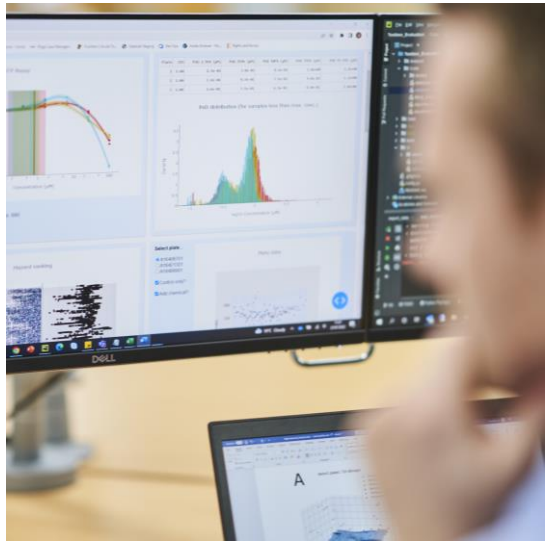
Assessing the safety of consumer products by integrating new approach methodologies (NAMs) within the next generation risk assessment (NGRA)

Dr Renato Ivan de Ávila
Scientist – Human Safety
Unilever Safety and Environmental Assurance Centre (SEAC)



CBMAlt 2023
I Congresso Brasileiro de Métodos Alternativos ao Uso de Animais

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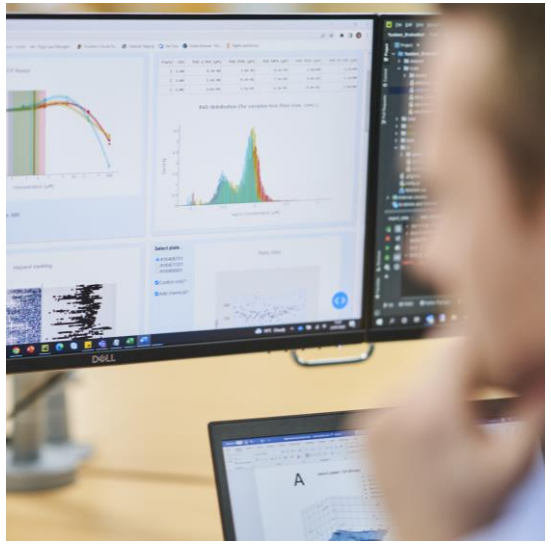
Agenda

1. Introduction to Unilever Safety and Environmental Assurance Centre (SEAC)
2. Assessing ingredient & product safety without animal testing
3. Next-Generation Risk Assessment (NGRA)
4. Bioactivity exposure ratio (BER) approach
5. NGRA: from principles to application
6. Unilever NGRA frameworks for decision-making on human safety
7. Concluding remarks

Unilever

Introduction to SEAC

Unilever's Global Centre of Excellence in Safety & Sustainability Sciences



Unilever

Unilever's Safety & Environmental Assurance Centre (SEAC)

SEAC is Unilever's global centre of excellence in Safety & Sustainability Sciences, part of R&D's Safety, Environment & Regulatory Sciences Capability.

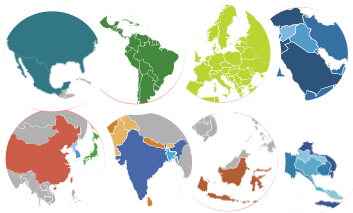
Diverse, multi-disciplinary team of ~150 scientists based at Colworth, UK; ~70 miles north of London

Highly collaborative, working with over 70 academic, industry, government & NGO partners worldwide

Business Group R&D

Global Teams

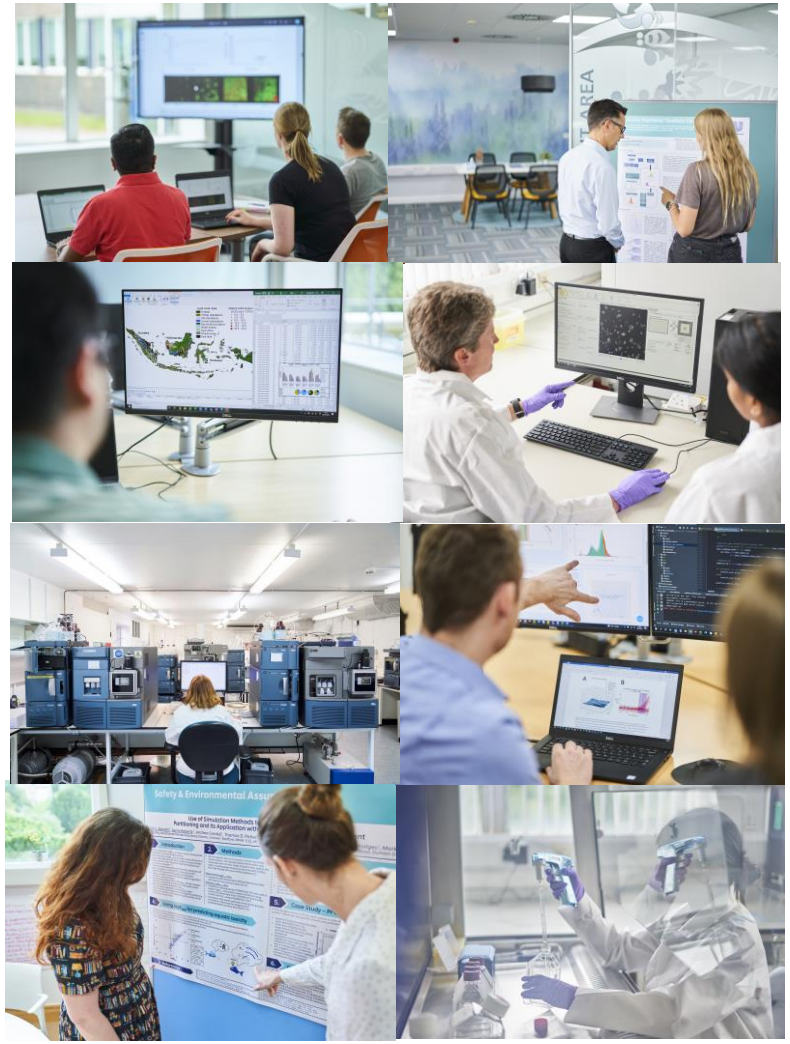
Business Units



'One R&D' Centre

- Safety, Environment & Regulatory
- Digital & Partnerships
- Sustainable Packaging

Team SEAC's purpose is to protect people & the environment



SEAC is a diverse, multi-disciplinary team of ~150 scientists covering:

- Cell Biology
- Chemistry
- Computational Modelling
- Environmental Safety
- Environmental Sustainability
- Exposure Science
- Informatics & Data Science
- Mathematics
- Microbiology
- Molecular Biology
- Process Safety
- Statistics
- Toxicology

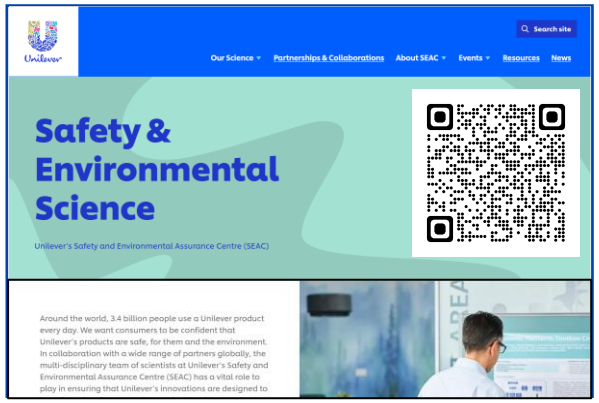
20+ Nationalities
15+ Languages

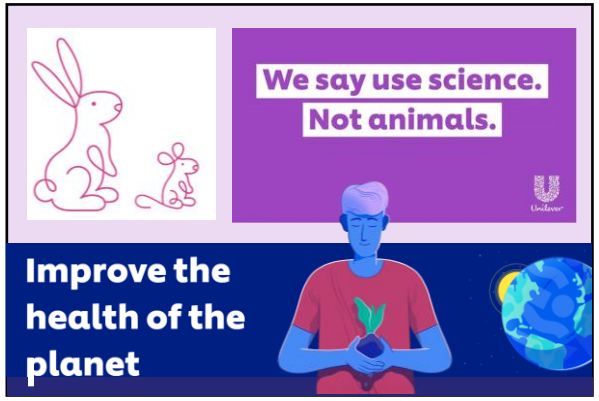
- Deploy expertise on higher risk business projects
- Collaborate with leading external research teams to develop & apply new capability
- Leverage science & global networks for consumer trust & freedom to operate

Safety Risk Assessments
- Consumers, Workers, Environment

Life Cycle Assessments
- Environmental Impacts

Unilever





Team SEAC's purpose is to **protect people & the environment** by ensuring:

1. Unilever's products & innovations are **Safe & Sustainable by Design without animal testing**
2. Our scientists & capabilities are **industry-leading with high business impact via Unilever's Products & Brands**
3. Safety & Env. Sustainability **policies & regulations are based on modern science**

Much of our strength lies in our shared Values – to be an **inclusive**, **supportive** & **collaborative** Team that is **pioneering**, **transparent** & **high-performing** with a strong focus on **learning** & **wellbeing**.

Unilever

Agenda

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Can we use a new ingredient safely?

Can we safely use x% of ingredient y in product z?

Risk = Hazard x Exposure

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2007 →

"Advances in toxicogenomics, bioinformatics, systems biology, and computational toxicology could transform toxicity **testing from a system based on whole-animal** testing **to one founded primarily on *in vitro* methods** that evaluate changes **in biologic processes using cells, cell lines, or cellular components, preferably of human origin**."

Unilever

2008 →

Brazil Moves Toward the Replacement of Animal Experimentation

Alternatives to Laboratory Animals 2019, Vol. 47(2) 71–81 © The Author(s) 2019 Article reuse guidelines: sagepub.com/journals-permissions DOI: 10.1177/0261192919856806 journals.sagepub.com/home/atl SAGE

Renato Ivan de Ávila and Marize Campos Valadares

Brazilian National Network of Alternative Methods (RENAMA) 10th Anniversary: Meeting of the Associated Laboratories, May 2022

de Ávila et al. Altern. Lab. Anim. (ATLA), article in press, 2023.

Brazil paves the way to end animal testing thro...

To find out more about the state of animal testing in Brazil, Cosmetics Design USA spoke with Dr. Gavin Maxwell, safe...

www.cosmeticsdesign.com

https://www.cosmeticsdesign.com/Article/2023/09/12/brazil-paves-the-way-to-end-animal-testing-throughout-latam

Presidência da República
Casa Civil
Subchefia para Assuntos Jurídicos

LEI Nº 11.794, DE 8 DE OUTUBRO DE 2008.

Regulamenta o inciso VII do § 1º do art. 225 da Constituição Federal, estabelecendo procedimentos para o uso científico de animais; revoga a Lei nº 6.638, de 8 de maio de 1979; e dá outras providências.

2008: Law no. 11,794/2008 (Lei Arouca) represents a regulatory milestone in the implementation of alternative methods

2012: creation of the RENAMA

Ministério da Ciência, Tecnologia e Inovação

GABINETE DO MINISTRO

PORTARIA Nº 491, DE 3 DE JULHO DE 2012

Institui a Rede Nacional de Métodos Alternativos - RENAMA e sua estrutura no âmbito do Ministério da Ciência, Tecnologia e Inovação - MCTI, que será supervisionada por um Conselho Diretor.

2012: ANVISA publishes the guide for cosmetics safety assessment

Agência Nacional de Vigilância Sanitária

Ministério da Ciência, Tecnologia e Inovação

CONSELHO NACIONALDE CONTROLE DE EXPERIMENTAÇÃO ANIMAL

RESOLUÇÃO NORMATIVA Nº 17, DE 3 DE JULHO DE 2014

Dispõe sobre
no Brasil e dá

2014: CONCEA recognized alternative methods

DIÁRIO OFICIAL DA UNIÃO

Publicado em: 17/01/2022 | Edição: 11 | Seção: 1 | Página: 18

Órgão: Ministério da Ciência, Tecnologia e Inovações/Conselho Nacional de Controle de Experimentação Animal

RESOLUÇÃO NORMATIVA CONCEA Nº 54, DE 10 DE JANEIRO DE 2022

Dispõe sobre o reconhecimento de métodos alternativos ao uso de animais em atividades de ensino e pesquisa científica e dá outras providências.

