



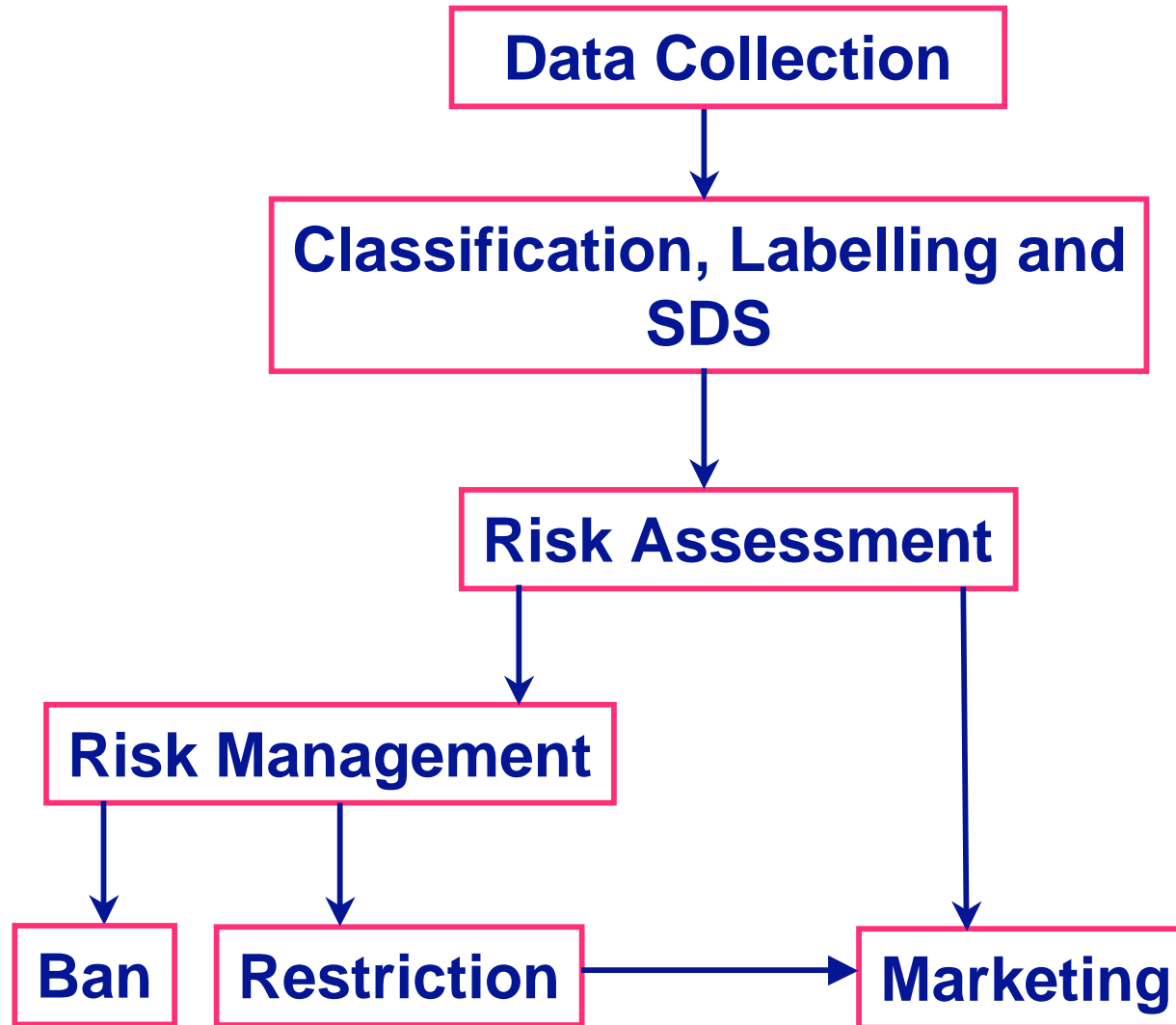
european consensus platform on 3R-alternatives



Ecopa REACH Animal Use Calculator

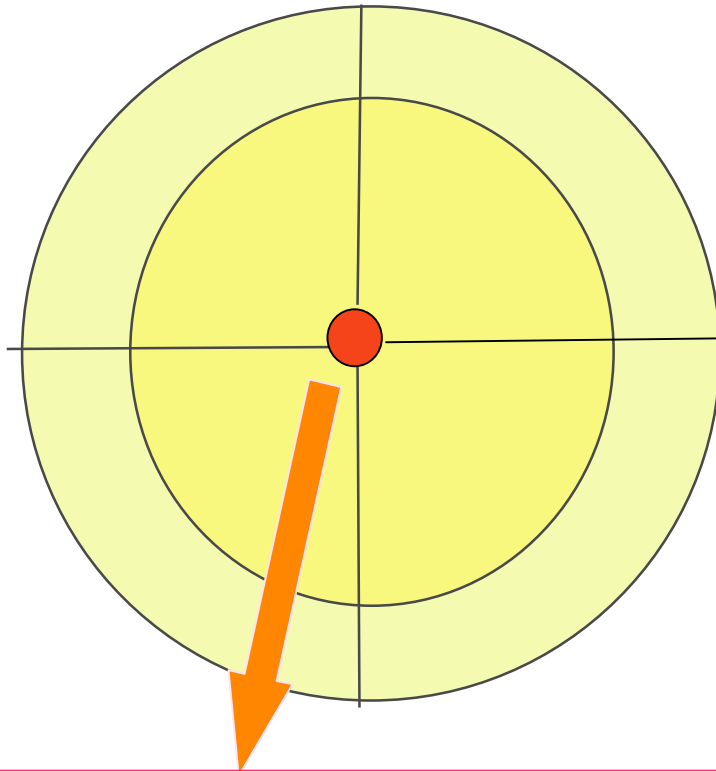
**Karsten Müller &
Simon Webb**

Apply the Same Principle as Today...



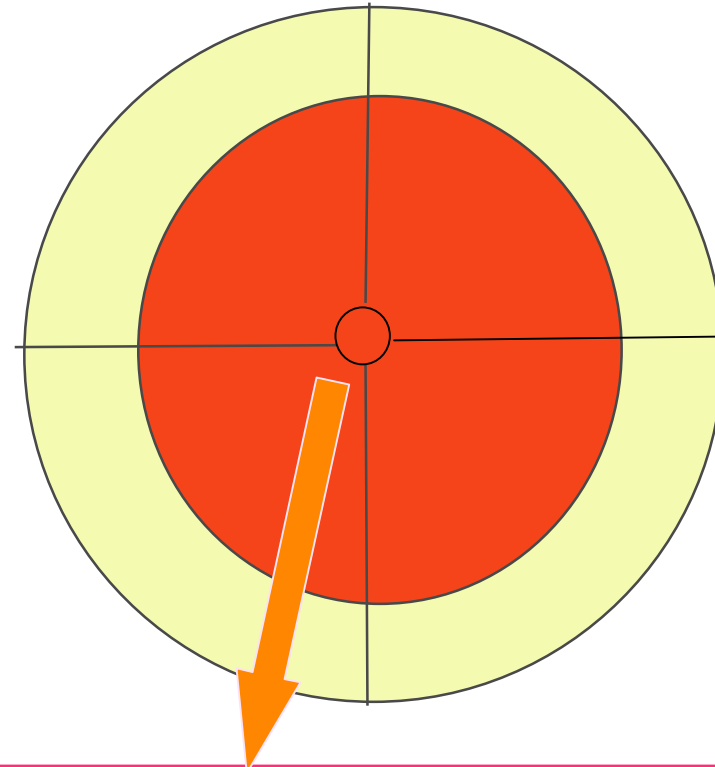
...but Bigger Scope...

