Alternatives to Animal Tests: Progress and Challenges

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Humane Society Legislative Fund

SCHC – September 30, 2014

Collaboration: International Animal Protection

International Council on Animal Protection at the Organisation for Economic Cooperation and Development Programmes

Kristie Sullivan, Secretariat of ICAPO

International Harmonisation

Worldwide Impact

OECD
BETTER POLICIES FOR BETTER LIVES


Animal Alliance
of Canada

ICAPO

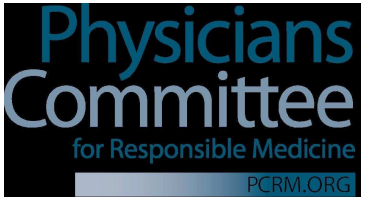

BUAV


ANIMAL WELFARE
ACADEMY


EUROGROUP
FOR ANIMALS


THE HUMANE SOCIETY
OF THE UNITED STATES


Advancing
Animal
Advocacy


Physicians
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for Responsible Medicine
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JAVA
JAPAN ANTI-VIVISECTION ASSOCIATION


PETA INTERNATIONAL
SCIENCE CONSORTIUM, LTD.

ICAPO ACTIVITIES

- Internal and external ICAPO nominees participate in OECD working group and *ad hoc* expert group mtgs
- Provides comments to draft test guidelines and other documents
- Draft chapters or sections of documents; partner with member countries on projects
- ICAPO and its member groups provide financial and in kind support to the development of new tools

ICAPO ACTIVITIES

- ICAPO has taken an active role in promoting the OECD AOP Programme
- Member group dues and individual organizations pay for meeting travel costs
- ICAPO considered "invited expert"—not an official member country
- Confidentiality rules
- OECD consensus organization

Potential for immediate and substantial animal savings

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Harmonised Templates
Focus
Mutual Acceptance of Data (MAD)
Adverse Outcome Pathways, Molecular Screening and Toxicogenomics
OECD assists internationally collaborative efforts on Molecular Screening and Toxicogenomics with the aim of defining needs and possibilities for their application in a regulatory context.
Read more
Find out more:
Test Guidelines Programme
Animal welfare
Endocrine Disrupters
Cutting Costs in Chemicals Management: How OECD Helps Governments and Industry, 2010

CHALLENGES

- Pace of scientific advancement
- Mutual Acceptance of Data—not so simple
- Post-TG implementation of methods in member countries