2015: ANVISA starts to accept the methods recognized by CONCEA

Agência Nacional de Vigilância Sanitária

RESOLUÇÃO - RDC Nº 35, DE 7 DE AGOSTO DE 2015

Dispõe sobre a aceitação dos métodos alternativos de experimentação animal reconhecidos pelo Conselho Nacional de Controle de Experimentação Animal - Concea.

A Diretoria Colegiada da Agência Nacional de Vigilância Sanitária, no uso das atribuições que lhe conferem os incisos III e IV, do art. 15, da Lei nº 9.782, de 26 de janeiro de 1999, inciso V e §§

CONCEA recognizes some innovative methods

+40 testing guidelines:
- 30 1R (replacement) guidelines
- 11 2R (refinement & reduction) guidelines

Ministério da Ciência, Tecnologia e Inovação

GABINETE DO MINISTRO

RESOLUÇÃO NORMATIVA Nº 18, DE 24 DE SETEMBRO DE 2014

nhece métodos alternativos ao uso de animais em atividades de pesquisa no B
lução Normativa nº 17, de 03 de julho de 2014, e dá outras providências.

Ministério da Ciência, Tecnologia, Inovações e Comunicações

CONSELHO NACIONAL DE CONTROLE DE EXPERIMENTAÇÃO ANIMAL

RESOLUÇÃO NORMATIVA Nº 31, DE 18 DE AGOSTO DE 2016

Reconhece métodos alternativos ao uso de animais em atividades de pesquisa no B

DIÁRIO OFICIAL DA UNIÃO - Seção

CONSELHO NACIONAL DE CONTROLE DE EXPERIMENTAÇÃO ANIMAL

RESOLUÇÃO Nº 45, DE 22 DE OUTUBRO DE 2019

Reconhece método alternativo ao
em atividades de pesquisa no Bras

DIÁRIO OFICIAL DA UNIÃO

Publicado em: 07/10/2022 | Edição: 192 | Seção: 1 | Página: 15

Órgão: Ministério da Ciência, Tecnologia e Inovações/Conselho Nacional de Controle de Experimentação Animal

RESOLUÇÃO Nº 56, DE 5 DE OUTUBRO DE 2022

Reconhece métodos alternativos ao uso de animais em atividades de pesquisa no Brasil.

DIÁRIO OFICIAL DA UNIÃO

Publicado em: 01/03/2023 | Edição: 41 | Seção: 1 | Página: 8

Órgão: Ministério da Ciência, Tecnologia e Inovação/Conselho Nacional de Controle de Experimentação Animal

RESOLUÇÃO Nº 58, DE 24 DE FEVEREIRO DE 2023

Dispõe sobre a proibição do uso de animais vertebrados, exceto seres humanos, em pesquisa científica, desenvolvimento e controle de produtos de higiene pessoal, cosméticos e perfumes que utilizem em suas formulações ingredientes ou compostos com segurança e eficácia já comprovadas cientificamente e dá outras providências.

https://www.gov.br/mcti/pt-br/composicao/conselhos/concea/paginas/publicacoes-legislacao-e-guia/metodos-alternativos-reconhecidos-pelo-concea

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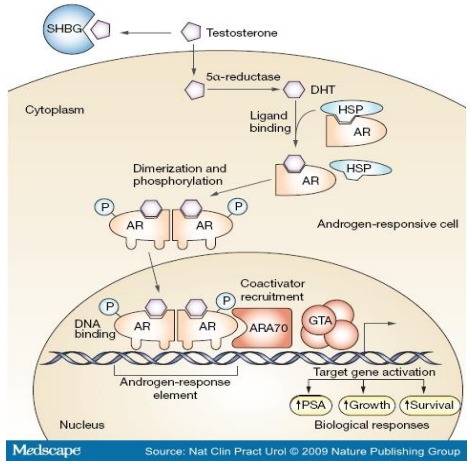
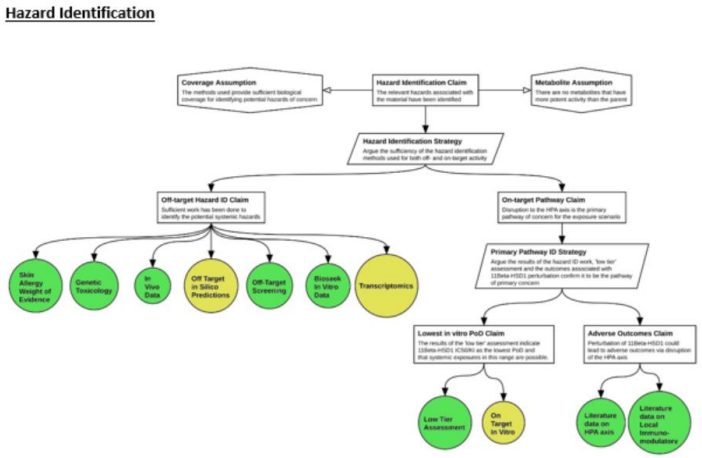
What is Next-Generation Risk Assessment (NGRA)?

- Using different data inputs from , e.g. new approach methodologies (NAMs), which characterise the chemical-biological interactions & effects at the molecular & cellular level
- An exposure-led risk assessment solution to biological pathway-indicated hazard concerns

Exposure led



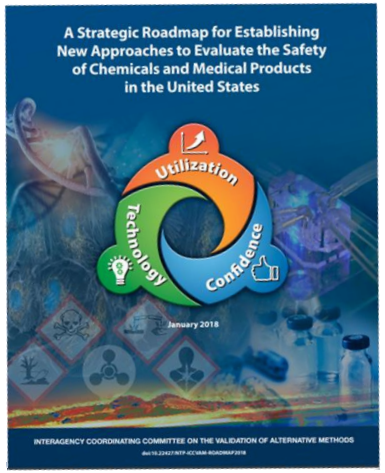
Mechanistic



Hypothesis driven

Maximising use of existing information

- All available safety data (of suitable quality)
  - public domain, historical *in house* data, supplier data etc
  - chemistry data, *in vitro* data, clinical data, epidemiological data, animal toxicology data etc
- Exposure-based waiving approaches
- History of safe use (HoSU)
- Read-across
- Use of existing *in vitro* data and approaches



"More recently, the term **"new approach methodologies" (NAMs)** has been adopted as a broadly descriptive reference to any **non-animal technology, methodology, approach, or combination** thereof that can be used to provide information on chemical hazard and risk assessment."

Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM), 2018

Available at: https://ntp.niehs.nih.gov/go/iccvam-rdmp

UNITED STATES ICCVAM Advancing Alternatives to Animal Testing

Unilever

Principles of Next Generation Risk assessment (NGRA)

*NGRA is defined as **an exposure-led**, **hypothesis-driven** risk assessment approach that **integrates New Approach Methodologies (NAMs)** to assure **safety without the use of animal testing***

Dent et al. Principles underpinning the use of new methodologies in the risk assessment of cosmetic ingredients. Computational Toxicology, v. 7, p. 20-26, 2018.

ICCR
International Cooperation on Cosmetics Regulation

9 principles of NGRA

https://www.iccr-cosmetics.org/

Main overriding principles:

1. The overall goal is a human safety risk assessment
2. The assessment is exposure led
3. The assessment is hypothesis driven
4. The assessment is designed to prevent harm

Principles describe how a NGRA should be conducted:

5. Following an appropriate appraisal of existing information
6. Using a tiered and iterative approach
7. Using robust and relevant methods and strategies

Principles for documenting NGRA:

8. Sources of uncertainty should be characterized and documented
9. The logic of the approach should be transparently and documented

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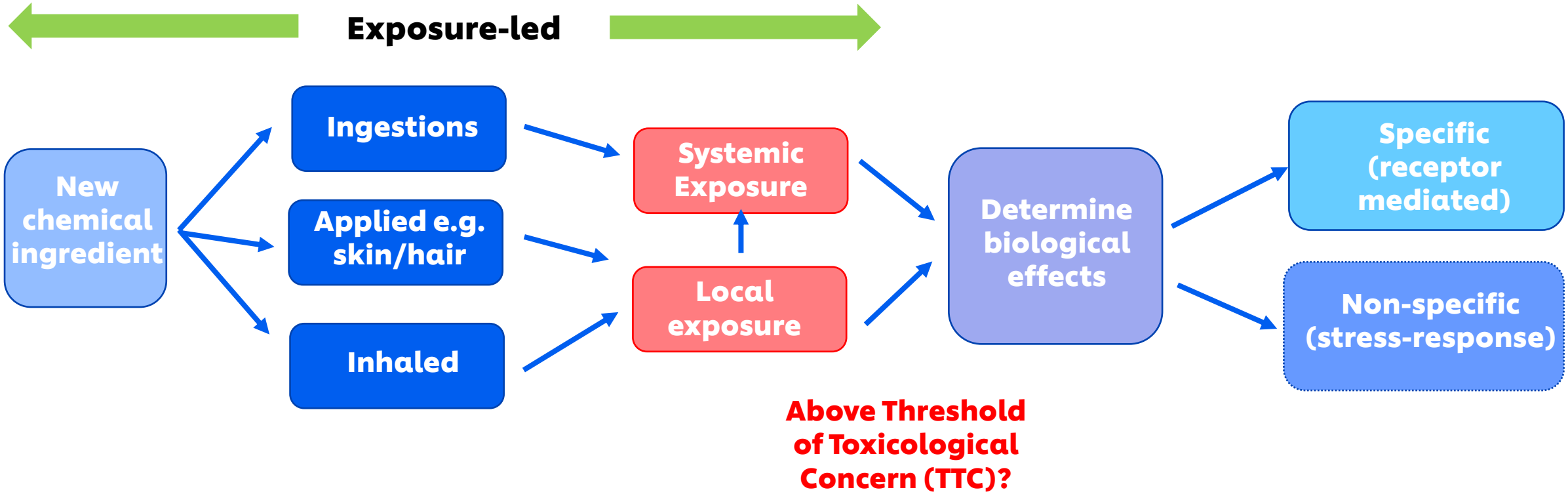
NGRA is an Exposure-led approach



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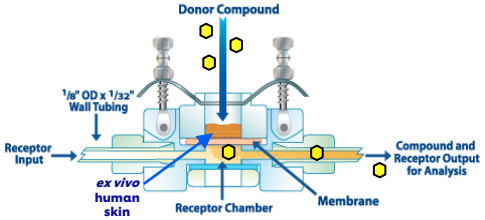
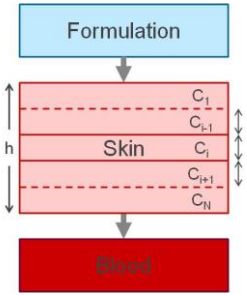
NGRA: The assessment is exposure-led

- Route of exposure
- Consumer use (Habits & Practices)
- Applied dose (external concentration)