Today



~3,000 new substances in the EU
~140 existing chemicals (>1000t/y)
Regulatory Evaluation
3,140 substances

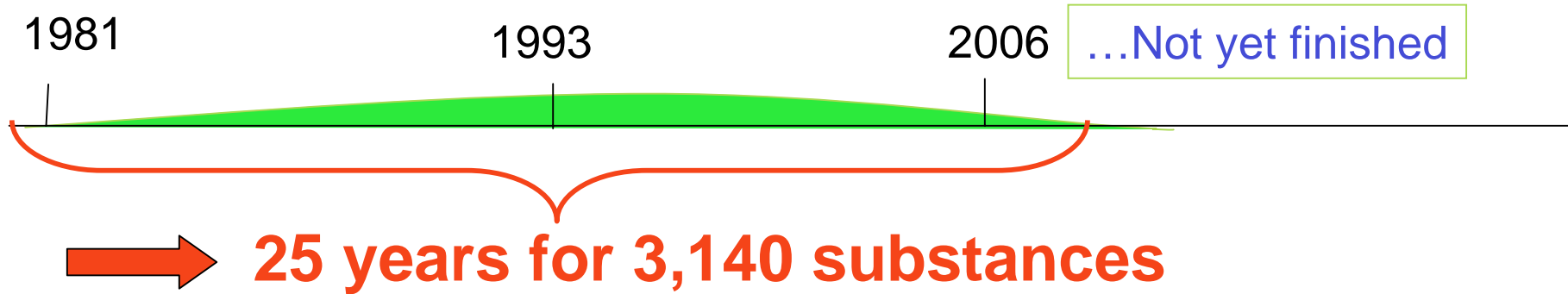
REACH



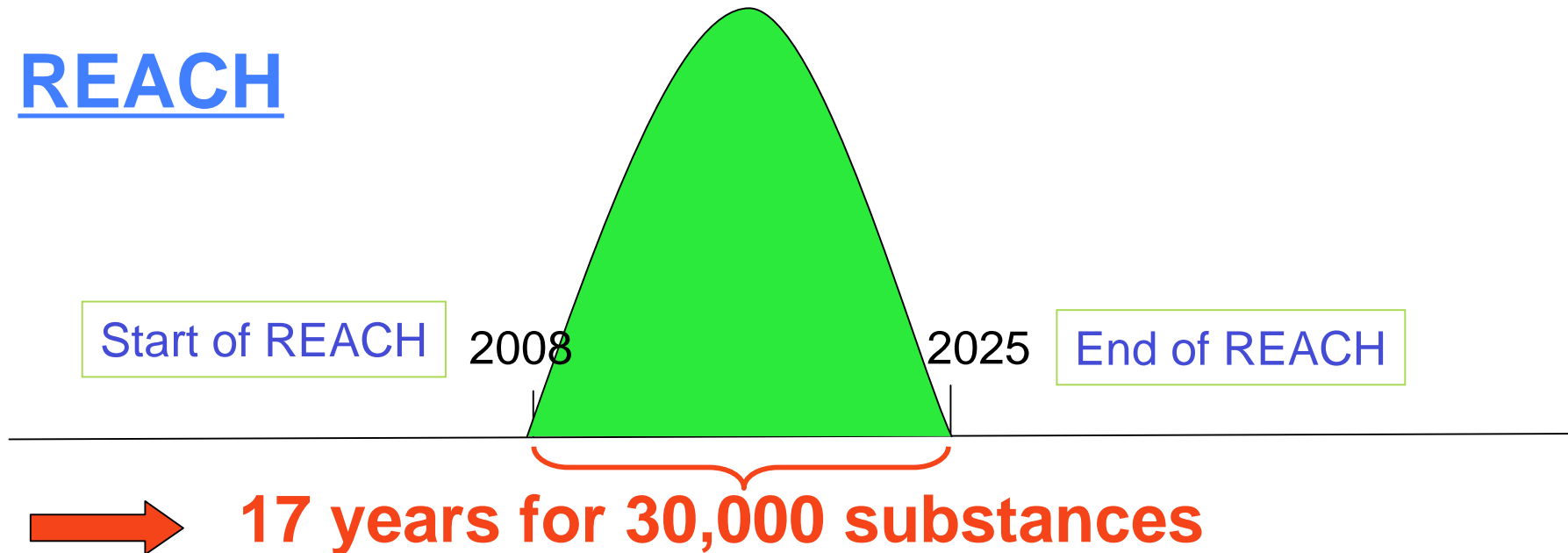
New and existing substances
>1t/y/manufacturer or importer
Regulatory Evaluation
30,000 substances

...and Much Quicker...

Until now



REACH



...and has Sparked a Debate!

Eurogroup for animal welfare - Campaigns - Microsoft Internet Explorer

File Edit View Favorites Tools Help

Address: http://www.eurogroupanimalwelfare.org/campaigns.htm

Home Members Login How can I help?

EUROGROUP for animal welfare

ISSUES

Chemicals Policy
Live animal transport
Government Agricultural

CHEMICALS

REACH (Registration, Evaluation and Authorisation & restriction of CHEMicals)

KEY ISSUES FOR ANIMAL WELFARE



ifhp
Institute for Health and Environmental Protection

ALTERNATIVE APPROACHES
CAN REDUCE THE USE OF TEST ANIMALS UNDER REACH

Attention to the report "Assessment of potential testing needs under REACH: Review of ICHHM, OECD based testing and voluntary industry initiatives"

September 2006
Prepared by: Dr. John, Sharon, Robert, Peter, Vanessa & Julia de Wit

11004



WWF **DETOX** CAMPAIGN **Factsheet**
Animal Testing and REACH

We have a once-in-a-generation opportunity to have safer chemicals and a healthier future for wildlife and people. The draft REACH regulation offers a chance to identify and phase out the worst chemicals, new markets for safer products, and increased trust, which means a good name for the chemical industry too.

Millions and people are exposed to chemicals in their daily lives every day. Eighty-two per cent of the 100 chemicals used in toys, for example, are not even tested for safety. Some are known to be harmful to children and babies. Others do not reach their targets, but contribute to air pollution, chemical use, and the release of toxic substances into the environment. REACH proposes that industry provides basic toxicological safety information on the chemicals it sells. It also sets the requirements for testing chemicals.

What is WWF's position on animal testing and REACH?

WWF does not believe that REACH will lead to a big increase in animal testing.

- For the 20,000 chemicals on the market in 1-10 ton quantities, testing will be greatly reduced (90-95%). This has been stated in the White Paper in 2001.
- Many chemicals belong to classes or groups of substances that do not require separate testing.
- REACH encourages the development of innovative alternatives to animal testing. This will further reduce animal testing.
- REACH will encourage the development of innovative alternatives to animal testing - alternatives that will also be suitable for other safety testing.

REACH is actively promoting the changes in REACH that will further reduce animal testing by encouraging the adoption of registration procedures with complete data sharing.

<http://www.panda.org/na>

Contact:

- WWF Europe, WWF House, 100 Chiswick Road, Uxbridge, Middlesex, UK. Tel: +44 (0)1895 833900. Email: enquiries@wwf.org.uk
- WWF USA, 2000 Market Street, Philadelphia, PA 19104, USA. Tel: +1 215 382 7400. Email: usa@wwf.org

SAFER CHEMICALS
FOR A HEALTHIER FUTURE

Welfare fully supports the objectives of the proposed new EU chemicals regulation. If the current proposal is left unchanged, REACH will result in the use of millions of

REACH - Amending the Commission's proposal

Background

The Commission's proposal for a new EU chemicals policy (REACH) is a landmark step towards a safer and more sustainable chemical industry. It aims to ensure that chemicals are safe for people and the environment, while maintaining the competitiveness of the European chemical industry.

Key Issues

The Commission's proposal for a new EU chemicals policy (REACH) is a landmark step towards a safer and more sustainable chemical industry. It aims to ensure that chemicals are safe for people and the environment, while maintaining the competitiveness of the European chemical industry.

Conclusion

REACH is a positive step towards a safer and more sustainable chemical industry. However, it is essential that the Commission's proposal is amended to ensure that it fully meets the objectives of animal welfare and the protection of the environment.

Replacing animal based toxicity tests - REACH and beyond

The Commission's proposal for a new EU chemicals policy (REACH) rightly raises concerns about the safety of chemicals. But a new and improved regulatory system for chemicals must not rely on outdated and cruel animal tests.

Key Messages

- REACH must not rely on outdated and cruel animal tests.
- REACH must encourage the development of innovative alternatives to animal testing.
- REACH must ensure that chemicals are safe for people and the environment.

Conclusion

REACH is a positive step towards a safer and more sustainable chemical industry. However, it is essential that the Commission's proposal is amended to ensure that it fully meets the objectives of animal welfare and the protection of the environment.