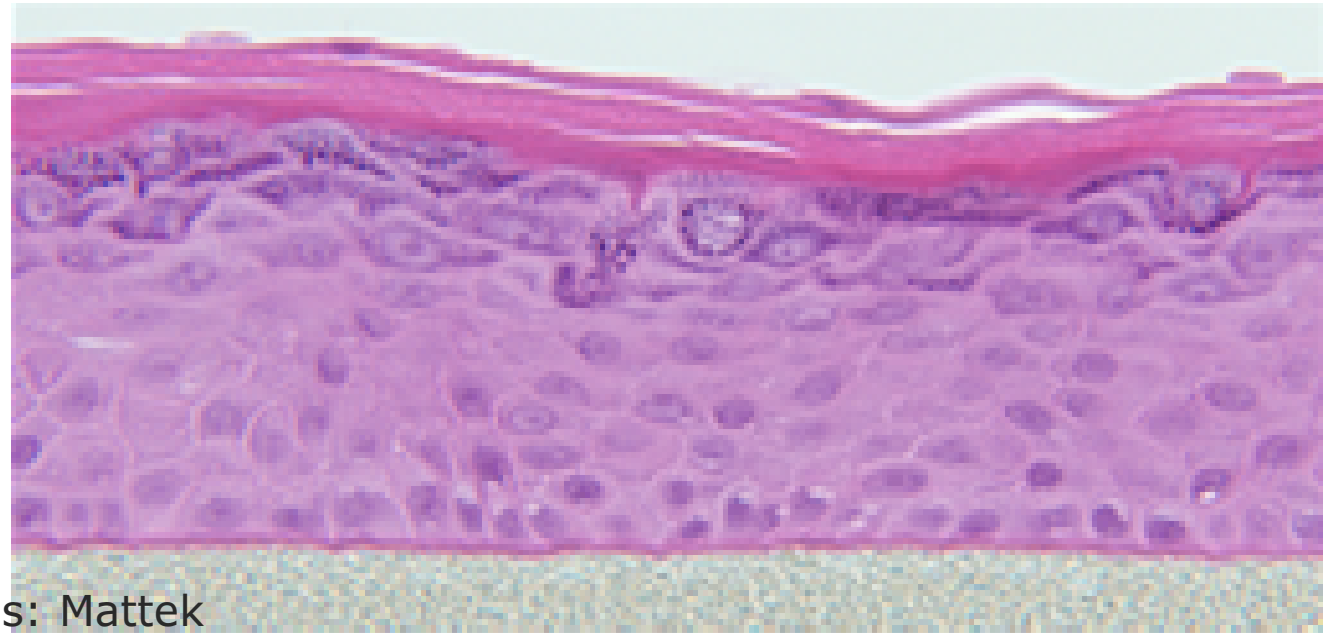
CHALLENGES

- Education of Regulators
- Certainty for Companies
- Continuing to take advantage of tradition of harmonization

Alternatives Advancement: U.S.

- Worked with industry to pass ICCVAM Authorization Act, P.L. 106-545

- Negotiated animal protection agenda in EPA's High Production Volume Chemical Program, including $4.75M in funding for alternatives research, development and validation



Pictures: Mattek

Collaborations in the United States

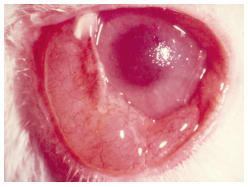
- Worked with industry to increase EPA's Computational Toxicology Program appropriations by 20% or $4M
- Worked with industry to prioritize research, development and relevance of 21st century toxicological methods for EPA and NIH appropriations
- Passed laws in CA, NJ, NY requiring the used of alternatives validated by the ICCVAM for all but pharma

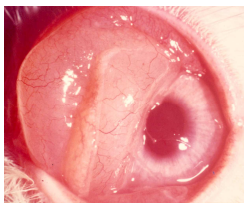
Implementing the 3Rs:

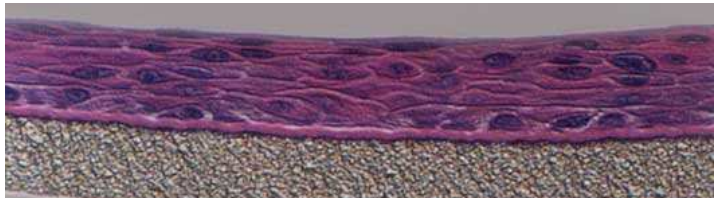
Prioritizing reduction, refinement and replacement of traditional animal tests for key endpoints/areas

Eye irritation/corrosion

Health concern	Animal test	3R best practice
Reversible eye damage (irritation) or irreversible tissue destruction (corrosion)	Chemical/product is applied to the eye of live rabbits; not washed for 24 hrs; animals observed at defined time points for 3 wks, then killed (OECD TG 405).	Validated *ex vivo* cow & chicken eye (OECD TGs 437/438) & fluorescein leakage (OECD TG 460) tests accepted for detection of severe irritants/corrosives (& non-irritants); *in vitro* human cornea tests for mild/moderate irritants in OECD acceptance process.