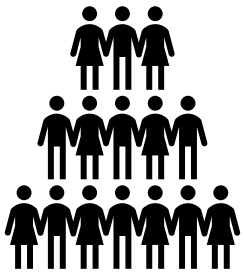
ADME parameters



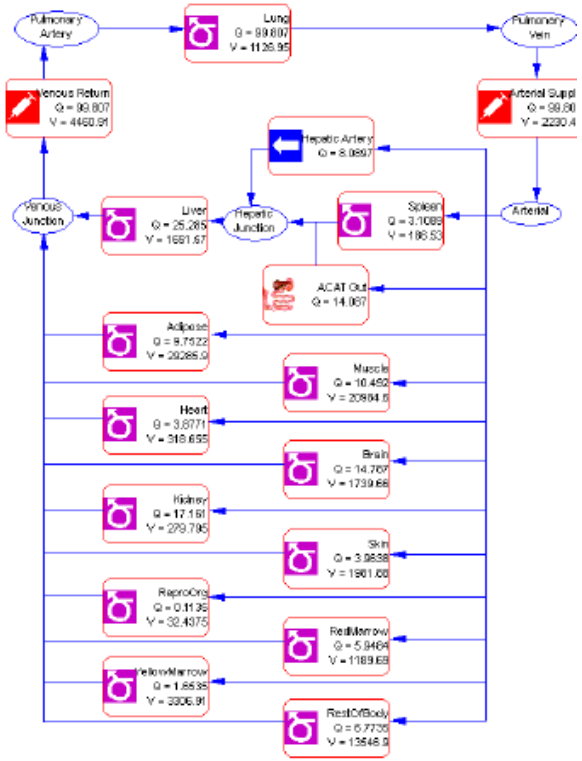


- Skin penetration
- Phys-chem properties
- Hepatic clearance
- Fraction unbound
- blood:plasma ratio

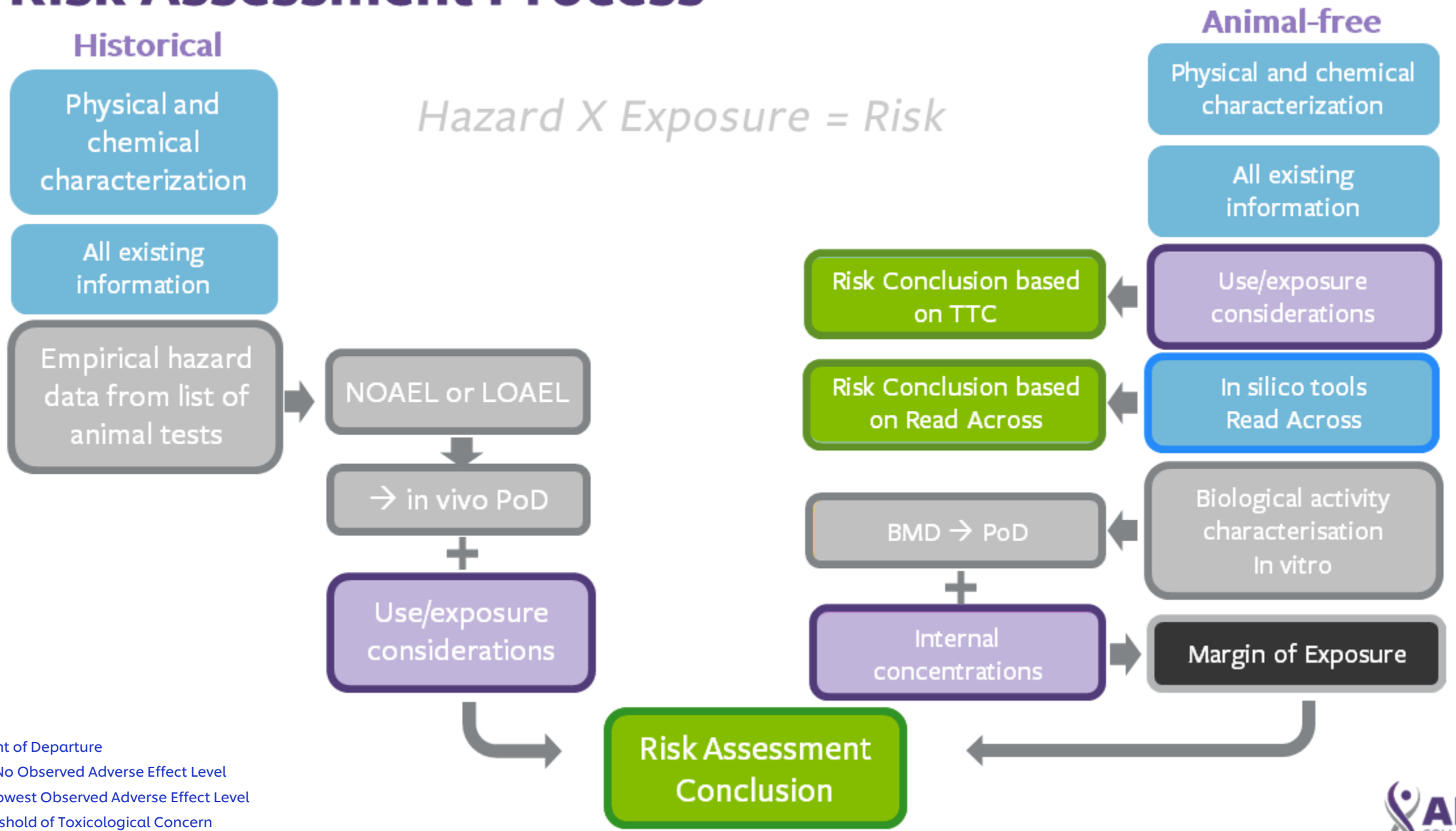
Uncertainty analysis- Population simulation



Physiologically-based kinetic (PBK) modelling – Internal concentration (plasma, urine, organ-level)



Risk Assessment Process

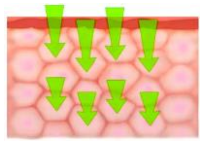


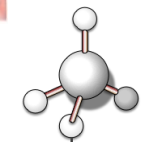
PoD – Point of Departure
NOAEL – No Observed Adverse Effect Level
LOAEL - Lowest Observed Adverse Effect Level
TTC - Threshold of Toxicological Concern
BMD – benchmark dose

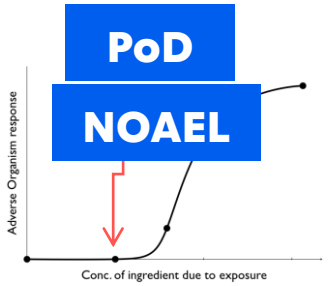
https://afsa.talentlms.com/index

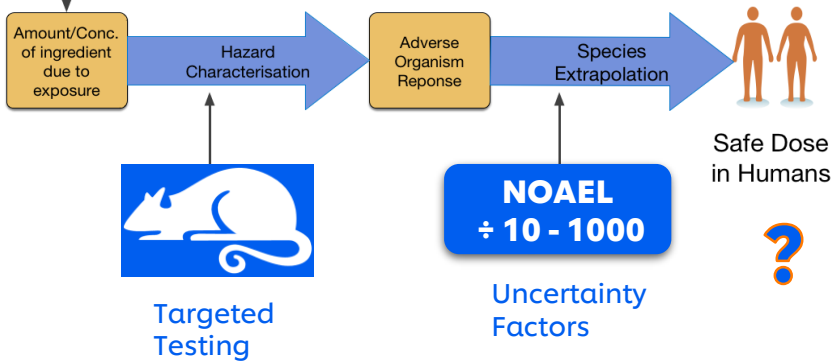
NGRA: the bioactivity exposure ratio (BER) approach and decision making

Is it safe?

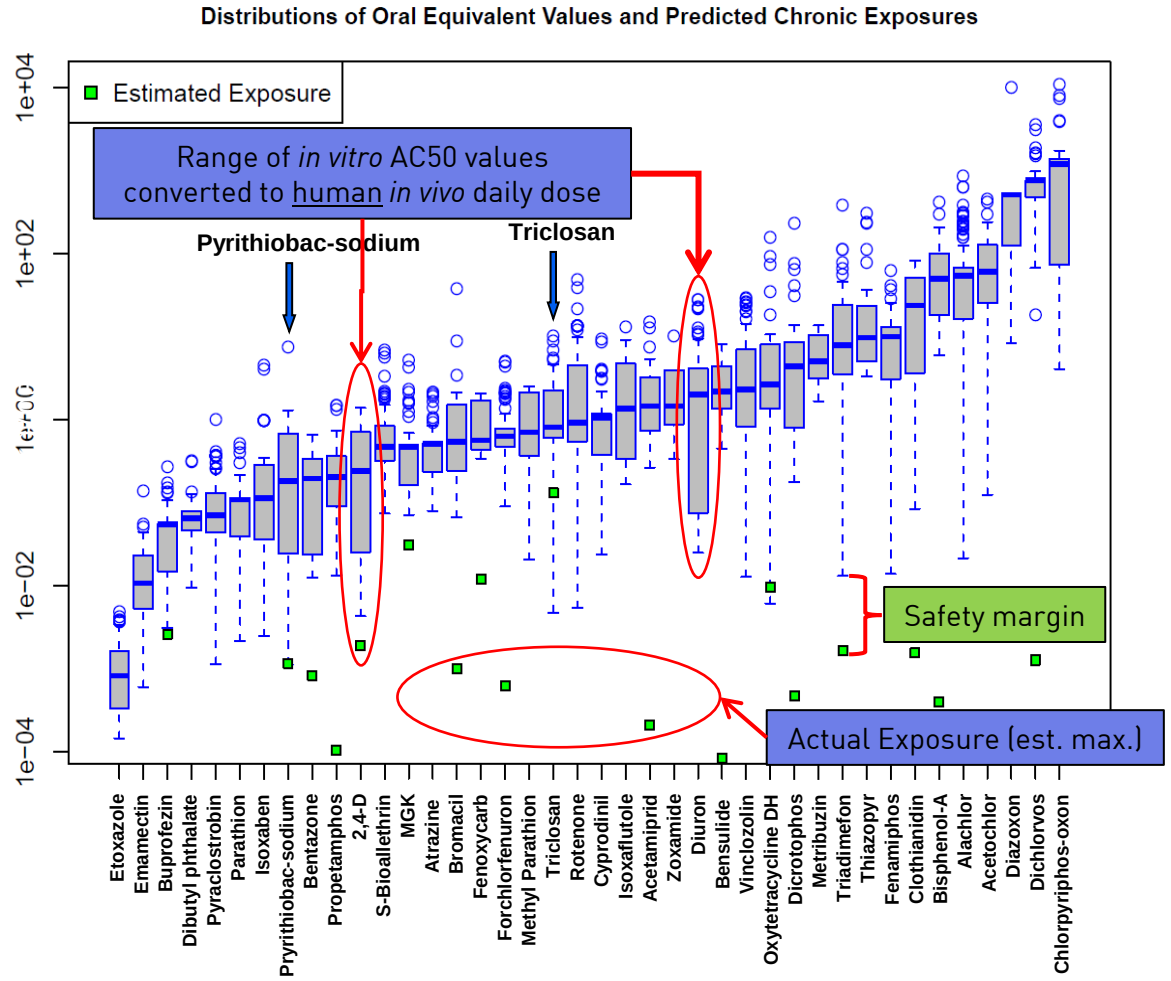








e.g. 90 Day Repeat Dose Study



PoD – Point of Departure

NOAEL – No Observed Adverse Effect Level

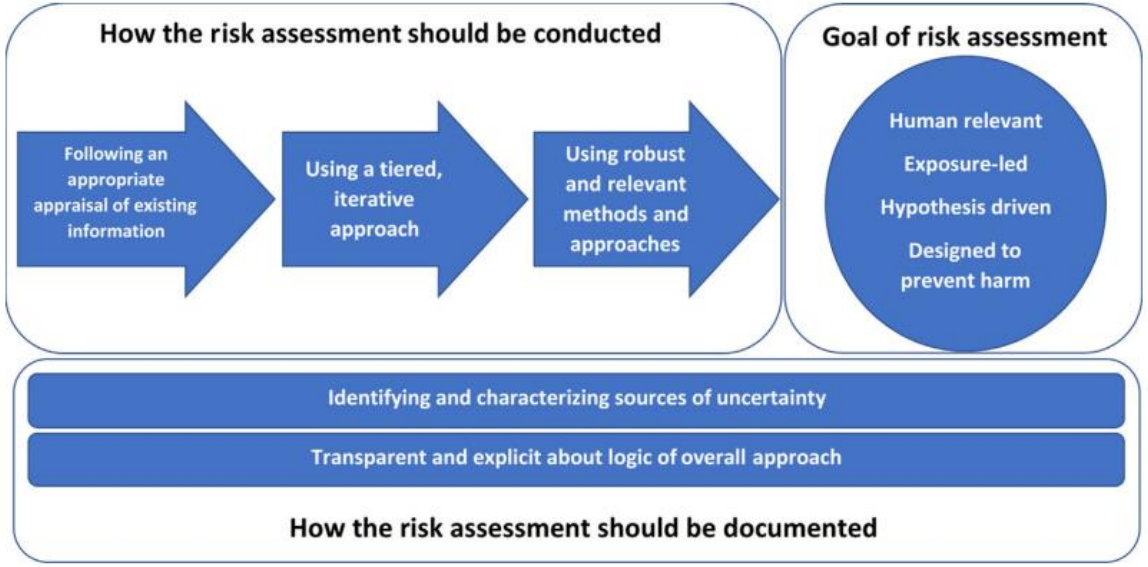
Graph from Rusty Thomas EPA, with thanks. Rotroff et al. Toxicological Sciences , 117, 348-358, 2010.