Webb-SF

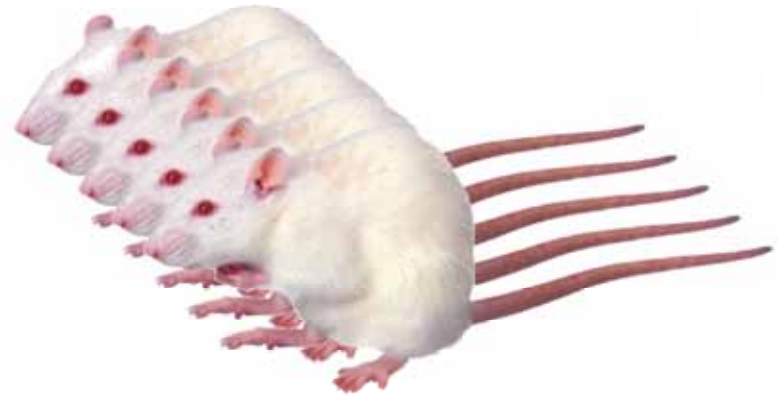
Principle of the Calculator

**REACH
Test Requirements**

**Test
Protocols**

**Availability of
Existing Data**

**Projected
Need to Test**



REACH Test Requirements

Microsoft Excel - AnimalUseReach_beta version_07.xls

		no. of substances acc. to "Advanced Options"		
		19,200	4,977	2,461
Test Protocol	Protocols	Annex V >1 Tonnes	Annex VI >10 Tonnes	Annex VII > 100 Tonnes
Corrosion Skin	OECD 430 & 431	Standard	Standard	Standard
Iritation Eye	-	Standard	Standard	Standard
Acute Dermal Irritation/Corrosion	OECD 404	-	Standard	Standard
Acute Eye Irritation/Corrosion	OECD 405	-	Standard	Standard
Skin Sensitisation - Maximisation	OECD 406	-	-	-
Skin Sensitisation - Buehler	OECD 406	-	-	-
Repeated Dose Toxicity: 28 Day Short Term (Rodents)	OECD 407	-	Standard	Standard
Repeated Dose Toxicity: 90 Day Subchronic (Rodents)	OECD 408	-	Potential	Standard
Repeated Toxicity: 365 Day Chronic (Rodents)	OECD 452	-	-	-

OECD 404
Acute Dermal Irritation/Corrosion:
Standard Annex VI – VIII
(>10, >100 & >1000 tonnes)

1 of 24 - Clipboard
Item collected.

start | User Interface | Advanced options | Test Protocols + defaults | Details for Calculation | Graph_Animal use per test_high | 5:37 PM

Data Availability/Actual Testing Need

Microsoft Excel - AnimalUseReach_beta version_07.xls

AD scenario reflects available/promised data estimated in Pedersen et al. (2003), with RDN scenario reflects acceptance of QSAR and waiving as estimated in Pedersen et al.

	C	D	N	O	P	Q	R
			Annex V	Annex V	Annex VI	Annex VI	Annex
			AD Scenario	RDN Scenario	AD Scenario	RDN Scenario	AD Scer
	Test Protocol	Protocols	Test Needs (%)	Test Needs (%)	Test Needs (%)	Test Needs (%)	Test Need
7	Corrosion Skin	OECD 430 & 431	50	16	0	0	0
8	Irritation Eye	-	50	28	0	0	0
10	Acute Dermal Irritation/Corrosion	OECD 404	0	0	35	11	33
11	Acute Eye Irritation/Corrosion	OECD 405	0	0	35	20	33
12							
13	Skin Sensitisation - Maximisation	OECD 406	83	37	83	37	78
			83	37	83	37	78
			83	37	83	37	78
			50	12	35	9	33
			50	12	35	9	33
			0	0	35	6	33
			97	23	97	23	93
			0	0	35	9	33
			0	0	83	20	78
			0	0	83	20	78
			0	0	35	9	33
			0	0	83	20	78
			0	0	83	20	78
			0	0	80	17	71
			0	0	97	6	93
			0	0	0	0	0

Calculation / Graph_Animal use per test_high

OECD 404
Acute Dermal Irritation/Corrosion
Annex VI (>10 t)
Data Available 65%
Testing Required 11%
(Pedersen et al., 2003)

Projected Animal Use

	C	D	Y	Z	AA	AB	AC
1			the no. of substances acc. to "Advanced Options", animal numbers acc. to "Advanced op				
2			4,977	4,977	2,461	2,461	2,704
3			Annex VI	Annex VI	Annex VII	Annex VII	Annex
4			AD Scenario	RDN Scenario	AD Scenario	RDN Scenario	AD Scen
5	Test Protocol	Protocols	Numbers	Numbers	Numbers	Numbers	Numb
6							
7	Corrosion Skin	OECD 430 & 431	0	0	0	0	0
8	Irritation Eye	-	0	0	0	0	0
9							
10	Acute Dermal Irritation/Corrosion	OECD 404	5,226	1,642	2,436	812	568
11	Acute Eye Irritation/Corrosion	OECD 405	5,226	2,986	2,436	1,403	568
12							
13	Skin Sensitisation - Maximisation	OECD 406	0	0	0	0	0
14	Skin Sensitisation - Buehler	OECD 406	0	0	0	0	0
				46,037	47,990	20,919	32,44
				0	0	0	0
				0	0	0	0
				0	0	0	0
				57,236	114,437	27,071	83,82
				5,375	9,746	2,363	7,46
				39,816	76,783	18,704	24,87
				0	0	0	0
				0	0	0	0
				0	0	0	0
				0	0	0	0
				33,844	69,892	12,797	40,01
				23,890	183,098	25,594	186,0
				0	0	0	411,0

OECD 404

Acute Dermal Irritation/Corrosion

Annex VI 1,642 - 5,226 animals

Annex VII 812 - 2,436 animals

Annex VIII 162 – 568 animals

Tests 872 – 2,743

Use of the Calculator


The screenshot displays a Microsoft Excel spreadsheet with a yellow background. The title bar reads "Microsoft Excel - AnimaluseReach_beta version_07.xls". The menu bar includes "File", "Edit", "View", "Insert", "Format", "Tools", "Data", "Window", and "Help". The toolbar contains various icons for file operations and formatting. The spreadsheet content includes the ecopa logo (a blue and yellow star) and the text "ecopa european consensus-platform for alternatives". Below the logo, the title "Calculator for estimating animal use under the future European Chemicals Legislation (REACH)" is displayed. The "Input:" section contains a paragraph of text and an "Advanced" button. The "Output:" section features a "Calculate" button, a "Clear" button, and a "Print Screen" button. Below these are two input fields: "Animals needed" with a "Plot AD" button and "Reduced Data Need (RDN) Scenario:" with a "Plot RDN" button. A paragraph of text provides further information about the calculation process. At the bottom, a "Remarks:" section contains two paragraphs of text. The status bar at the bottom of the Excel window shows "Ready" and the taskbar at the bottom of the screen displays the Windows start button, several application icons, and the system clock showing "5:40 PM".

Microsoft Excel - AnimaluseReach_beta version_07.xls

File Edit View Insert Format Tools Data Window Help

Type a question for help

A1

 **ecopa** european consensus-platform for alternatives

Calculator for estimating animal use under the future European Chemicals Legislation (REACH)

Input: ecopa has drawn upon various sources to gather the information required for calculating potential animal use under REACH. Testing requirements under REACH are as of December 2005 following the 1st reading in the Parliament and discussions in the Council. This information can be viewed and - if necessary - modified by pressing the "Advanced" button below. You can access the details before or after starting the calculation. Or simply skip this step and start the calculation right now with ecopa's default values.

Advanced

Output: Make your own estimation in mind. Now press here to see the result below.

Animals needed: "Available Data" (AD) Scenario: Plot AD

"Reduced Data Need" (RDN) Scenario: Plot RDN

Plots graphs with the fraction of animals needed per individual test for either the "Available Data" (AD) or the "Reduced Data Need" (RDN) scenario.

Further information (e.g., on the proportion of mammals, birds and fish and on the impact of the scenario on each individual test) can be viewed further down the page after having initiated the calculation. "Calculate" has to be pressed only once at the beginning. Calculations are subsequently updated automatically.

Remarks: Test requirements are based on the REACH proposal from October 29 2003, the amendments proposed after the 1st reading in the European Parliament and Council negotiations.