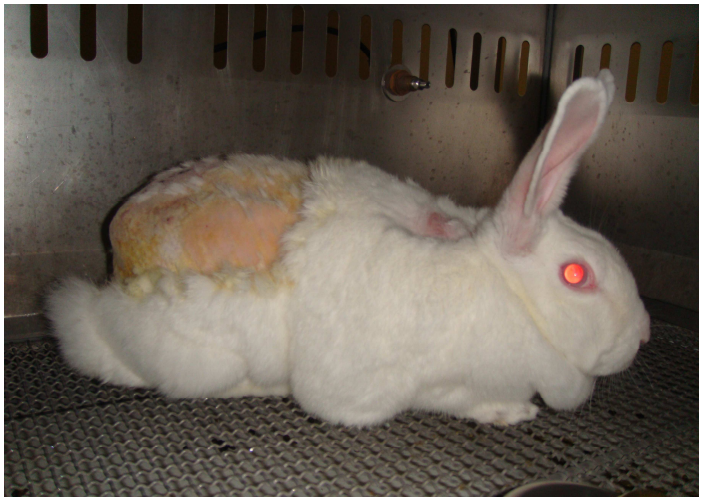


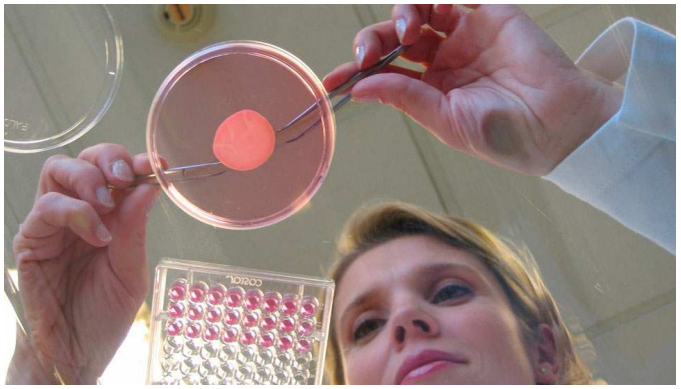


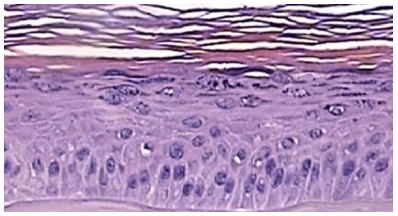


Skin irritation/corrosion

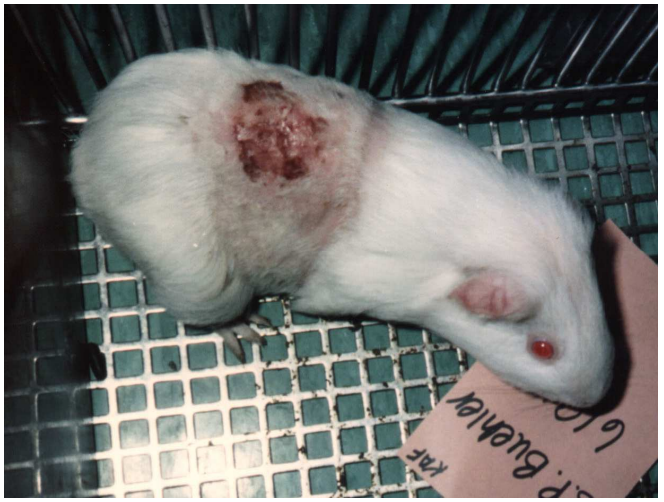
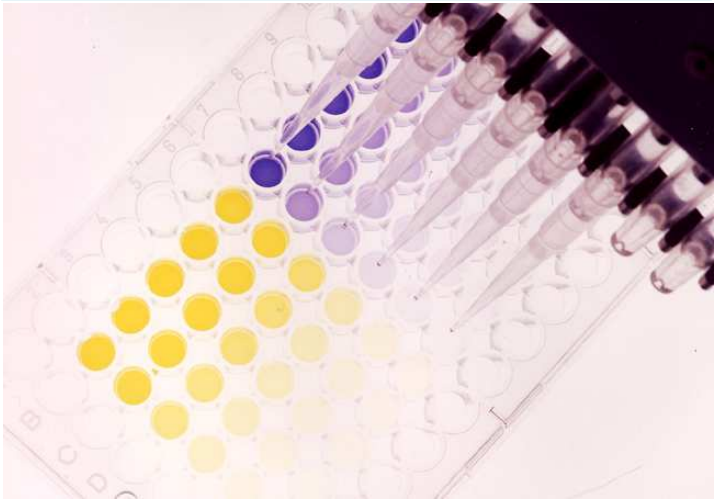
Health concern	Animal test	3R best practice
Reversible skin damage (irrit'n) or irreversible tissue destruction (corrosion)	Chemical/product is applied to the shaved backs of live rabbits for 4 hrs, then washed off; animals observed at defined time points for 2 wks, then killed (OECD TG 404).	Validated/accepted *in vitro* tests (OECD TG 431/corrosion & TG 439/irritation) are reconstructed human skin models that assess cell viability using colour-change MTT test. Full replacement in most cases if both tests run in sequence (back to back).







