.1%	26.7%
Pr(C=0 | T)	65.2%	53.5%	66.7%	72.9%	73.3%

Threshold Probabilities (reproducability):

for a positive conclusion	**79%**
for a negative conclusion	**77%**

Posterior Probability of the qWoE conclusion

for a positive conclusion	**27%**
for a negative conclusion	**73%**



Information Gap:

for a positive conclusion	**53%**	**TEST PROPOSAL needed**
for a negative conclusion	**4%**	**TEST PROPOSAL needed**

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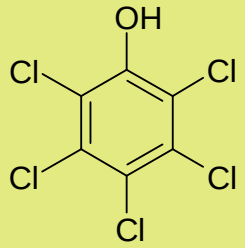
Case (proof-of-principle) of qWoE ITS: Skin Sensitization

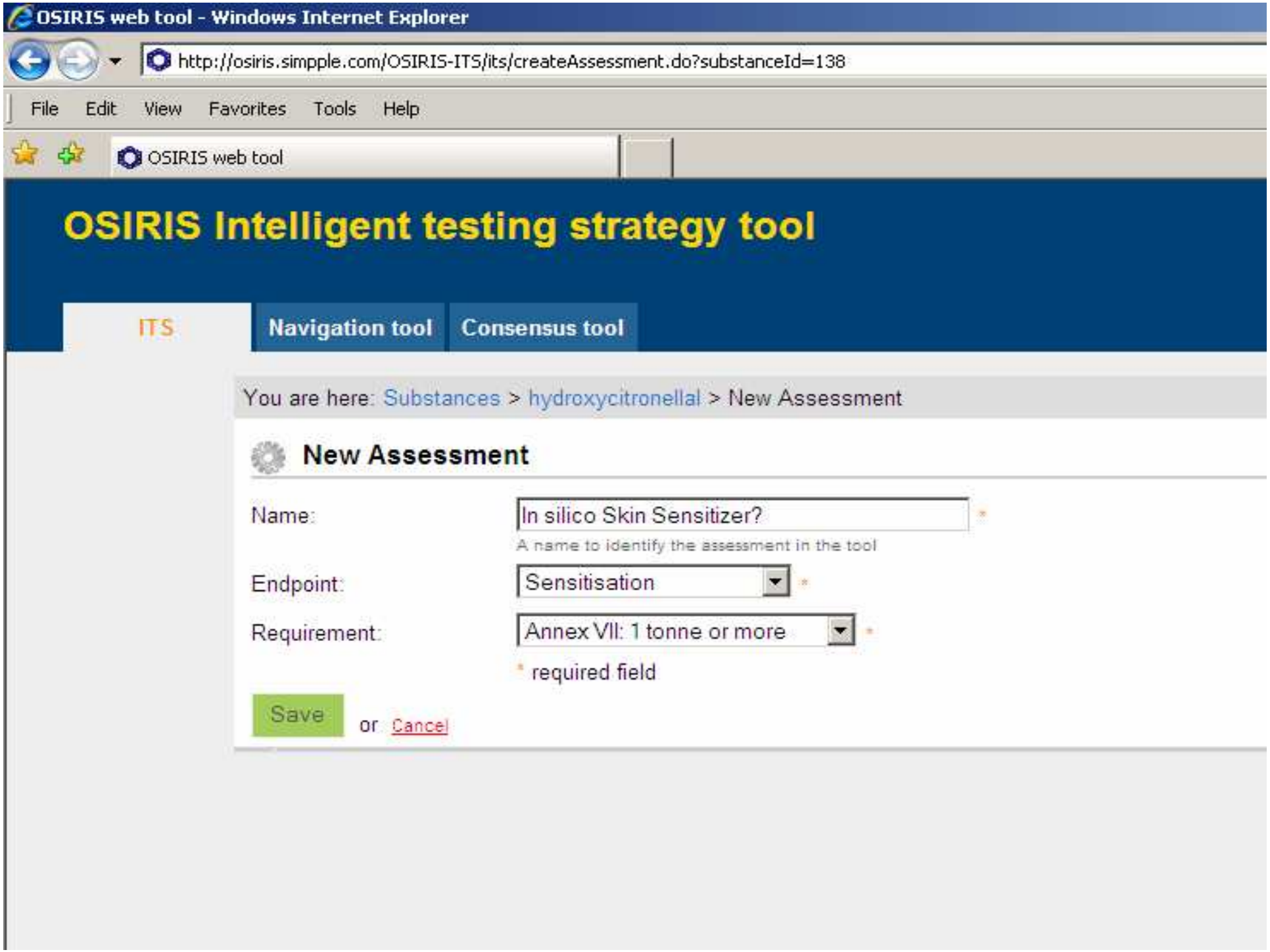
- Excel implementation

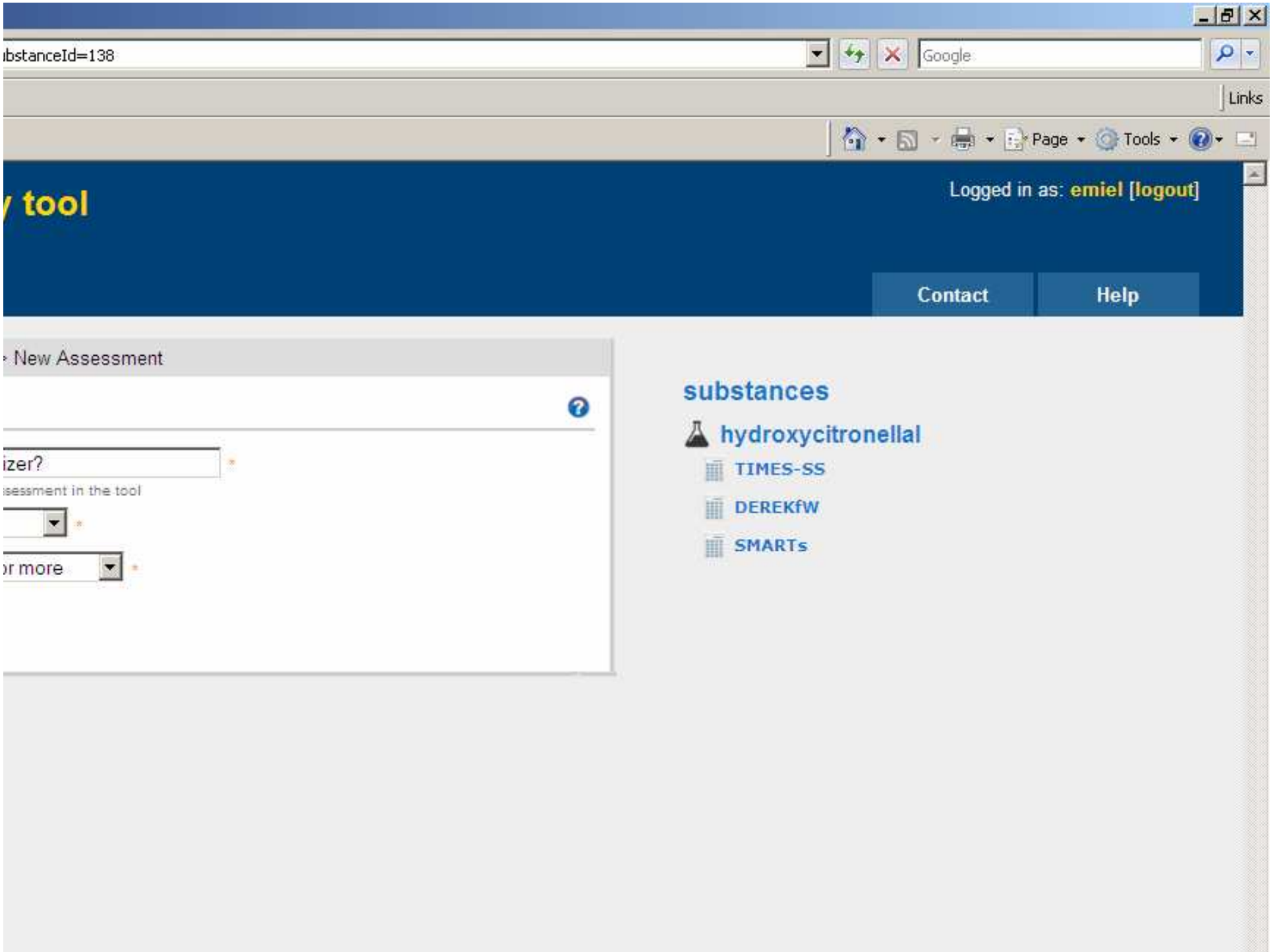


- Pentachlorophenol 87-86-5

- DEREK	no alert found	negative
- SMARTs	alert found	positive
- TIMES-SS	no alert found	negative
- TOPKAT	probability<0.7	negative
- MultiCASE	alert found	positive
- LLNA test (2 results)		**positive**