Animal number per test has been taken from the corresponding OECD guidelines and supplemented by expert

User Interface / Advanced options / Test Protocols + defaults / Details for Calculation / Graph Animal use per test_high

Ready

start | > ecopa logo's ... | Microsoft Excel... | ~3259926.put | ecopaREACH... | +3160194.PPT | 5:40 PM

Modification of Assumptions

Microsoft Excel - AnimalUseReach_beta version_07.xls

File Edit View Insert Format Tools Data Window Help

Arial 10 B I U

A1

		Annex V (>1 to/year)							
		Inclusion in scenario		Test needs			Inclusion in		
		Calculation		Calculation		Calculation	Calculation		
		↓		↓		↓	↓		
		Include in Scenario for Annex V	Include in Scenario for Annex V (default)	Test needs AD scenario	Test needs AD scenario (default)	Test needs RDN scenario	Test needs RDN scenario (default)	Include in Scenario for Annex VI	
		(Yes/No)	(Yes/No)	%	%	%	%	(Yes/No)	
43	Test Protocol	Protocols							
44									
45	Corrosion Skin	OECD 430 & 431	yes	yes	50	50	16	16	yes
46	Irritation Eye	-	yes	yes	50	50	28	28	yes
47									
48					0	0	0	0	yes
49					0	0	0	0	yes
50									
51					83	83	37	37	no
52	Skin Sensitisation - Buehler	OECD 406	no	no	83	83	37	37	no
53	Skin Sensitisation - Local Lymph Node Assay LLNA	OECD 429	yes	yes	83	83	37	37	yes
54	Mutagenicity								

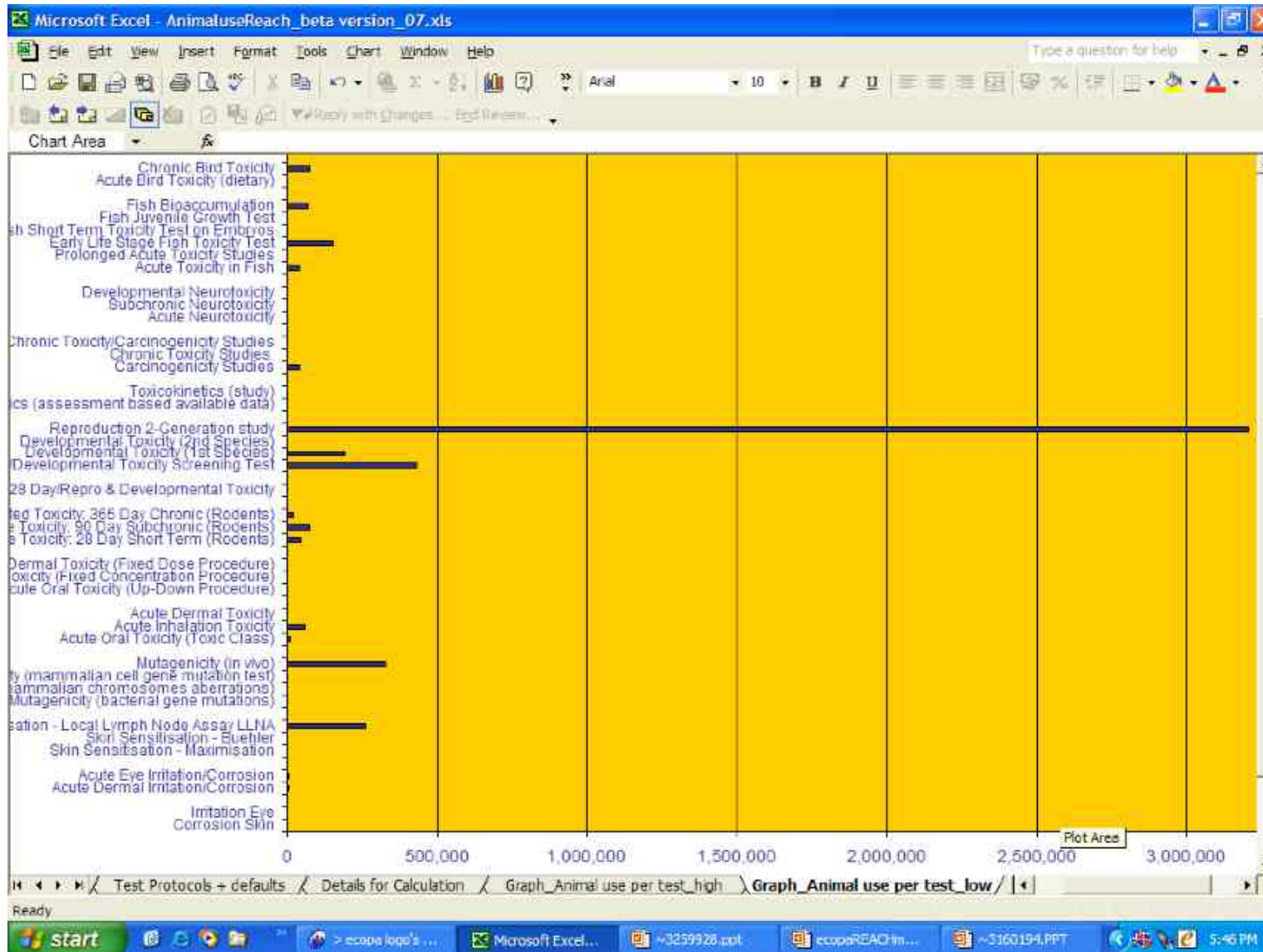
Substance Number, Test Requirement, Data Availability & Animal Number per Test

User Interface | Advanced options | Test Protocols + defaults | Details for Calculation | Graph_Animal use per test_high

Ready

start | > ecopa logo's ... | Microsoft Excel... | ~3259928.cort | ecopaREACHm... | ~3160194.PPT | 5:42 PM

Graphical Output



1 - 10t/y (Annex V)

- ✓ **Skin Corrosion/Irritation (assessment or *in vitro*)**
- ✓ **Eye Irritation (assessment or *in vitro*)**
- ✓ **Bacterial Gene Mutation**
- ✓ **Skin Sensitization (LLNA)**
- ✓ **Acute Oral Toxicity**

10 - 100 t/y (Annex VI)

Those tests already mentioned for 1 - 10 t/y and:

- ✓ *In vivo* Skin Irritation
- ✓ *In vivo* Eye Irritation
- ✓ *In vitro* Cytogenicity Test in Mammalian Cells
- ✓ *In vitro* Gene Mutation Test in Mammalian Cells
- ✓ Acute Toxicity (2nd route)
- ✓ 28 day Repeat Dose Study
- ✓ Reproductive & Developmental Screening Study
- ✓ Acute Aquatic Toxicity-Fish

100 - 1000 t/y (Annex VII)

Those tests already mentioned for 10 - 100 t/y and:

- ✓ **90 day Sub-Chronic Toxicity Study**
- ✓ **Developmental Toxicity Study (one species)**
- ✓ **Two-Generation Reproductive Study**
- ✓ **Fish Early-life Stage, Embryo or Juvenile Growth Test**
- ✓ **Bioconcentration in one Aquatic Species (Fish)**