Vision of NGRA

Protection-not-prediction Concept

If there is no bioactivity observed at consumer-relevant concentrations, there can be no adverse health effects.

If there is bioactivity observed at consumer-relevant concentrations, we need to work out if that could result in an adverse effect.



Dent et al. Principles underpinning the use of new methodologies in the risk assessment of cosmetic ingredients. Computational Toxicology, v. 7, p. 20-26, 2018.

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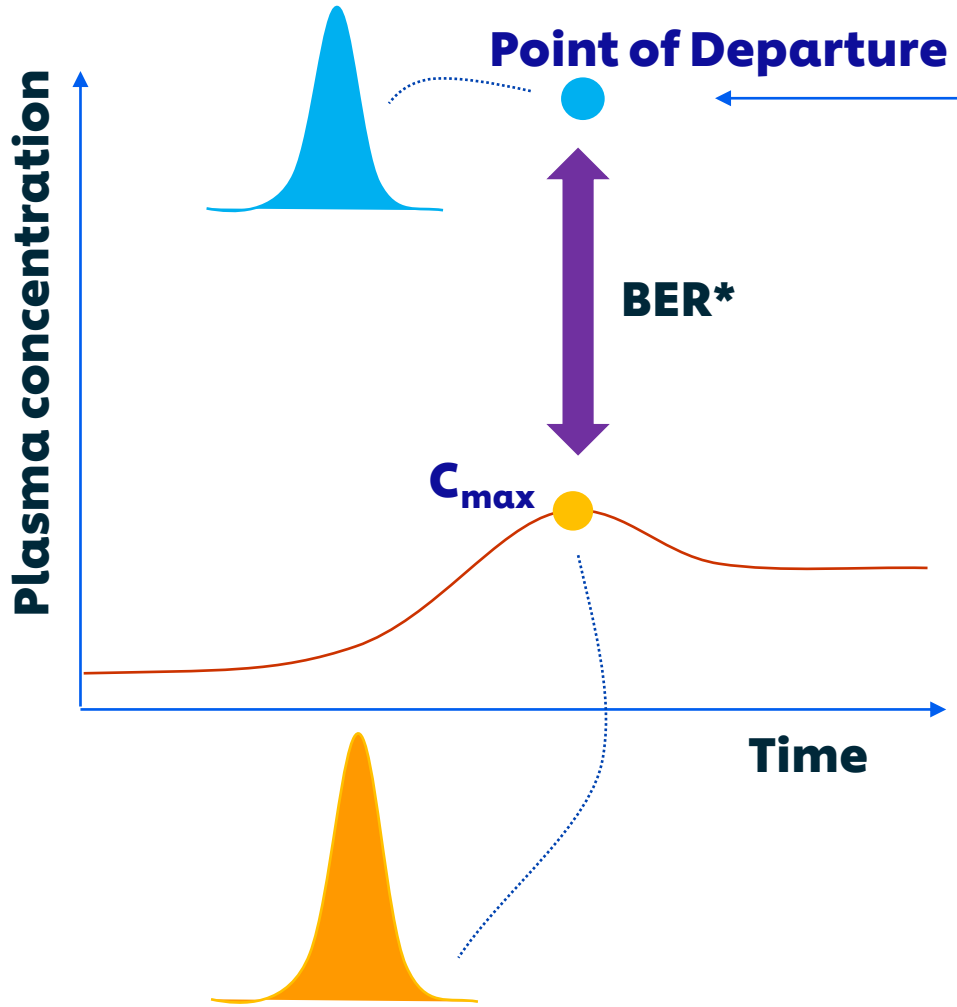
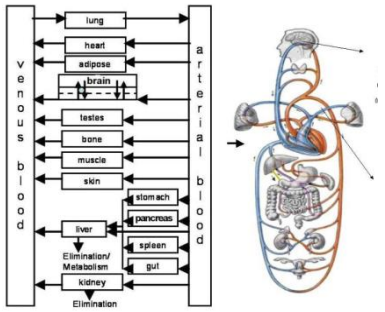
Bioactivity Exposure Ratio (BER)

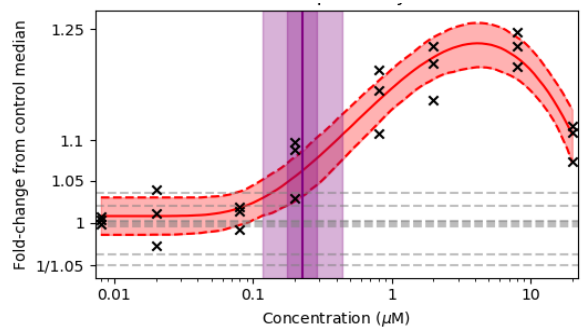
- The ratio of the PoD and the relevant exposure estimate



Exposure models (PBK, free/total concentration)



PoD derived from *in vitro* concentration-response



*Related terms: margin of safety (MoS); margin of exposure (MoE)

Bioactivity Exposure Ratio (BER) approach:

interpreting *in vitro* NAMs data for assessing chemical safety

https://www.epa.gov/chemical-research/accelerating-pace-chemical-risk-assessment-apcra

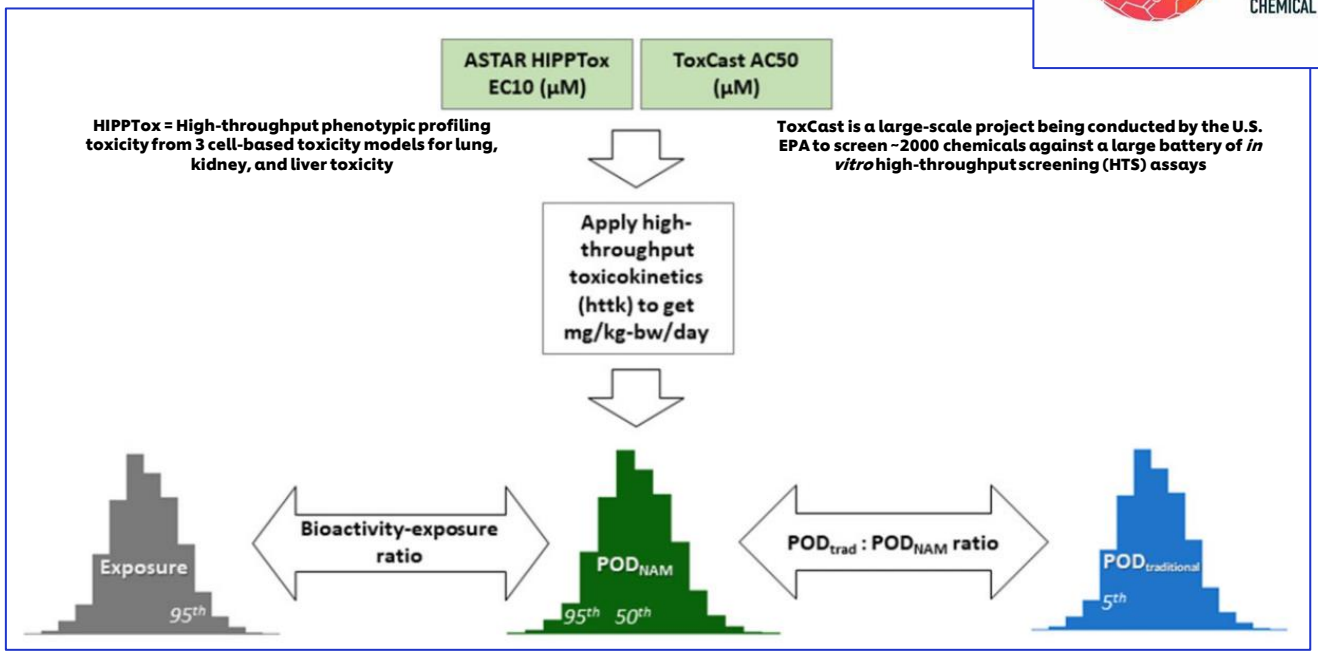
APCRA
ACCELERATING THE PACE OF CHEMICAL RISK ASSESSMENT

OXFORD SOT Society of Toxicology academic.oup.com/toxsci Tox Spotlight article

TOXICOLOGICAL SCIENCES, 173(1), 2020, 202–225
doi: 10.1093/toxsci/kfz201
Advance Access Publication Date: September 18, 2019
Research Article

Utility of *In Vitro* Bioactivity as a Lower Bound Estimate of *In Vivo* Adverse Effect Levels and in Risk-Based Prioritization

Katie Paul Friedman ,*,1 Matthew Gagne,† Lit-Hsin Loo,‡ Panagiotis Karamertzanis,§ Tatiana Netzeva,§ Tomasz Sobanski,§ Jill A. Franzosa,¶ Ann M. Richard,* Ryan R. Lougee,*,|| Andrea Gissi,§ Jia-Ying Joey Lee,‡ Michelle Angrish,|| Jean Lou Dorne,|| Stiven Foster,# Kathleen Raffaele,# Tina Bahadori,|| Maureen R. Gwinn,* Jason Lambert,* Maurice Whelan,** Mike Rasenberg,§ Tara Barton-Maclaren,† and Russell S. Thomas *



- ✓ Evaluation of *in vitro* new approach methodologies (NAMs), exposure modelling and dose-response models
- ✓ For 89% chemicals (n=448), PoD_{NAM} was more conservative than $PoD_{traditional}$
- ✓ BER approach is useful to accelerate screening and chemicals assessment using NAMs for hazard and exposure

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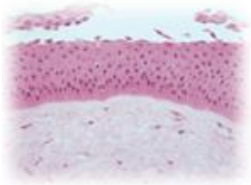
NGRA: Using relevant methods to test hypotheses

Established Methods

OECD test methods

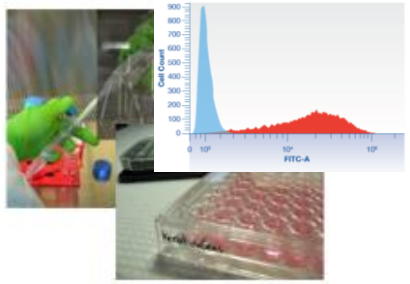


OECD TG437

OECD TG430/431
OECD TG439

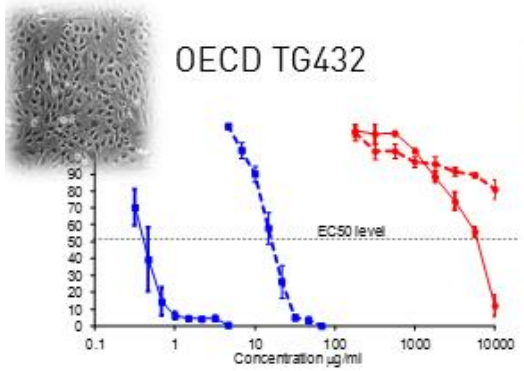
Skin and eye irritation

OECD TG442C OECD TG442E



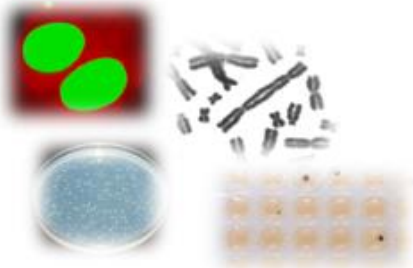
OECD TG442D

Skin sensitisation



Phototoxicity

OECD TG473



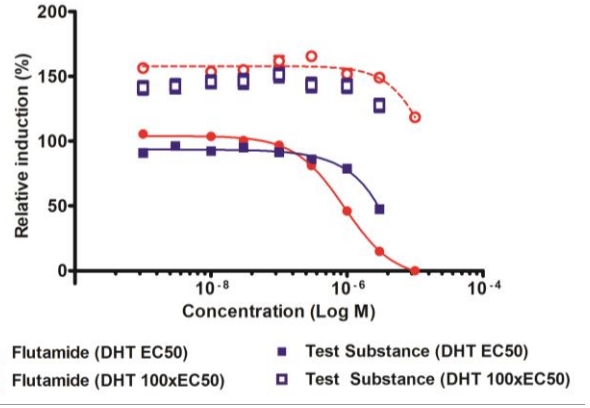
OECD TG471 OECD TG476

Genotoxicity

New Approach Methodologies (NAMs)