OSIRIS web tool - Windows Internet Explorer
http://osiris.simpple.com/OSIRIS-ITS/its/welcome.do
Google
File Edit View Favorites Tools Help
Links
OSIRIS web tool
Page
Tools
OSIRIS Intelligent testing strategy tool
Logged in as: emiel [logout]
ITS
Navigation tool
Consensus tool
Contact
Help
OSIRIS web tool
This is the fourth version of the web tool implementation of the Integrated Testing Strategies (ITS) to be develope within OSIRIS.
New features in this version are:
• Integration with Chemprop database: test data contained in Chemprop datasets can be imported into a substance.
• Current version includes two new endpoints, Aquatic Toxicity, using a preliminary ITS, and Sensitisation, using an ITS that includes qWoE.
• Advanced probabilistic-based decision methods are supported by the tool. They are included in the ITS for Sensitisation.
Internet
100%


OSIRIS web tool - Windows Internet Explorer
http://osiris.simpple.com/OSIRIS-ITS/its/createAssessment.do?substanceId=138
File Edit View Favorites Tools Help
OSIRIS web tool
OSIRIS Intelligent testing strategy tool
ITS
Navigation tool
Consensus tool
You are here: Substances > hydroxycitronellal > New Assessment
New Assessment
Name:
In silico Skin Sensitizer?
A name to identify the assessment in the tool
Endpoint:
Sensitisation
Requirement:
Annex VII: 1 tonne or more
* required field
Save
or Cancel