Skin sensitization

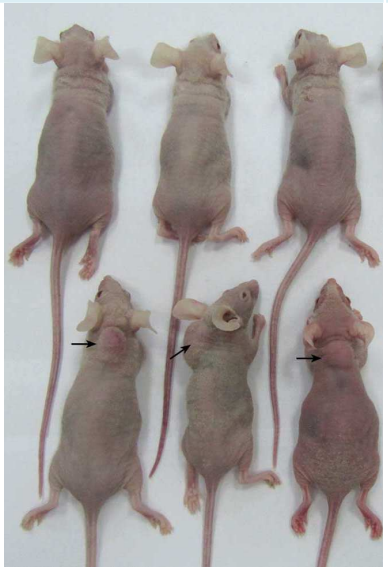
Health concern	Animal test	3R best practice
Skin allergy	Chemical/product applied to shaved skin of guinea pigs (OECD TG 406) or to ears of mice (OECD TGs 429, 442a/b); animals given an immune challenge & later killed to assess the immune response.	TG 429 limit test reduces animal use 50%; several *in vitro* tests undergoing validation/acceptance as sequential strategy measuring protein reactivity (DPRA), human cell line activation test (hCLAT) & skin cell (KeratinoSens) test.
		

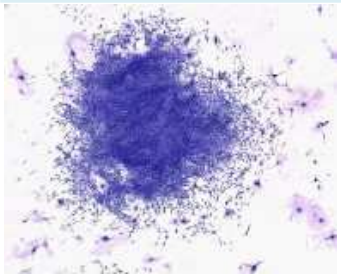
Genotoxicity

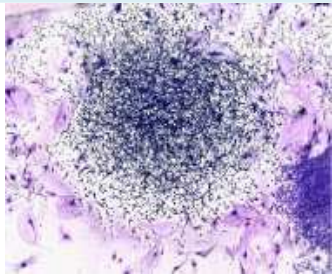
Health concern	Animal tests	3R best practice
Damage to genetic material leading to cancer or heritable genetic	In the micronucleus test (OECD TG 474) & chromosomal aberration test (OECD TG 475), a chemical is force-fed to animals, who are bled or killed at defined time points for bone marrow extraction. See also rodent dominant lethal (OECD TG 478), unscheduled DNA synthesis (OECD TG 486) & transgenic rodent cell gene mutation tests (OECD TG 488).	Accepted *in vitro* methods include the *Salmonella* bacterial reverse mutation test (OECD TG 471), chromosomal aberration test (OECD TG 473), cell gene mutation test (OECD TG 476), micronucleus test (OECD TG 487), typically as battery of 2-3 tests, with results assessed in a weight-of-evidence approach.

Carcinogenicity

Health concern	Animal tests	3R best practice
Cancer via genotoxic or non-genotoxic mechanisms	Animals fed chemically-laced food or water for 1.5-2 years & observed for signs of cancer, then killed & for extensive necropsy (OECD TGs 451, 453). Test often uses animals from 2 rodent species (400 rats + 400 mice).	Discontinuing use of mice as 2nd species reduces animal use 50%. A combination of *in vitro* genotox & cell transformation tests (e.g., Syrian hamster embryo, OECD GD 163) can predict 90-95% of human cancers.







Our challenge

Animal testing is <u>legally required</u> in most product sectors & countries

- Pre-market approval of a new drug or pesticide can involve dozens of separate animal tests
- New & revised laws requiring extensive testing of tens of thousands of 'existing' (& new) chemicals
- Cross-sector testing programs being created to address emerging health concerns (endocrine disruption, nanoparticles)
- 70% of the most severe pain & suffering in animal labs is related to toxicity testing
- Progress depends on development & international regulatory acceptance of non-animal approaches/3R best practices

Case study: pesticides

- Testing to meet regulatory data requirements can consume ~**10,000 animals** in **dozens** of separate toxicity studies for a **single** new pesticide active ingredient
- No global alignment of data requirements (vs. pharma/ICH model)
- In some cases, different regulations for agricultural ("plant protection") vs. non-agricultural ("biocidal/antimicrobial") products