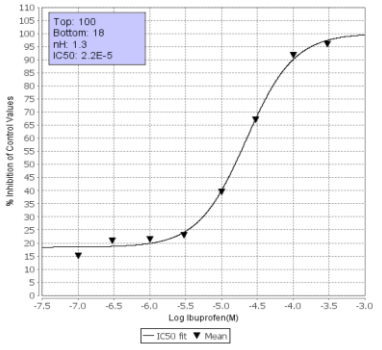
Receptor-binding assays

e.g. AR-CALUX® assay to measure androgen receptor activity



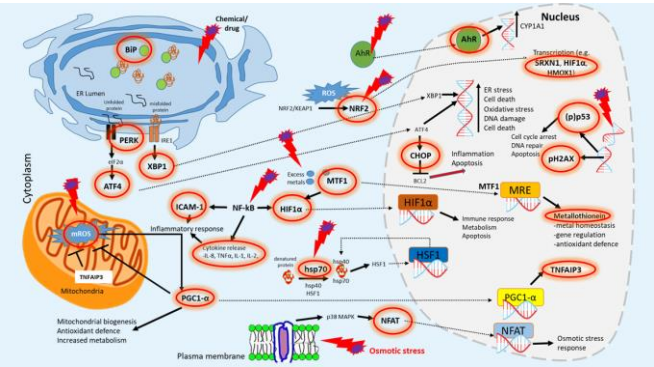
Dent et al . Toxicological Science, 167, 375-384, 2019.

Ibuprofen – Cox-1.



Biological activity characterisation using NAMs

Cellular stress



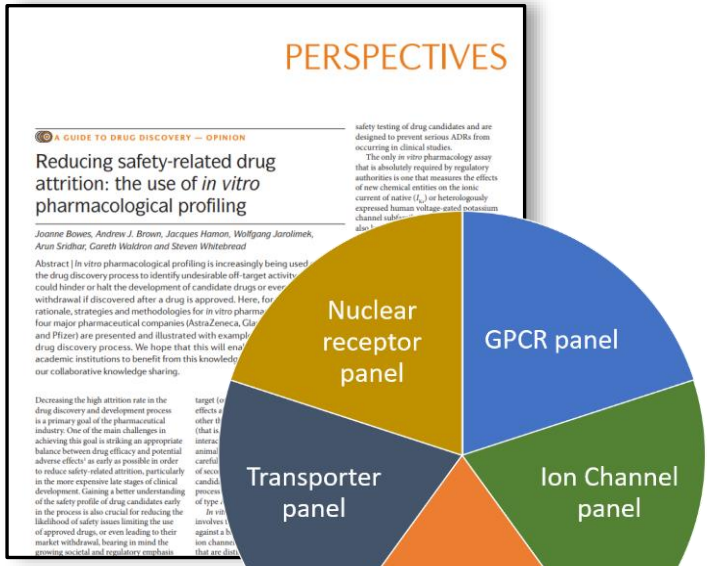
cyprotex AN EVOTEC COMPANY

Image kindly provided by Paul Walker (Cyprotex)

36 biomarkers identified that were representative of key stress pathways, mitochondrial toxicity and cell health.

Hatherell et al. Toxicological Sciences, 176, 11-33, 2020.

Receptor-binding assays

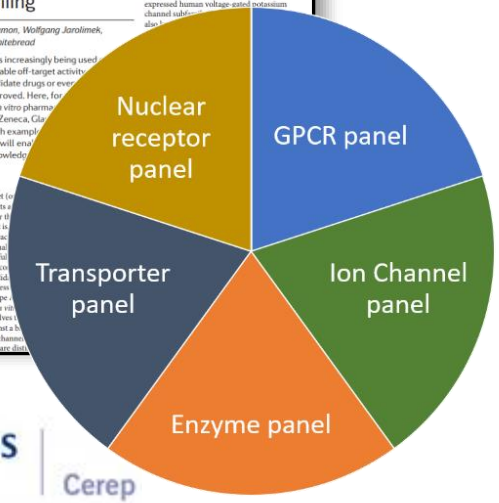

PERSPECTIVES

A GUIDE TO DRUG DISCOVERY — OPINION

Reducing safety-related drug attrition: the use of *in vitro* pharmacological profiling

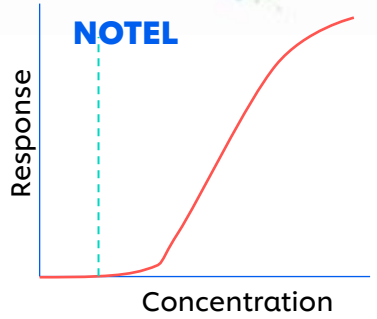
Joanne Bowes, Andrew J. Brown, Jacques Hamon, Wolfgang Jarolimek, Arun Sridhar, Gareth Waldron and Steven Whitebread

Abstract | *In vitro* pharmacological profiling is increasingly being used



eurofins | Cerep

High throughput transcriptomics



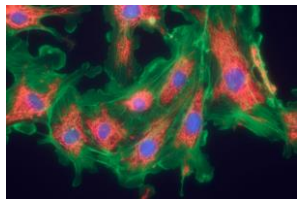
Mechanism based gentox assessment

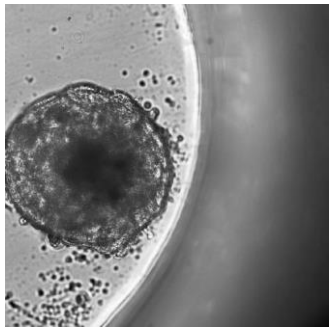
toxys

ToxTracker®

DNA Damage
P53 Binding
Oxidative Stress
Protein Damage

Advanced cell systems and microtissues





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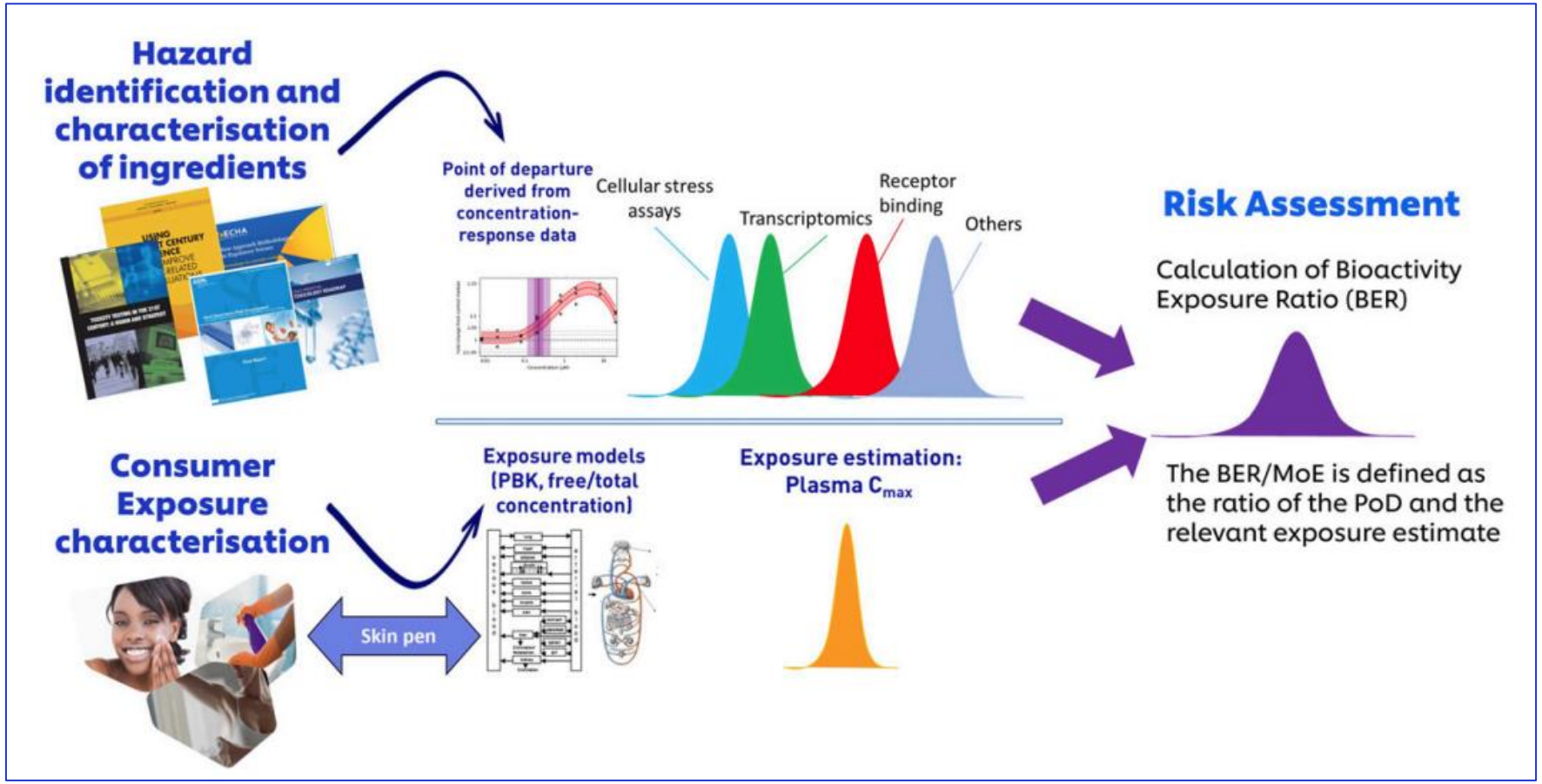
NGRA approaches enable the integration of non-animal data for decisions on the safety of chemicals used in cosmetics and other consumer products



Fentem, J. The 19th FRAME Annual Lecture, November 2022: Safer Chemicals and Sustainable Innovation Will Be Achieved by Regulatory Use of Modern Safety Science, Not by More Animal Testing. Altern. Lab. Anim. (ATLA), v. 51, p. 90-101, 2023.