bstanceId=138
Google
Links
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Tools
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Logged in as: emiel [logout]
Contact
Help
New Assessment
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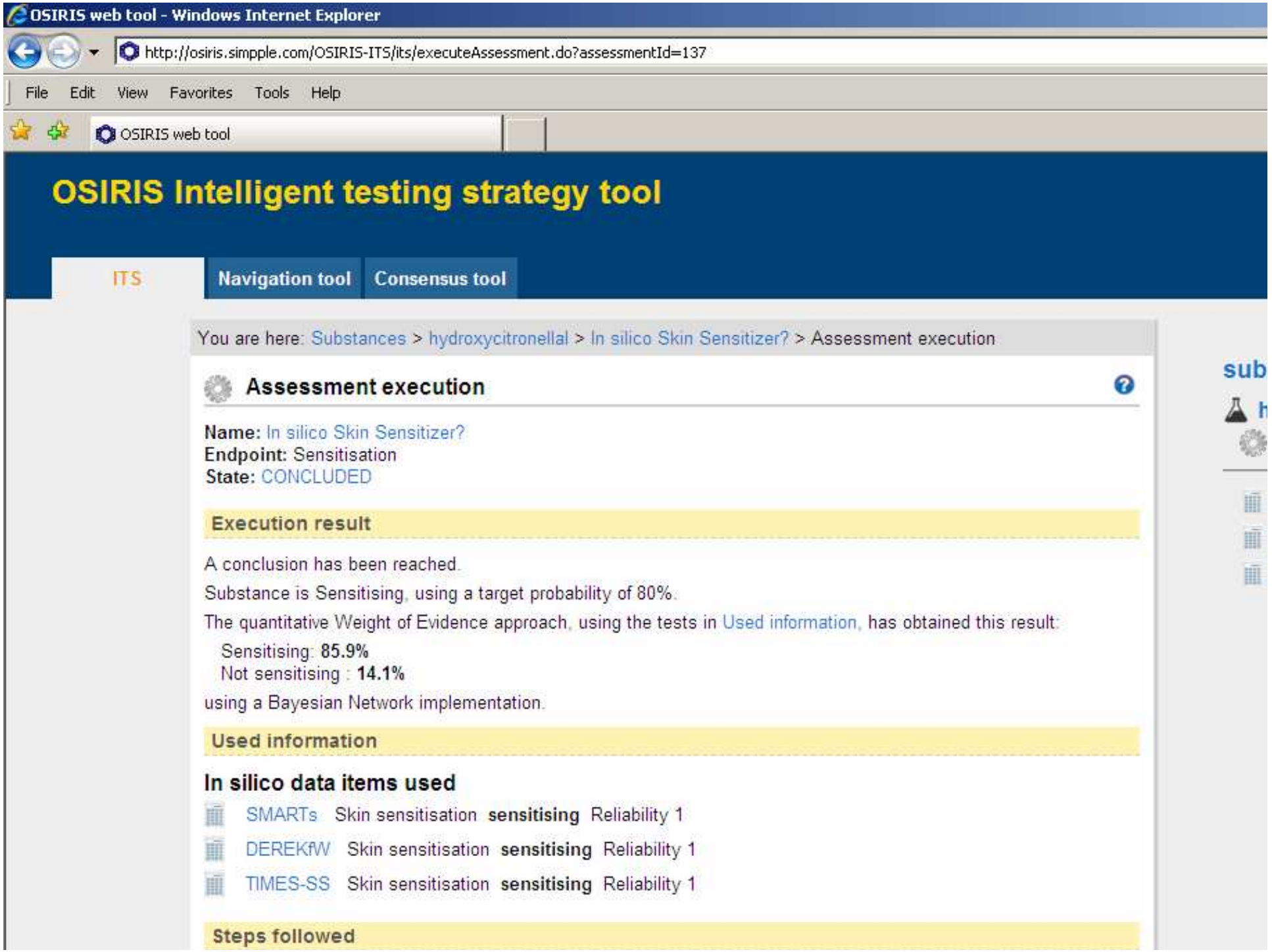
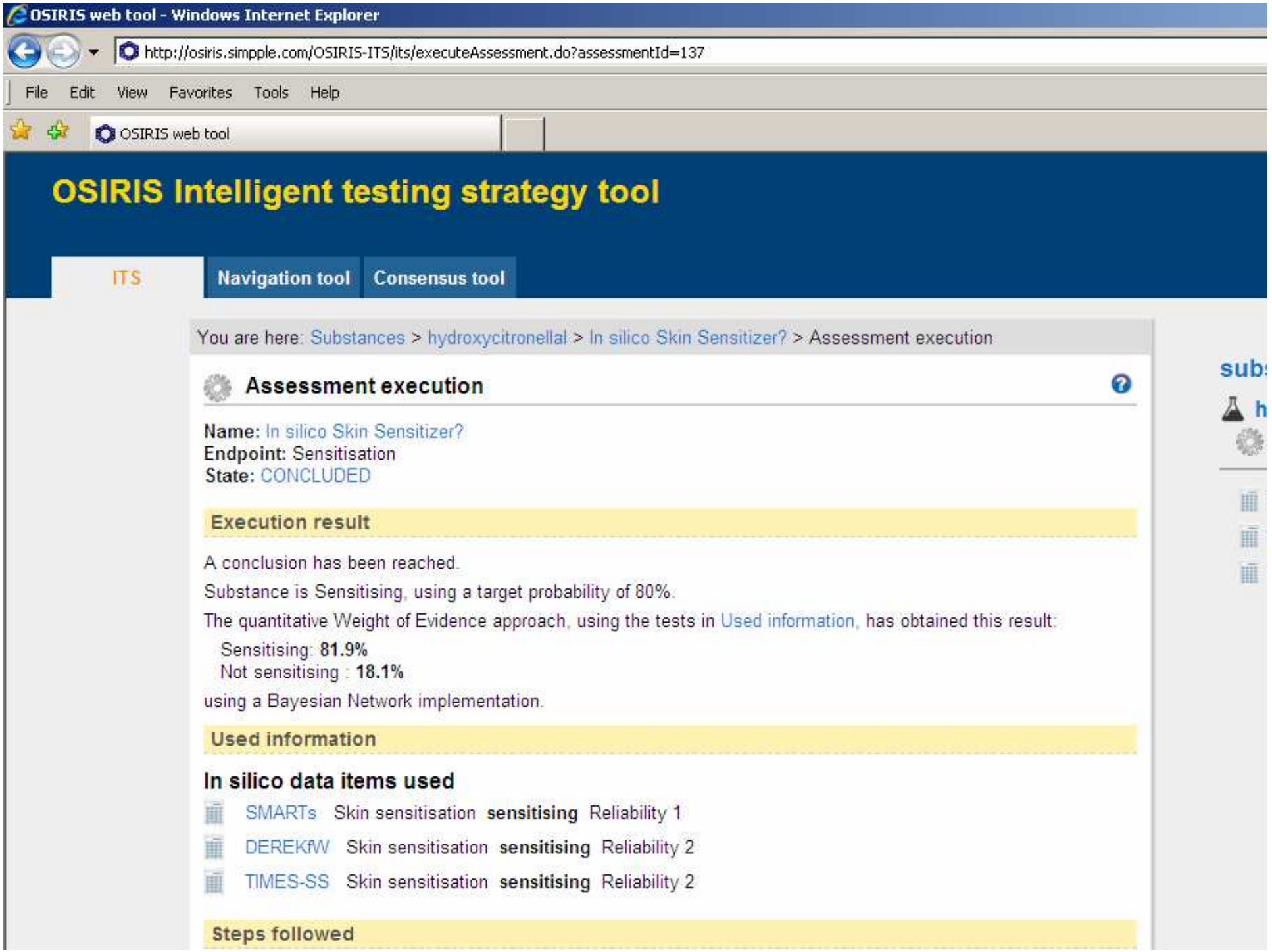
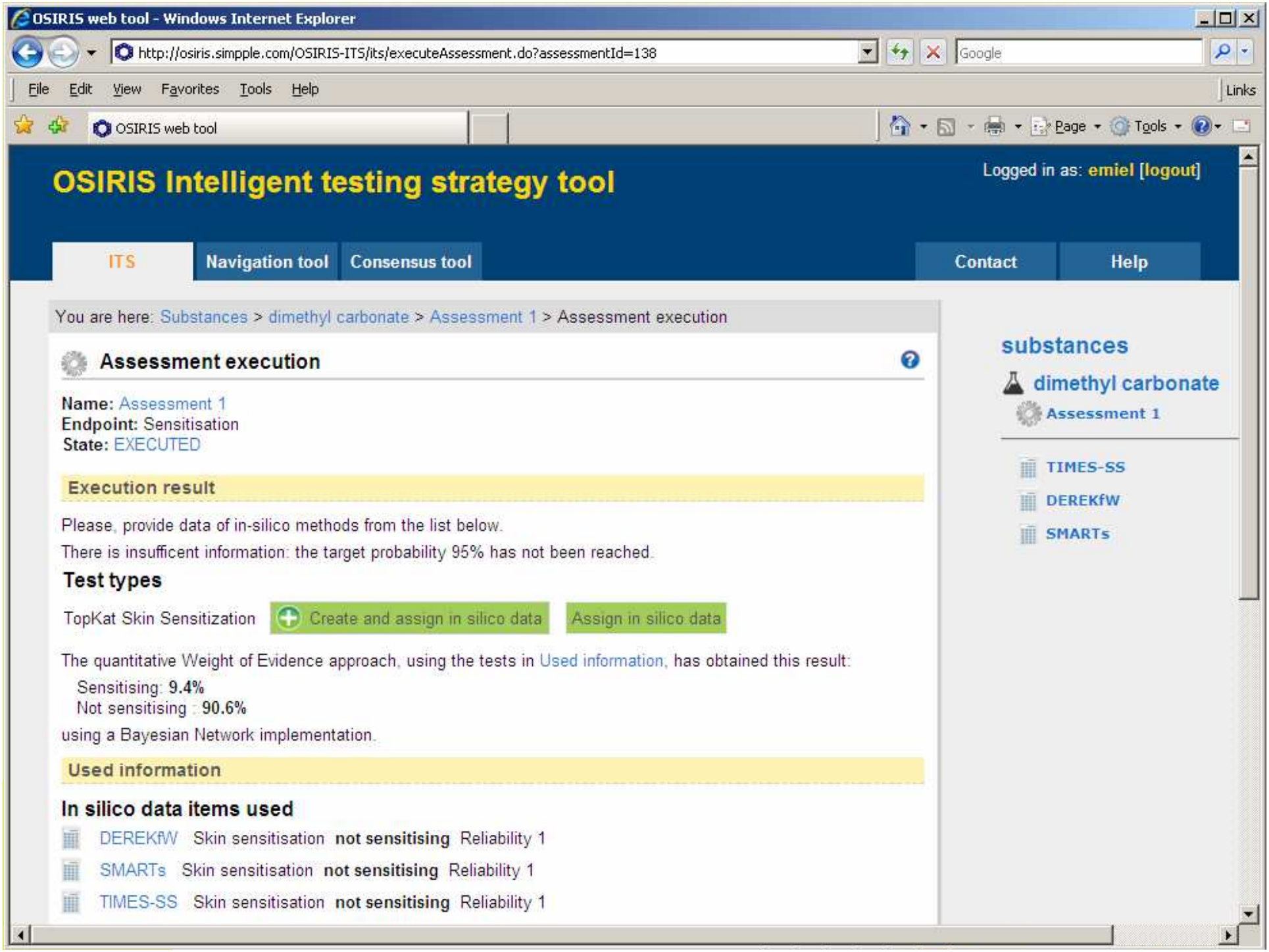
r more
substances
hydroxycitronellal
TIMES-SS
DEREKfW
SMARTs