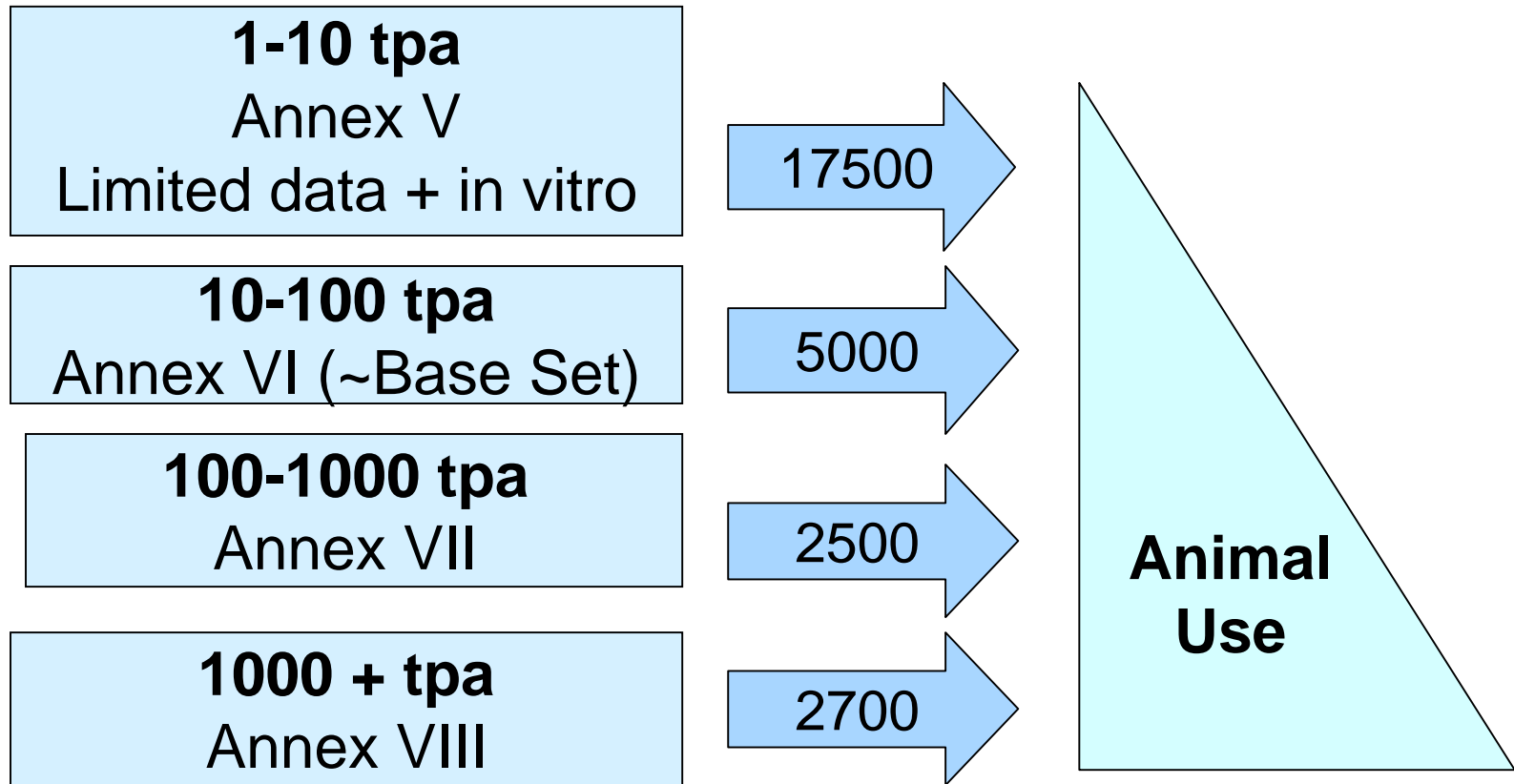
>1000 t/y (Annex VIII)

Those tests already mentioned for 100-1000t/y and if appropriate:

- ✓ **Further Mutagenicity Test**
- ✓ **Long-term Repeat Dose Study**
- ✓ **Carcinogenicity Study**
- ✓ **Long-term Reproductive Toxicity to Birds**

Overall Data Requirements

No. of chemicals

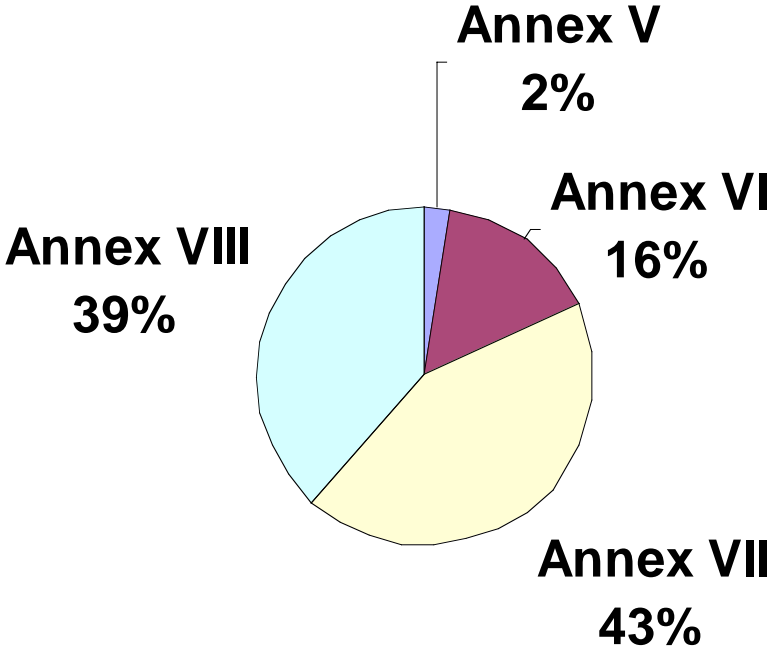


Key Input Assumptions

- Calculator is highly dependent upon input assumptions
- Data availability and testing need is taken from ECB JRC (Pedersen *et al.*, 2003)
- Data availability is based on US EPA and ICCA HPV, IUCLID, VCI Voluntary Initiative etc.
- Two default scenarios with Standard tests: “*Available Data*” (AD) & “*Reduced Data Need*” (RDN)
- “*Available Data*” assumes that data is required in all cases if it does not exist already (“tick-box”)
- “*Reduced Data Need*” assumes that testing is required for a subset of substances based on application of read-across, grouping, (Q)SAR, exposure-based waiving etc.

Comparison of Scenarios (Standard Tests Only)