Standard testing requirements for a pesticide chemical

1. Toxicokinetics	11. 28-day dermal [CR]	21. Chronic (1y) dog	31. Avian acute oral*
2. Acute oral*	12. 28-day inhal. [CR]	22. Carcino rat	32. Avian dietary
3. Acute dermal*	13. 90-day dermal [CR]	23. Carcino mouse	33. Avian repro
4. Acute inhalation*	14. 90-day inhal. [CR]	24. Repro 2-gen rat	34. Fish acute x2*
5. Skin irritation*	15. *Vitro* mutation x3	25. Prenat dev. rat	35. Fish chronic juv.
6. Eye irritation*	16. *Vivo* micronuc. [CR]	26. Prenat dev. rabbit	36. Fish early life stg.
7. Skin sensitisation*	17. Mouse spot [CR]	27. Neurotox hen[CR]	37. Fish lifecycle[CR]
8. 90-day oral rat	18. *Vivo* cytogen. [CR]	28. Dermal absorpt.	38. Fish bio[ ]
9. 90-day oral dog	19. *Vivo* germ cell [CR]	29. Addn'l studies[CR]	39. Mecososm[CR]
10. 28-day oral [CR]	20. Chronic (2y) rat	30. Livestock feed*	…

* Test required for **both** active ingredient **and** finished product CR = Conditional Requirement

Necessary redundancy?

AGRICULTURAL CHEMICAL
SAFETY ASSESSMENT
TECHNICAL COMMITTEE

Health and
Environmental
Sciences
Institute

"In most cases, when the database is complete using the large number of animals mandated by the test guidelines, **only one study is used to set the RfD** [reference dose] **for each risk assessment**. The question then arises: Would it have been possible to eliminate the studies which were not used for risk assessment and still protect human health?"

— Doe et al., Crit Rev Toxicol. 2006; 36: 37-68

Revision of EU pesticide data requirements*

1. Uptake of all applicable OECD 3R guideline methods, as well as other scientifically-supported alternative testing strategies
2. Move away from redundant *in vivo* testing
   - Multiple exposure routes (oral & skin & inhalation)
   - Multiple species (rodent & dog/rabbit)
3. Encourage 'thoughtful toxicology'
   - Examine 2 or more endpoints within a single test
   - Adopt more efficient & informative study designs
   - Waiving *in vivo* studies based on *in vitro* data

* Regulation (EU) No 528/2012 concerning the making available on the market and use of biocidal products

Commission Regulation (EU) No 283/2013 setting out the data requirements for active substances… concerning the placing of plant protection products on the market

Commission Regulation (EU) No 284/2013 setting out the data requirements for plant protection products

Summary

'3R BEST PRACTICE'

- >80 3R-oriented amendments proposed by Humane Society International (& fully supported by industry!) were adopted in revised EU pesticide data requirements
- **<u>Potential</u> for ±50% reduction in animal use** without compromising health or environmental protection

HOWEVER…

- Global trade requires improved regulatory alignment among major markets to achieve maximum animal reduction
- USA has taken small steps to align with EU & Canada has moved to align with USA

TIME TO EXPAND…

- To other countries & industry sectors (chemicals, pharma, etc.)