OSIRIS web tool - Windows Internet Explorer
http://osiris.simpple.com/OSIRIS-ITS/its/executeAssessment.do?assessmentId=137
File Edit View Favorites Tools Help
OSIRIS web tool
OSIRIS Intelligent testing strategy tool
ITS
Navigation tool
Consensus tool
You are here: Substances > hydroxycitronellal > In silico Skin Sensitizer? > Assessment execution
Assessment execution
Name: In silico Skin Sensitizer?
Endpoint: Sensitisation
State: CONCLUDED
Execution result
A conclusion has been reached.
Substance is Sensitising, using a target probability of 80%.
The quantitative Weight of Evidence approach, using the tests in Used information, has obtained this result:
Sensitising: 85.9%
Not sensitising : 14.1%
using a Bayesian Network implementation.
Used information
In silico data items used
SMARTs Skin sensitisation sensitising Reliability 1
DEREKfW Skin sensitisation sensitising Reliability 1
TIMES-SS Skin sensitisation sensitising Reliability 1
Steps followed


OSIRIS web tool - Windows Internet Explorer
http://osiris.simpple.com/OSIRIS-ITS/its/executeAssessment.do?assessmentId=137
File Edit View Favorites Tools Help
OSIRIS web tool
OSIRIS Intelligent testing strategy tool
ITS
Navigation tool
Consensus tool
You are here: Substances > hydroxycitronellal > In silico Skin Sensitizer? > Assessment execution
Assessment execution
Name: In silico Skin Sensitizer?
Endpoint: Sensitisation
State: CONCLUDED
Execution result
A conclusion has been reached.
Substance is Sensitising, using a target probability of 80%.
The quantitative Weight of Evidence approach, using the tests in Used information, has obtained this result:
Sensitising: 81.9%
Not sensitising : 18.1%
using a Bayesian Network implementation.
Used information
In silico data items used
SMARTs Skin sensitisation sensitising Reliability 1
DEREKfW Skin sensitisation sensitising Reliability 2
TIMES-SS Skin sensitisation sensitising Reliability 2
Steps followed


OSIRIS web tool - Windows Internet Explorer
http://osiris.simpple.com/OSIRIS-ITS/its/executeAssessment.do?assessmentId=138
File Edit View Favorites Tools Help
OSIRIS web tool
OSIRIS Intelligent testing strategy tool
Logged in as: emiel [logout]
ITS
Navigation tool
Consensus tool
Contact
Help
You are here: Substances > dimethyl carbonate > Assessment 1 > Assessment execution
Assessment execution
Name: Assessment 1
Endpoint: Sensitisation
State: EXECUTED
Execution result
Please, provide data of in-silico methods from the list below.
There is insufficent information: the target probability 95% has not been reached.
Test types
TopKat Skin Sensitization
Create and assign in silico data
Assign in silico data
The quantitative Weight of Evidence approach, using the tests in Used information, has obtained this result:
Sensitising: 9.4%
Not sensitising : 90.6%
using a Bayesian Network implementation.
Used information
In silico data items used
DEREKfW Skin sensitisation not sensitising Reliability 1
SMARTs Skin sensitisation not sensitising Reliability 1
TIMES-SS Skin sensitisation not sensitising Reliability 1
substances
dimethyl carbonate
Assessment 1
TIMES-SS
DEREKfW
SMARTs

Conclusion:

Bayesian network tool to Weight of Evidence seems

transparent, reproducible, flexible, objective, practical

Discussion:

specific **choices / information** required to make this work....

1. REACH Information Requirement → Threshold Probability
2. List of all possible data sources → statistical performance
3. Quality Factors – endpoint / method specific checklists?

4. Costs (animals, money, time) with an optimization algorithm

Acceptance?

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