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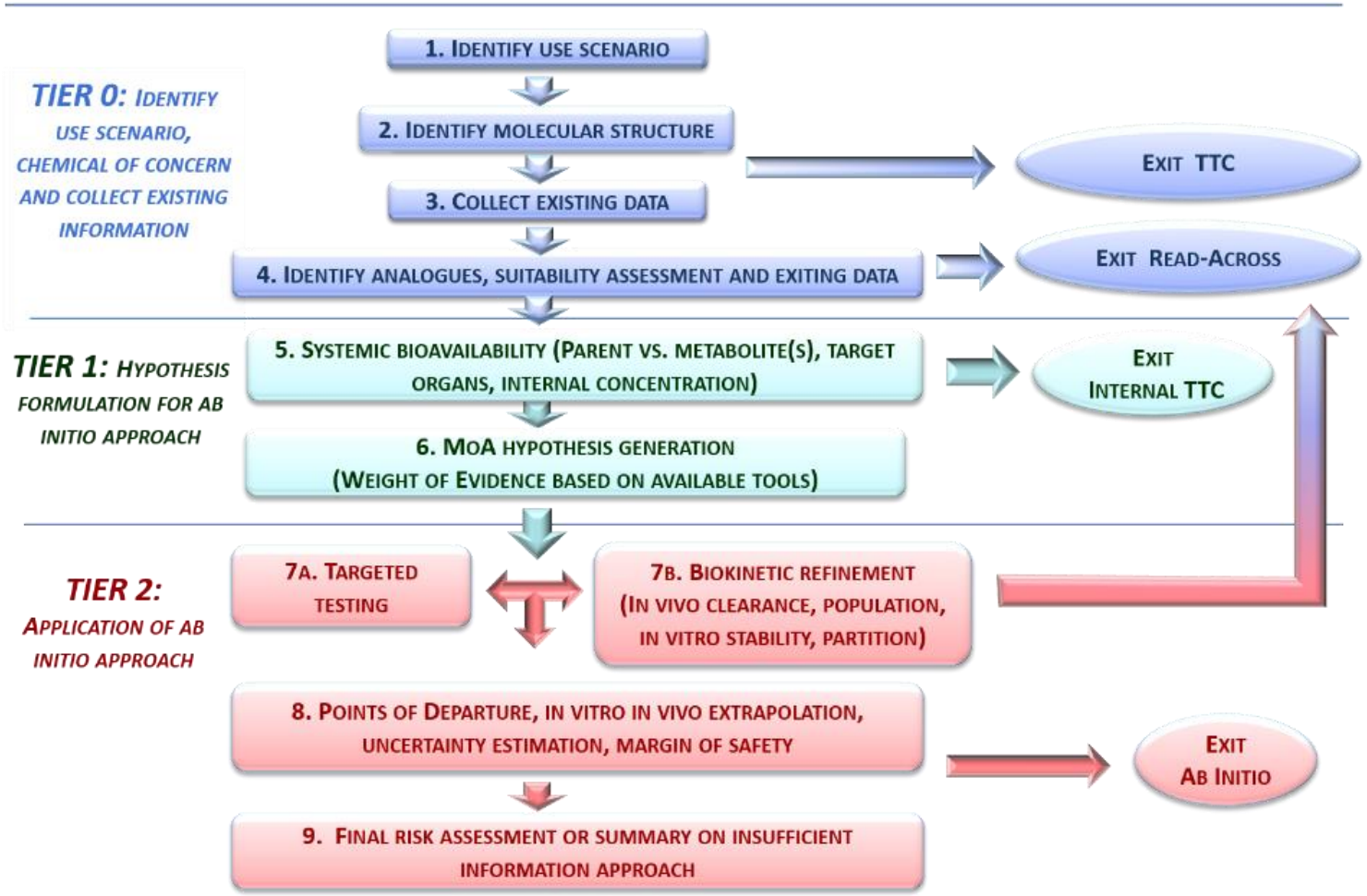
NGRA: from principles to application

Safety Evaluation Ultimately Replacing Animal Testing (SEURAT)

https://www.seurat-1.eu/



Berggren et al. Ab initio chemical safety assessment: A workflow based on exposure considerations and non-animal methods. Computational Toxicology, v. 4, p. 31-44, 2017.

NGRA: from principles to application

The summarization of NGRA case studies in cosmetics ingredients.

Ingredients	Toxicological endpoint	NAMs used	Advantages and valuables
1% phenoxyethanol	systemic toxicity	*in silico* (PBPK modeling, (Q)SAR, COSMOS nuclear Receptors Binding profilers, MIE Atlas, CERAPP, CoMPARA and CDOCKER), *in vitro* (*in vitro* metabolism, high throughput transcriptomics (HTTr), *in vitro* pharmacological profiling (SafetyScreen44) and cell stress panel)	To illustrates that one possible approach to evaluated both a parent chemical and its major stable metabolite in non-animal systemic toxicity risk assessment
0.1% coumarin	systemic toxicity	*in silico* ((Q)SAR, PBPK modeling), *in vitro* pharmacological profiling (SafetyScreen44 panel), immunomodulation panel (Diversity 8), ToxCast data *in vitro* cell stress panel, high-throughput transcriptomics, and ToxTracker tool	To demonstrate the value of integrating exposure science, computational modelling, and *in vitro* bioactivity data, to reach a safety decision without animal data
resorcinol	skin sensitization	*in silico* (read-across, TOXTREE, TIMES-M, TIMES-P), *in chemico* (protein binding assay; direct peptide reactivity assay, DPRA), *in vitro* (KeratinoSens, U-SENS, and SENS-IS)	To increase confidence, read-across was applied using analogues with skin sensitization data
caffeine	systemic toxicity	*in silico* (read-across, PBPK modeling, (Q)SAR, metabolite identification; Endocrine disruptome), *in chemico* (protein binding assay; direct peptide reactivity assay, DPRA), *in vitro* (genotoxicity assay and hepatocyte cultures)	Demonstrates the viability of a 10-step read-across framework in practice.
propyl paraben	skin sensitization	*in silico, in chemico*, and *in vitro* (KeratinoSens, U-SENS, h-CLAT, GARD and SENS-IS)	To show the important in considering the metabolization of chemical during risk assessment

Luo et al. The research progress of next generation risk assessment in cosmetic ingredients and the implications for traditional Chinese medicine risk assessment. Res. – Modern Chinese Medicine, v. 8, 100282, 2023.

More case studies available at:
https://www.oecd.org/chemicalsafety/testing/series-testing-assessment-publications-number.htm

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Agenda

1. Introduction to Unilever Safety and Environmental Assurance Centre (SEAC)
2. Assessing ingredient & product safety without animal testing
3. Next-Generation Risk Assessment (NGRA)
4. Bioactivity exposure ratio (BER) approach
5. NGRA: from principles to application
6. Unilever NGRA frameworks for decision-making on human safety
7. Concluding remarks

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Unilever NGRA frameworks for decision-making on human safety:

accelerate the transition to animal-free innovation with safe and sustainable ingredients

Some examples of current research topics:

- ✓ Systemic toxicity
- ✓ Skin allergy
- ✓ Inhalation
- ✓ Developmental and Reproductive Toxicity (DART)

https://seac.unilever.com/our-science/safety-without-animal-testing/

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Unilever NGRA framework for decision-making on human safety:

Systemic toxicity

NGRA tiered workflow for a systemic toxicity case study: 0.1% coumarin in consumer products

OXFORD | SOT Society of Toxicology
academic.oup.com/toxsci

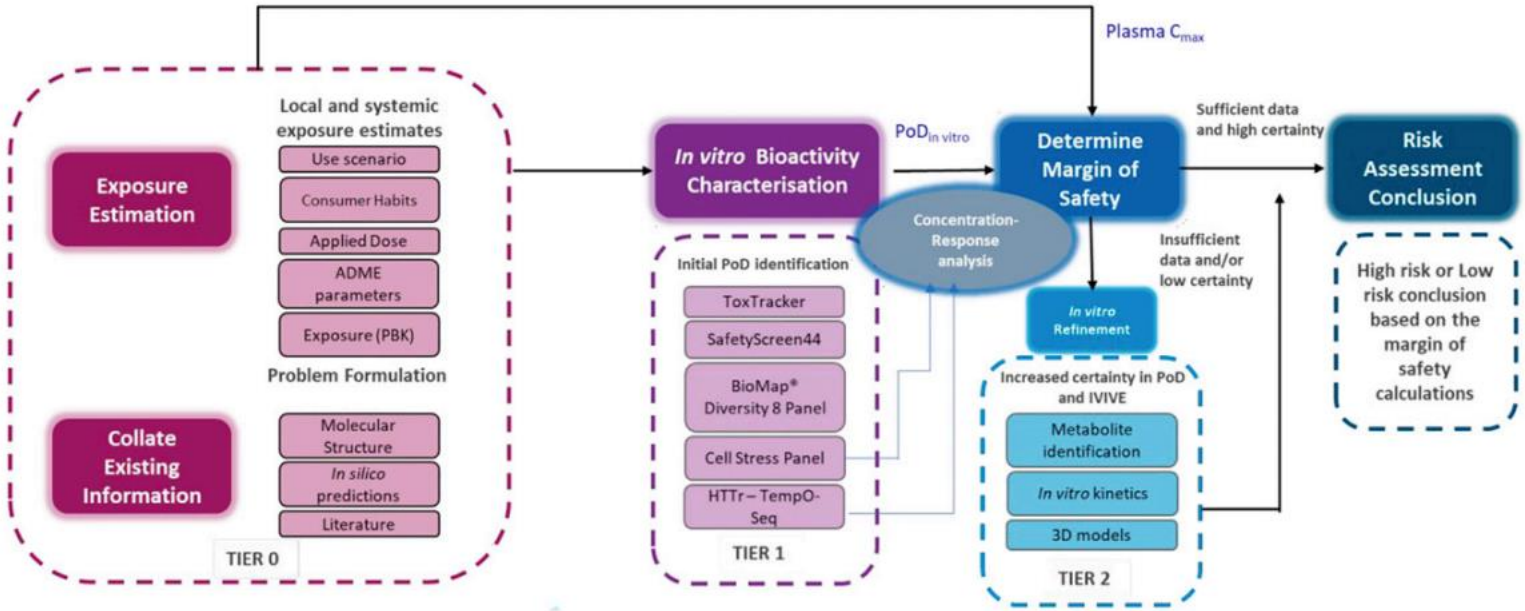
TOXICOLOGICAL SCIENCES, 176(1), 2020, 236–252
doi: 10.1093/toxsci/kfaa048
Advance Access Publication Date: April 10, 2020
Research article

A Next-Generation Risk Assessment Case Study for Coumarin in Cosmetic Products

Maria T. Baltazar,[1] Sophie Cable, Paul L. Carmichael, Richard Cubberley, Tom Cull, Mona Delagrange, Matthew P. Dent, Sarah Hatherell, Jade Houghton, Predrag Kukic, Hequn Li, Mi-Young Lee, Sophie Malcomber, Alistair M. Middleton, Thomas E. Moxon, Alexis V. Nathanail, Beate Nicol, Ruth Pendlington, Georgia Reynolds, Joe Reynolds, Andrew White, and Carl Westmoreland

Unilever Safety and Environmental Assurance Centre, Colworth Science Park, Sharnbrook, Bedfordshire MK44 1LQ, UK

[1]To whom correspondence should be addressed. Fax: +44(0)1234 264 744. E-mail: maria.baltazar@unilever.com.



Unilever NGRA framework for decision-making on human safety:

Systemic toxicity

Benchmarking against historical safety decisions to evaluate how protective the toolbox & workflow are

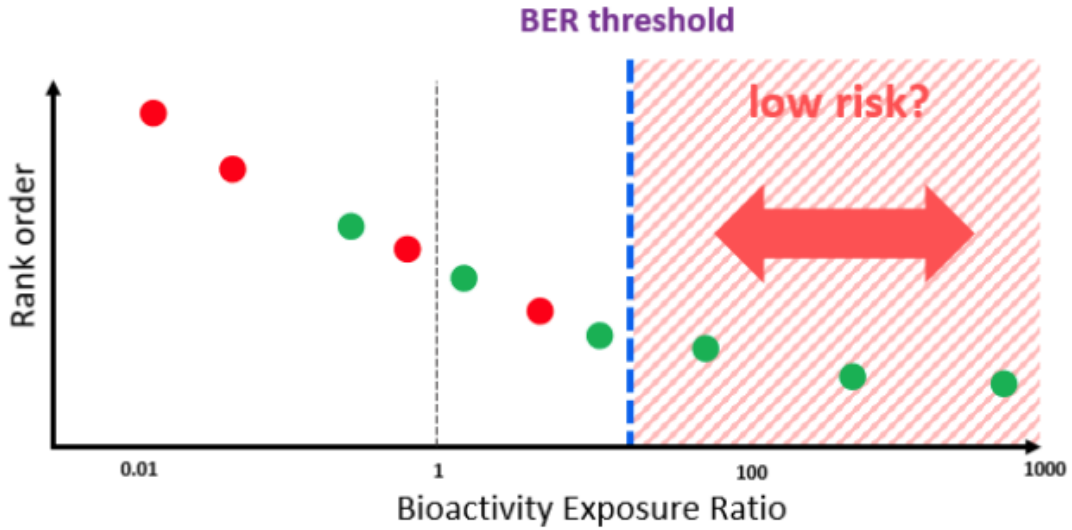
Caffeine

Oral dietary intake—400 mg/day	Low risk
Dermal 0.2% shampoo	Low risk
Oral tablets/overdose >10 g	High risk
Dermal clinical (2 mg/cm^2 of a solution containing 2.5% caffeine applied to a test area of 25 cm^2)	Low risk

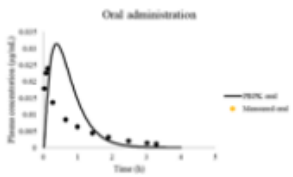
Adapted from Middleton et al. Toxicol. Sci., 1-24, 2022.