Credit: Troy Seidle, Humane Society International

U.S. Policy

Humane Cosmetics Act
H.R. 4148

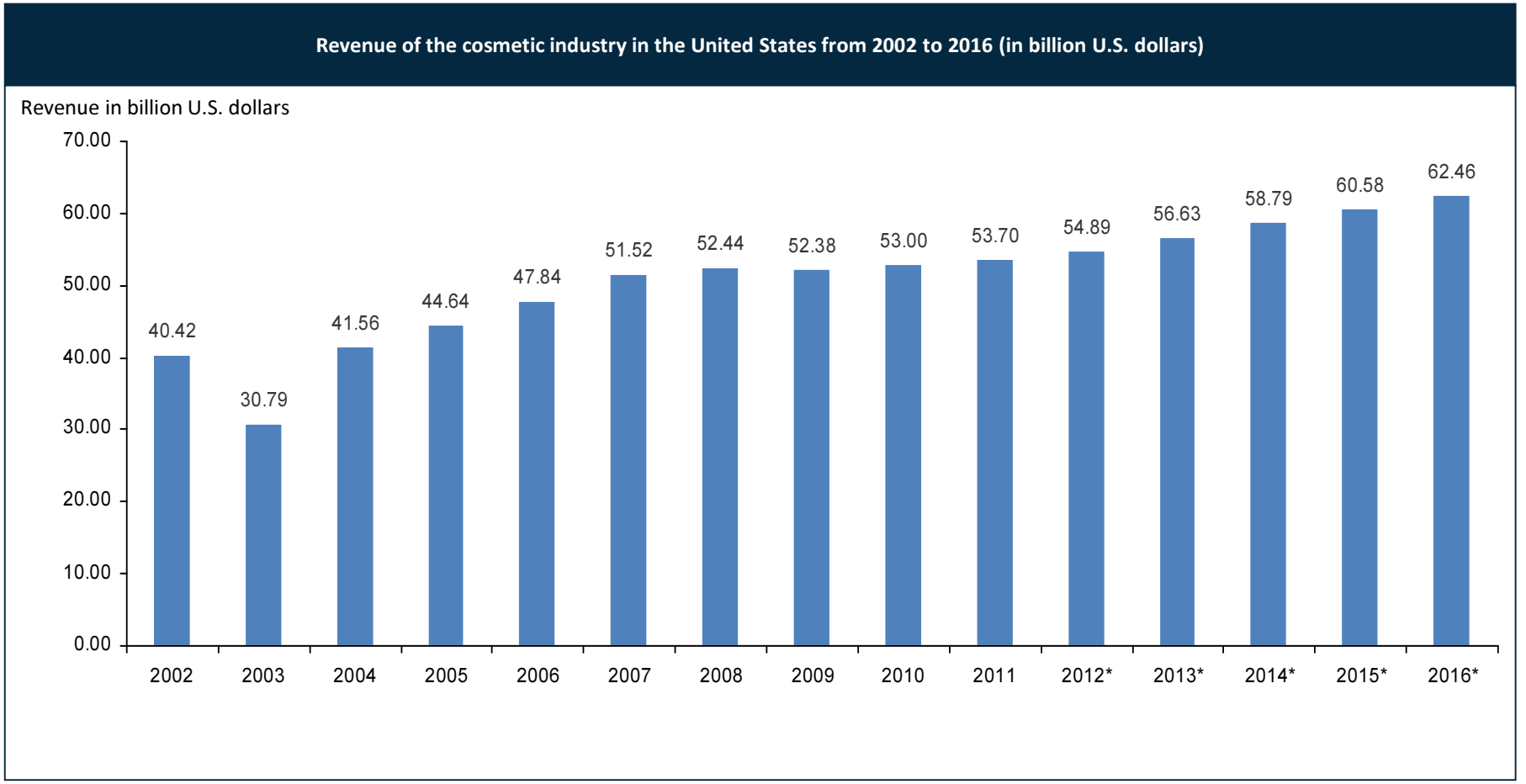
Climate for US Federal Legislation:

- *Decades of discussions with cosmetics industry and FDA for voluntary end to animal testing*
- *Administrative petition to mandate alternatives*
- *Industry negotiations with FDA*
- *Progress in other sectors of the world*

US Industry
The Market

Revenue of the cosmetic industry in the U.S. 2002-2016

United States



Note: further information regarding this statistic, such as comments and footnotes, can be found at the end of this Dossier on page 3