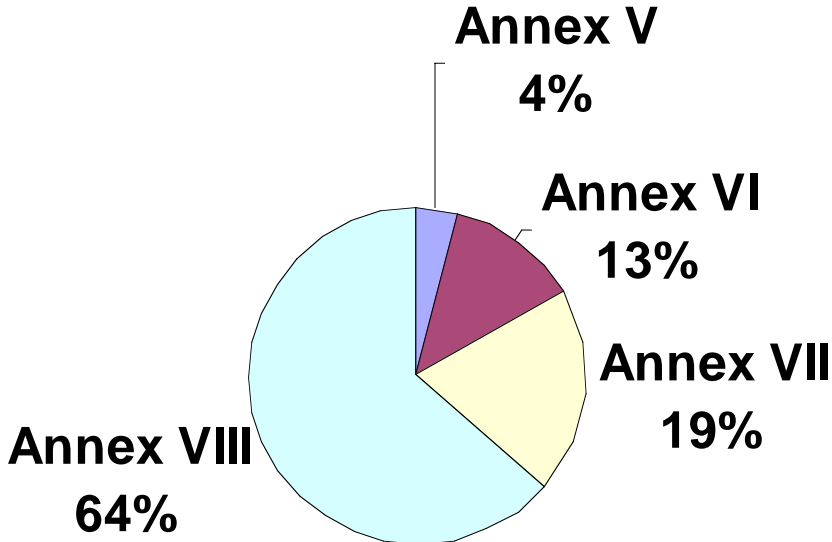
Available Data Scenario



16.21 Million Animals

7.00 Million Animals (- pups)

Reduced Data Need Scenario

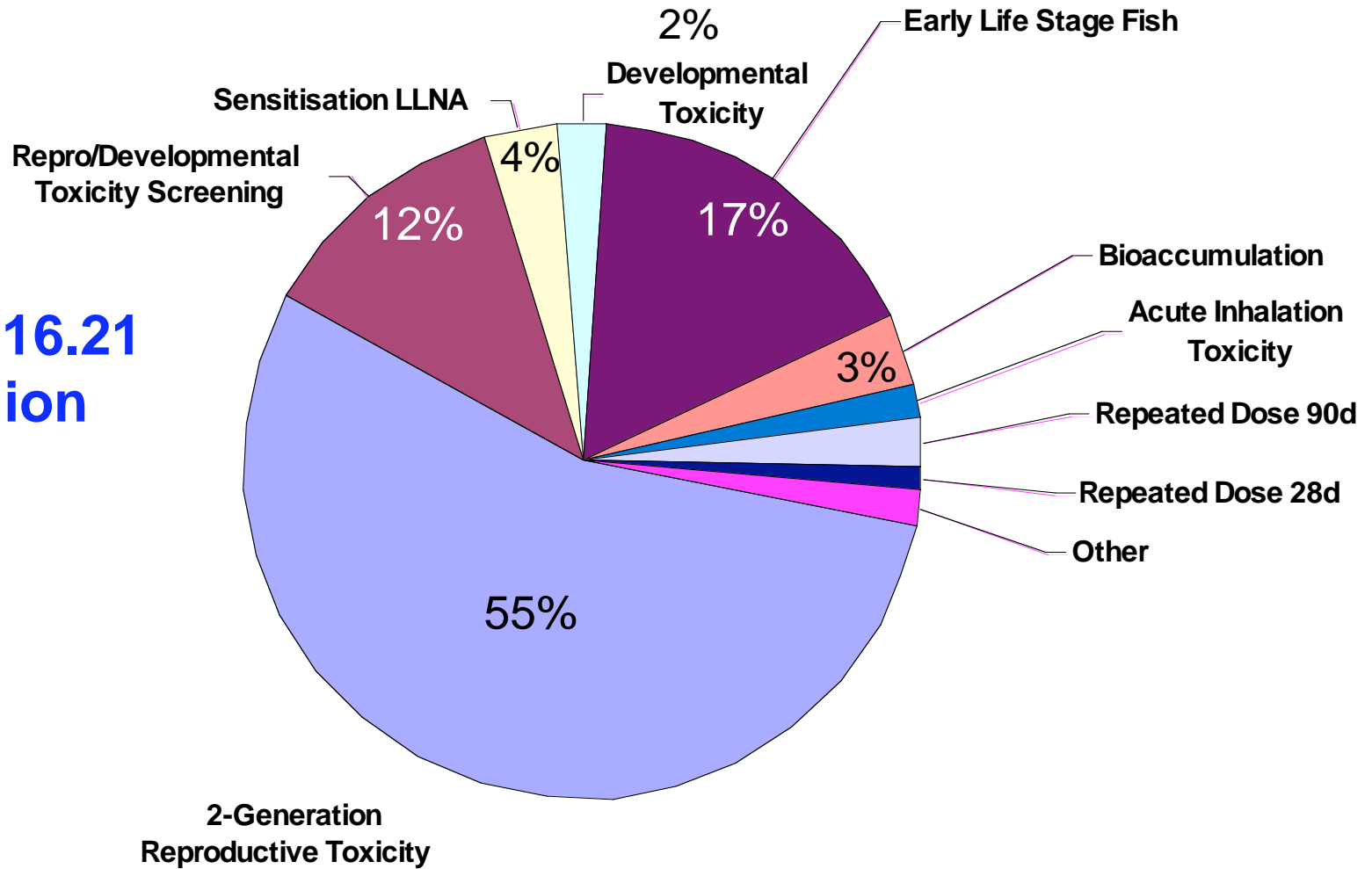


4.52 Million Animals

1.45 Million Animals (- pups)

Available Data Scenario

Total 16.21 million

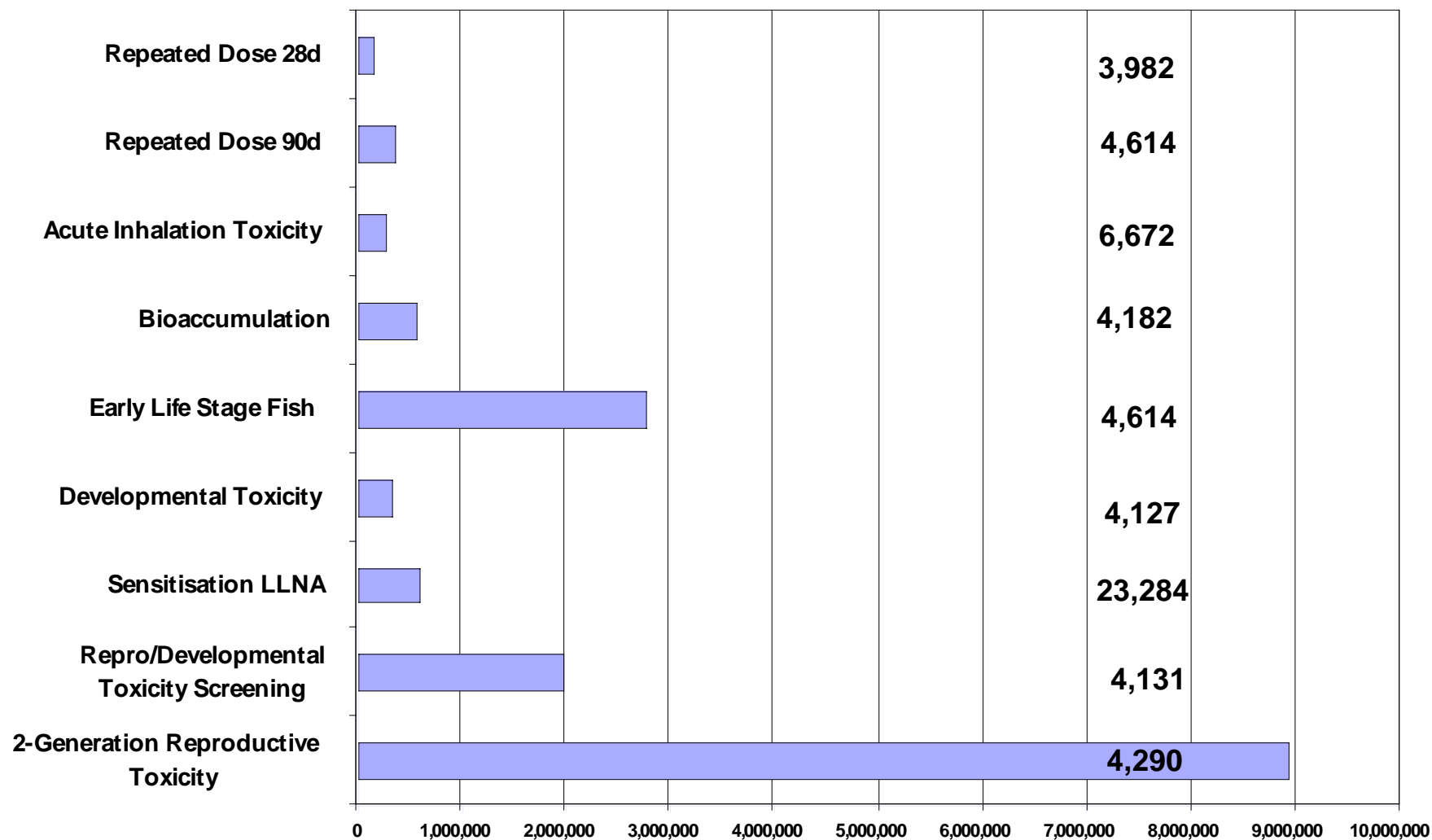


Available Data Scenario

Total 16.21 million

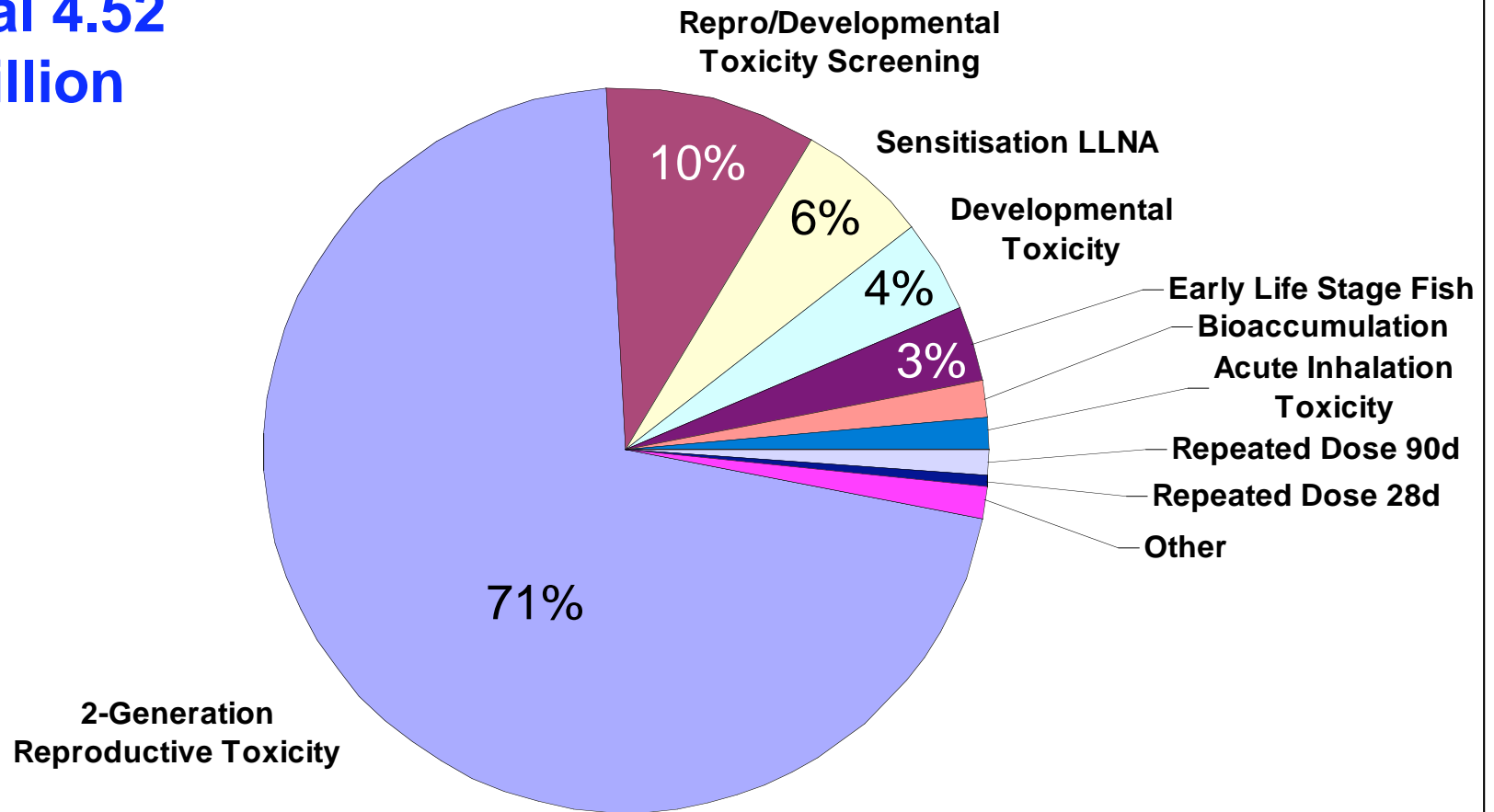
**Animal Use
Reduced Data Need Scenario**

Test #



Reduced Data Need Scenario

**Total 4.52
million**