Chemical exposures scenarios

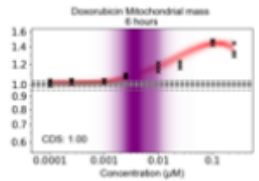
- 'Low' risk (from consumer goods perspective) – e.g. foods, cosmetics
- 'High' risk (from consumer goods perspective) – e.g. drugs



Define typical use-case scenarios & benchmark chemical-exposures; mix of high and low risk



PBK models of systemic exposure



in vitro assays, estimate PoDs

Calculate the Bioactivity-Exposure Ratio (BER)

Can we establish a BER threshold above which we consider a chemical exposure scenario to be low risk?

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Unilever NGRA framework for decision-making on human safety:

Systemic toxicity

OXFORD SOT Society of Toxicology academic.oup.com/toxsci

TOXICOLOGICAL SCIENCES, 2022, 1–24

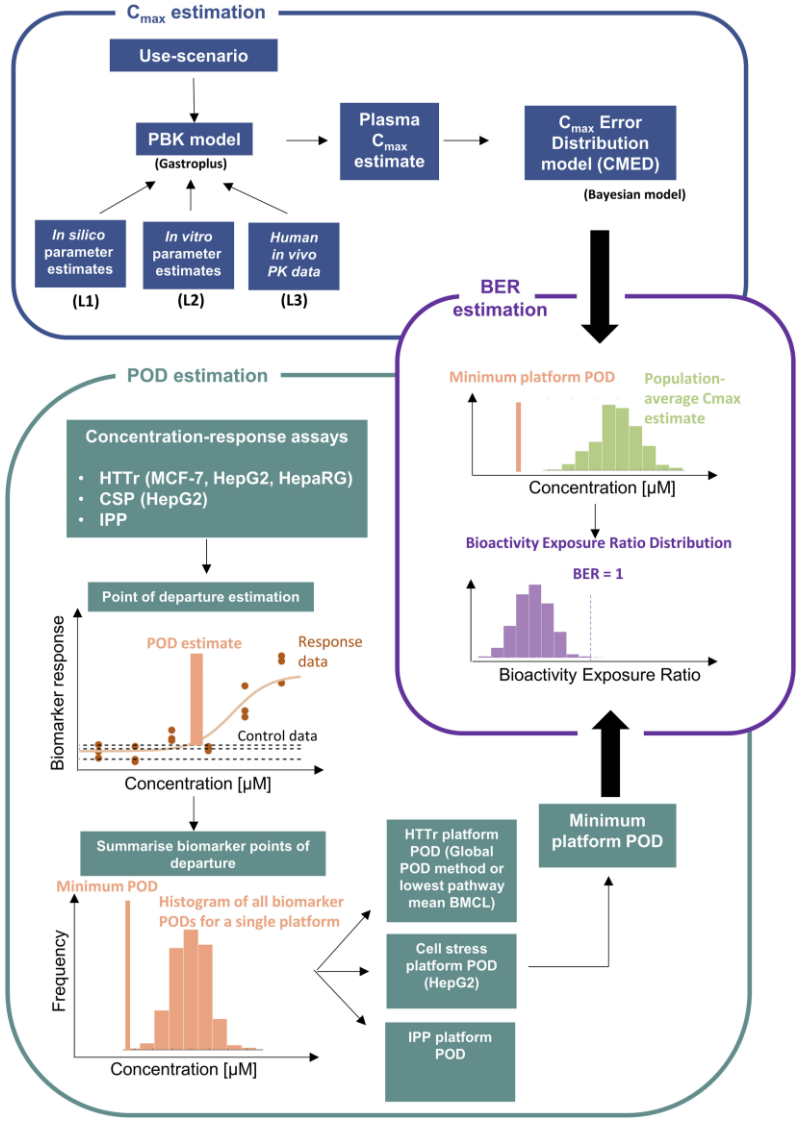
https://doi.org/10.1093/toxsci/kfac068
Dryad Digital Repository DOI: https://doi:10.5061/dryad.fbg79cnx1
Advance Access Publication Date: 13 July 2022
Research article

Are Non-animal Systemic Safety Assessments Protective? A Toolbox and Workflow

Alistair M. Middleton,*,[1] Joe Reynolds,* Sophie Cable,* Maria Teresa Baltazar,* Hequn Li,* Samantha Bevan,† Paul L. Carmichael,* Matthew Philip Dent,* Sarah Hatherell,* Jade Houghton,* Predrag Kukic,* Mark Liddell,* Sophie Malcomber,* Beate Nicol,* Benjamin Park,† Hiral Patel,‡ Sharon Scott,* Chris Sparham,* Paul Walker,† and Andrew White*

*Unilever Safety and Environmental Assurance Centre, Bedfordshire MK44 1LQ, UK; †Cyprotex Discovery Ltd, Cheshire SK10 4TG, UK and ‡Charles River Laboratories, Cambridgeshire, CB10 1XL, UK

[1]To whom correspondence should be addressed at Unilever Safety and Environmental Assurance Centre, Colworth Science Park, Sharnbrook, Bedfordshire MK44 1LQ, UK. E-mail: alistair.middleton@unilever.com.



Promising data for 24 different exposure scenarios covering 10 chemicals as a proof-of-concept study:

- up to 69% (9/13) of the low-risk scenarios could be identified
- protective against all (5/5) the high-risk scenarios

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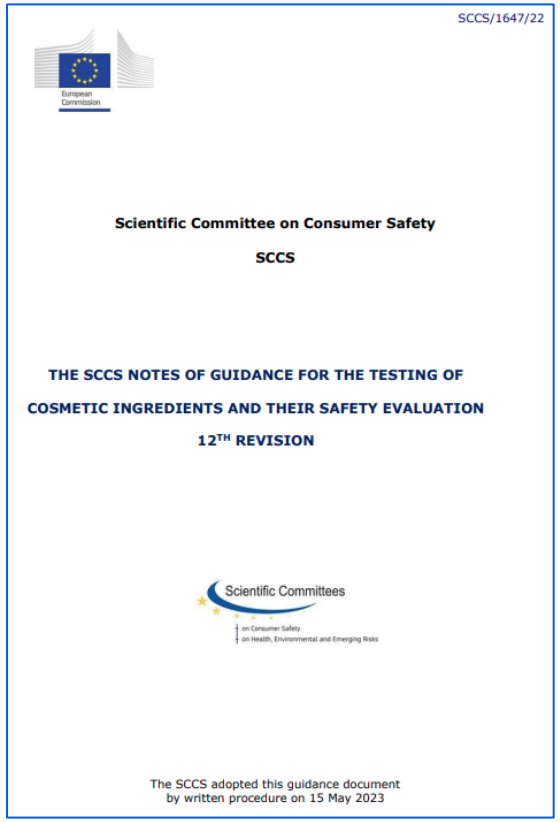
NGRA framework for human skin sensitisation

Scientific Committee on Consumer Safety (SCCS) 12th Notes of Guidance, 2023



SCCS/1647/22

European Commission

Scientific Committee on Consumer Safety

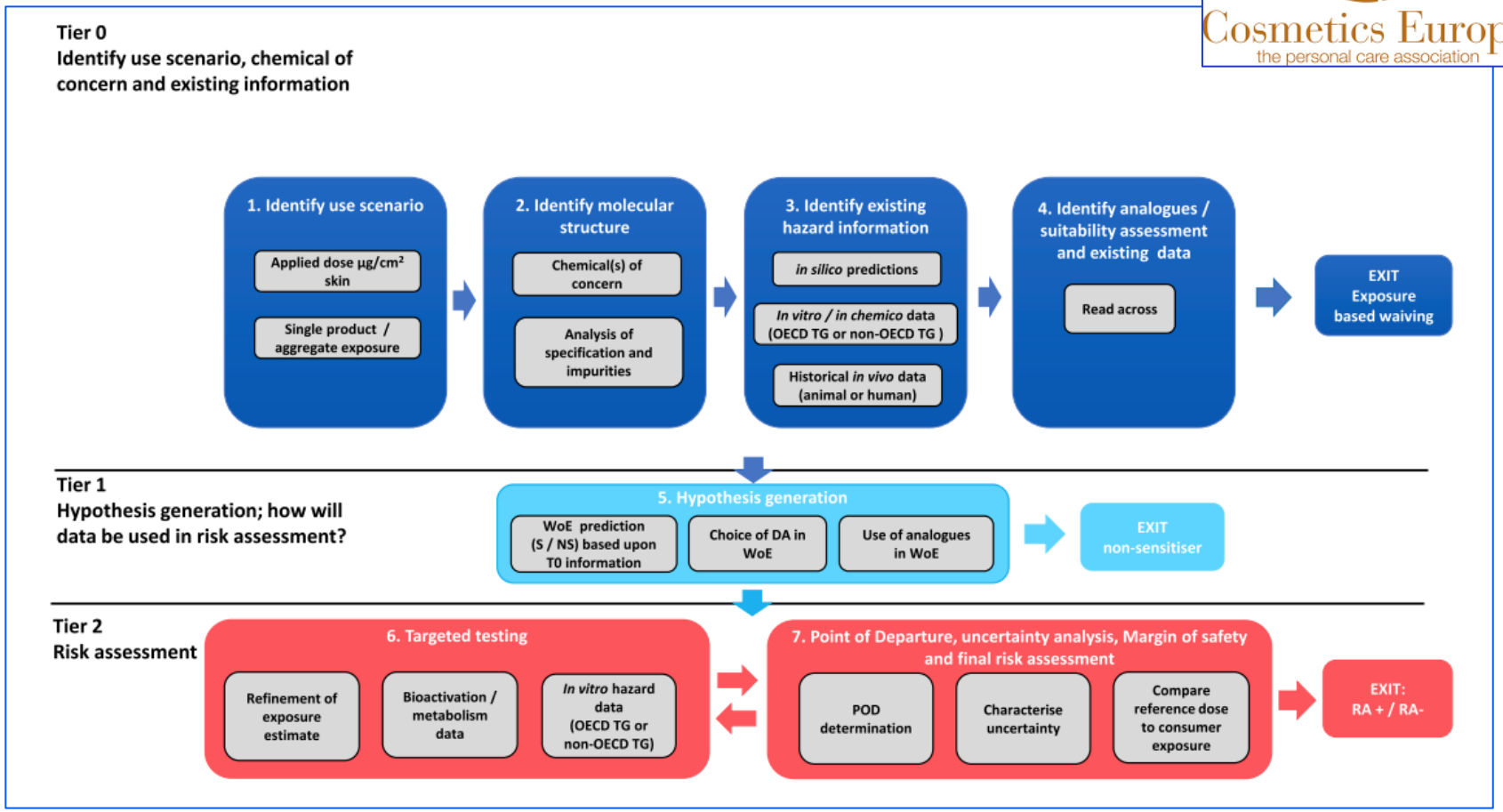
SCCS

THE SCCS NOTES OF GUIDANCE FOR THE TESTING OF COSMETIC INGREDIENTS AND THEIR SAFETY EVALUATION 12TH REVISION

Scientific Committees on Consumer Safety on Health, Environmental and Emerging Risks

The SCCS adopted this guidance document by written procedure on 15 May 2023

Cosmetics Europe
the personal care association



Gilmour et al. Development of a next generation risk assessment framework for the evaluation of skin sensitisation of cosmetic ingredients. Regul. Toxicol. Pharmacol. 116, 2020.