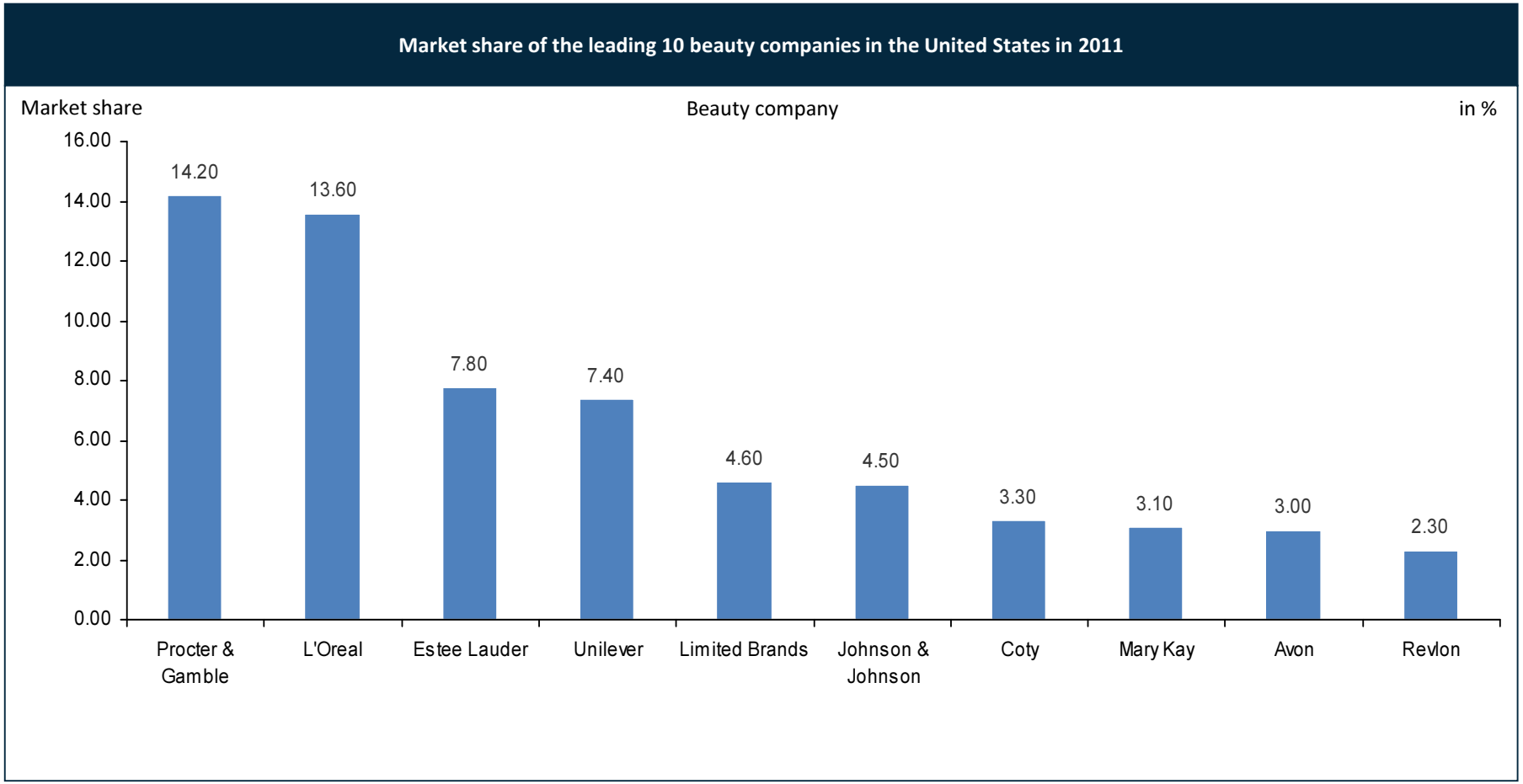
Source:

IBISWorld, Cosmetic & Beauty Products Manufacturing in the US 2011, page 31

ID 243742

Market share of the leading 10 beauty companies in the U.S. 2011

United States



Note: further information regarding this statistic, such as comments and footnotes, can be found at the end of this Dossier on page 3

Source:

L'Oreal, loreal-finance.com, page 15

ID 243953

Cosmetics

- ***What is a cosmetic?***
  - *A cosmetic is an article to be applied in any way to the human body with the intent of "cleansing, beautifying, promoting attractiveness, or altering the appearance", as well as any components used in such articles – excluding soap. 21 USC 321*

Who regulates this industry?

- *The Food and Drug Administration*
- *Cosmetic companies responsible for marketing safe products*
- *No premarket approval*
- *FDA does not require animal testing*

Humane Cosmetics Act
H.R. 4148

Sponsored by
Reps. Jim Moran (D-VA)
Michael Grimm (R-NY)

56 cosponsors

What does the bill do?

Testing: phases out animal testing one year after enactment

Sales: phases out sales of cosmetics tested on animals three years after enactment


LIZ CLAIBORNE
tarte™
PAUL MITCHELL
Bath & Body Works
smashbox
BARE ESCENTUALS
AVEDA
Murad
m
VICTORIA'S SECRET
BURT'S BEES
LUSH
wet n wild
PUREOLOGY
elf
eyes lips face
Crabtree & Evelyn
LONDON
MERLE NORMAN
ud
URBAN DECAY
Boots
stila
Too Faced
hourglass
THE BODY SHOP

American Public:

Support

- *73% of American voters would favor Congress enacting legislation that would phase out and eventually end new animal testing for cosmetic products and ingredients.*
- *55% of voters would favor this legislation strongly.*
- ***75% of voters say they would feel safer, or as safe, if non-animal methods** were used to test the safety of a cosmetic instead of animal testing.*

Thanks for inviting me to speak!