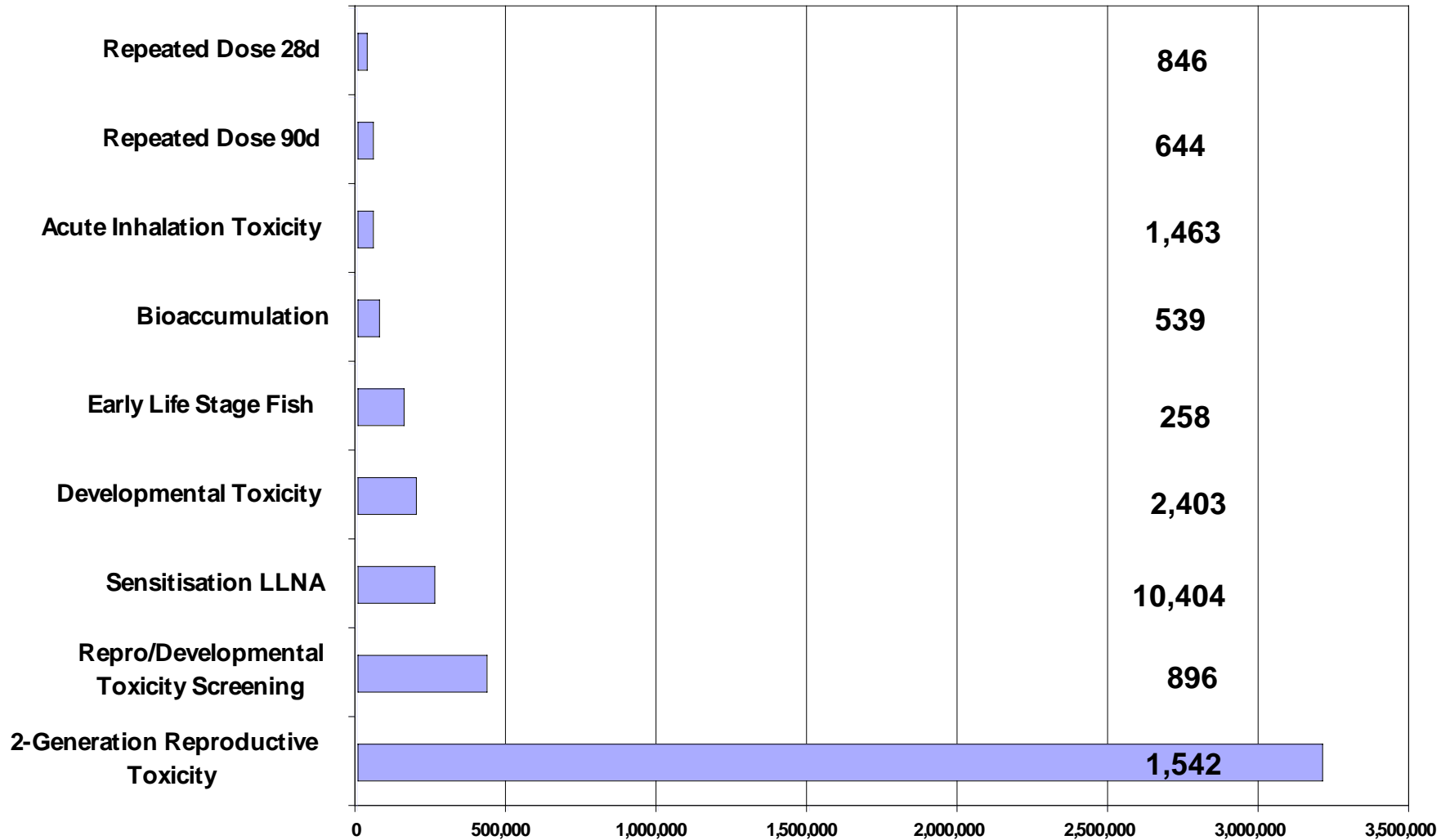


Reduced Data Need Scenario



Total 4.52 million

**Animal Use
Reduced Data Need Scenario**

Test #



2-Generation Reproductive Toxicity

- Data availability and test need from Pedersen *et al.* (2003)
- Largest number of animals for a single endpoint
- Calculator default includes pups so total animals per test are 2080 versus 320
- Regulatory “grey area”
- 3.2 million animals or 71% in “*Reduced Data Need*” Scenario (1,542 tests)

- 8.9 million or 55% in “*Available Data*” Scenario (4,290 tests)


2-Generation Reproductive Toxicity

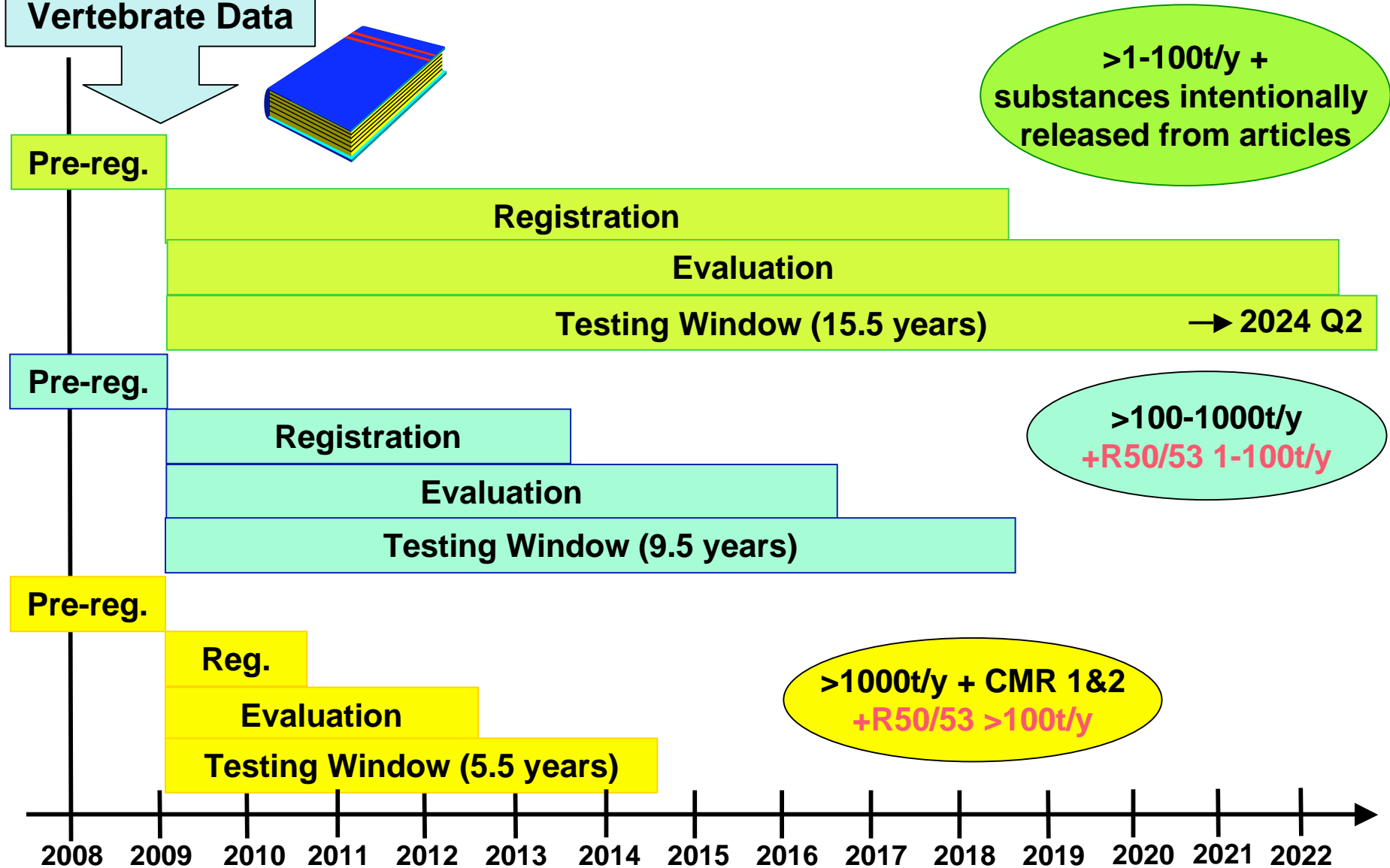
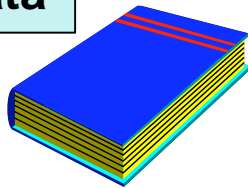
Annex V	Annex V	Annex VI (>10 Tonnes)
<ul style="list-style-type: none">• Availability• Test Need• Assumed trigger to test from Repeat Dose studies at approx. 15%	<ul style="list-style-type: none">• Availability• Test Need• Assumed trigger to test from Repeat Dose studies at approx. 15%• Possible underestimate as “Potential” – but not included in “Reduced Data Need”	<ul style="list-style-type: none">• Availability 3%• Test Need 12%• Assumed trigger to test from Repeat Dose studies at approx. 15%• Possible underestimate as “Potential” – but not included in “Reduced Data Need”• Additional 1.2 million?

Reproductive Toxicity

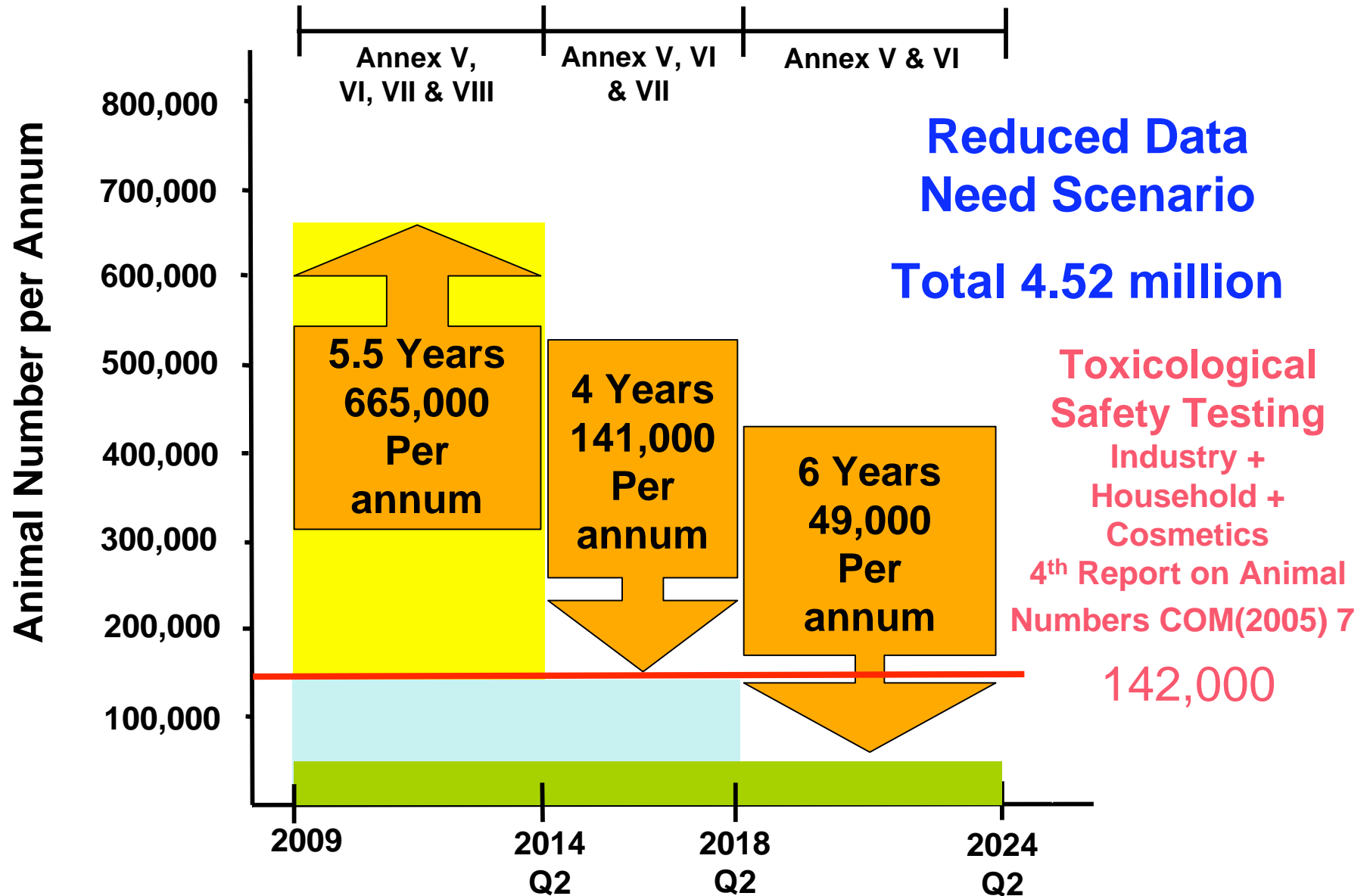
- Need to focus here (and other endpoints with high projected animal use) to refine predictions AND as priority for Intelligent Testing Strategies (ITS)
- ITS for Reproductive Toxicity proposed in RIP 3.3
- Tiered Approach in ILSI/HESI Agricultural Chemical Safety Assessment (ACSA)
- “ReProtect” aims to develop a suite of *in vitro* tests corresponding to the key components in the reproductive cycle (FP6 supported project)

Testing Window





Mandatory Sharing of Vertebrate Data



Animal Use Trend under REACH



Some Quick Observations

-  The numbers of laboratory animals required for REACH will dramatically increase animal use in the EU from 2010 until 2024 (especially <2014)
-  Actual animal use will be highly dependent upon the interpretation of test needs by regulators (c.f. SPORT)
-  “*Tick-box*” approaches will use many more animals
-  There is a need to focus on endpoints with high projected animal use as priority for Intelligent Testing Strategies

Summary of the Calculator



There is no “right answer” as the results are highly dependent upon input assumptions



The Calculator is an easily used tool that can be employed to quantify the impact of REACH in a transparent way



The Calculator can provide a rational basis to highlight areas that will most benefit from efforts to reduce overall animal use (c.f. fish acute toxicity <1% versus reproductive toxicity circa 55-71%)



The Calculator provides a clear rationale for ITS versus “box ticking” in terms of cost in animal lives



The Calculator can also be used within companies and test consortia to quantify animal use associated with Registration of their chemical portfolios