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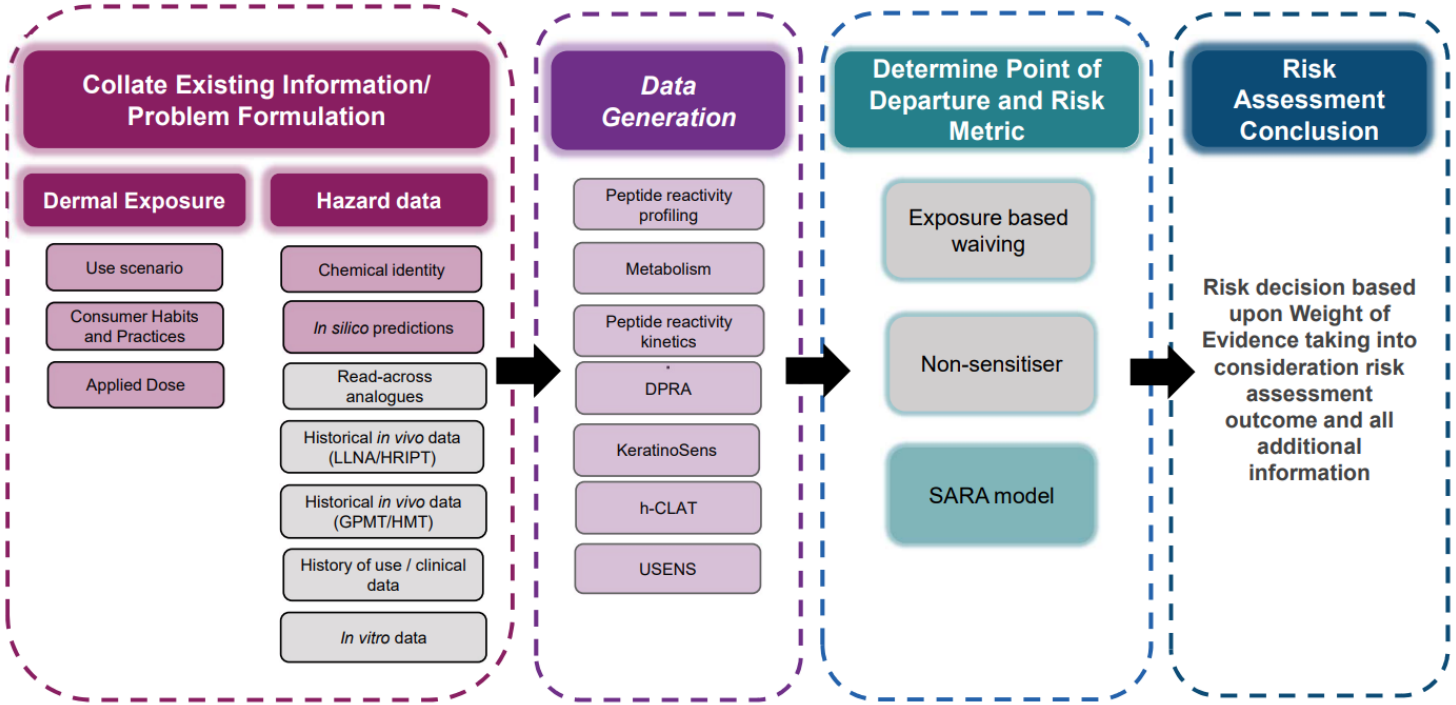
Unilever NGRA framework for decision-making on human safety:

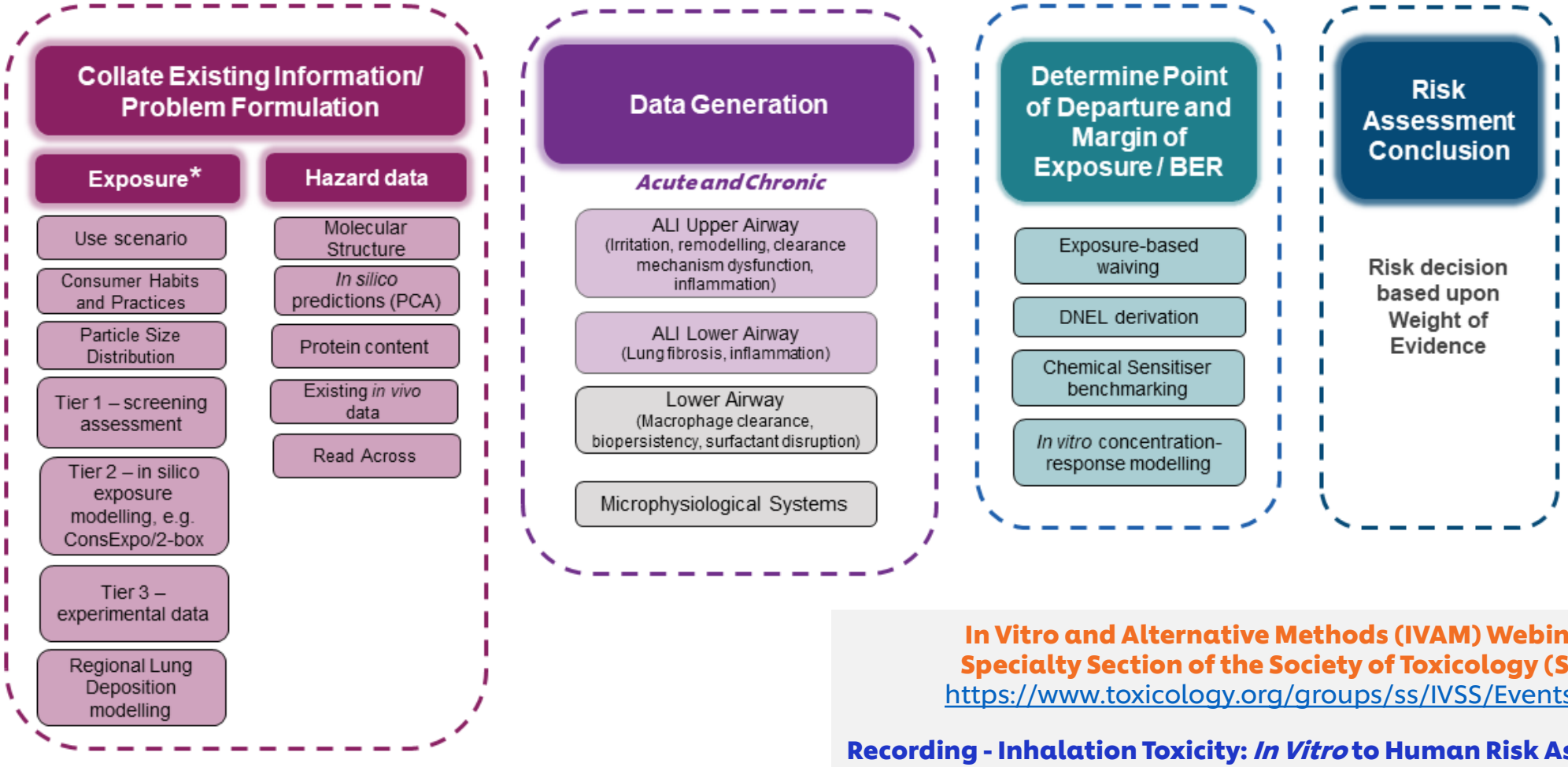
Skin allergy

NGRA tiered workflow for skin sensitisation case study materials in consumer products:

- coumarin in face cream (0.1%) and deodorant (1%)
- lactic acid in a shampoo (0.1%) and face cream (2%)
- geraniol at 0.02% in a face cream
- formaldehyde at 0.2% in a hand cream



Unilever NGRA framework for decision-making on human safety: inhalation



* https://www.youtube.com/watch?v=r5rGoihAbGI

In Vitro and Alternative Methods (IVAM) Webinar, Specialty Section of the Society of Toxicology (SoT)
https://www.toxicology.org/groups/ss/IVSS/Events.asp

Recording - Inhalation Toxicity: *In Vitro* to Human Risk Assessment:
https://player.vimeo.com/video/674986429 (January 2022)

Unilever NGRA framework for decision-making on consumer safety:

Developmental and Reproductive Toxicity (DART)

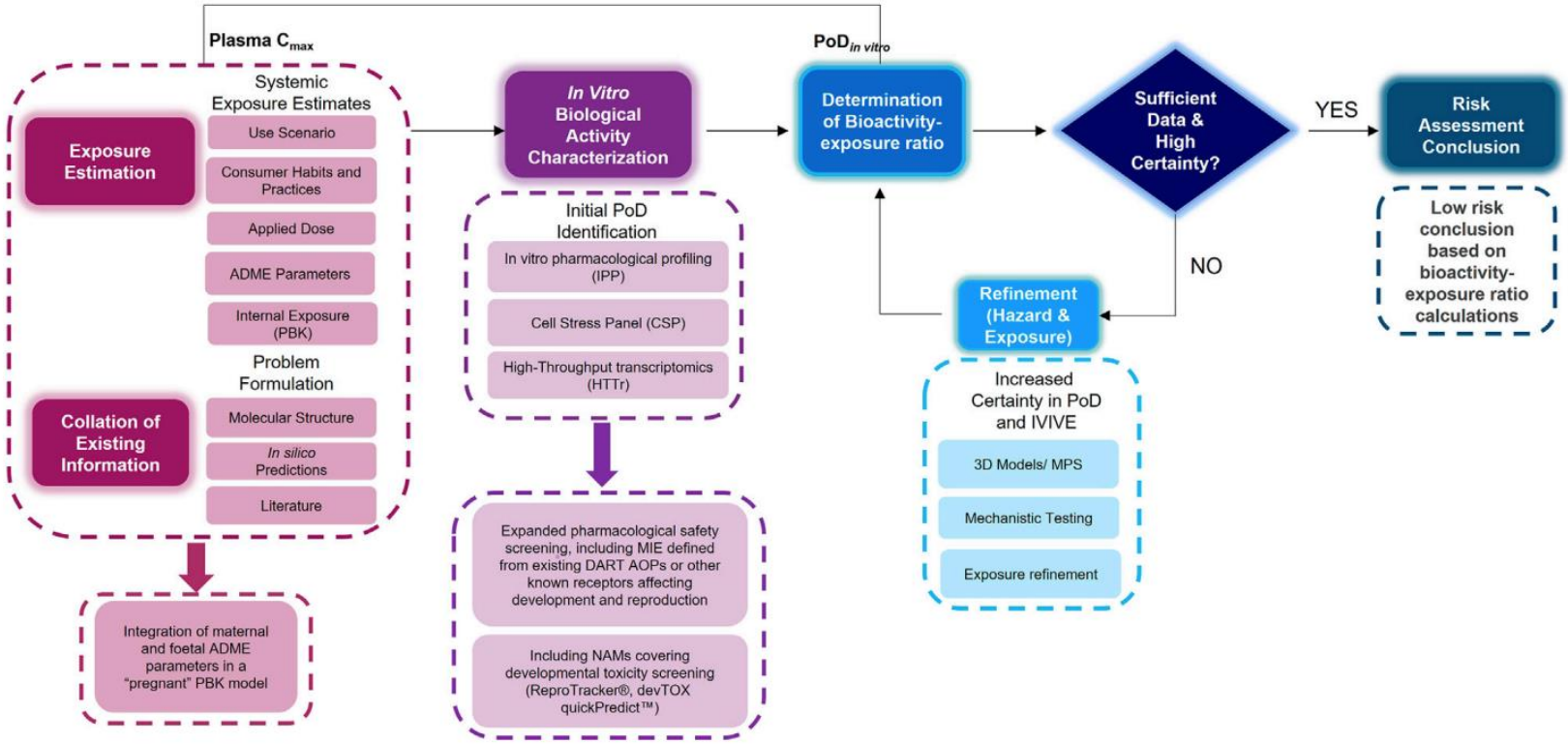
frontiers in Toxicology

ORIGINAL RESEARCH
published: 07 March 2022
doi: 10.3389/ftox.2022.838466

Beyond AOPs: A Mechanistic Evaluation of NAMs in DART Testing

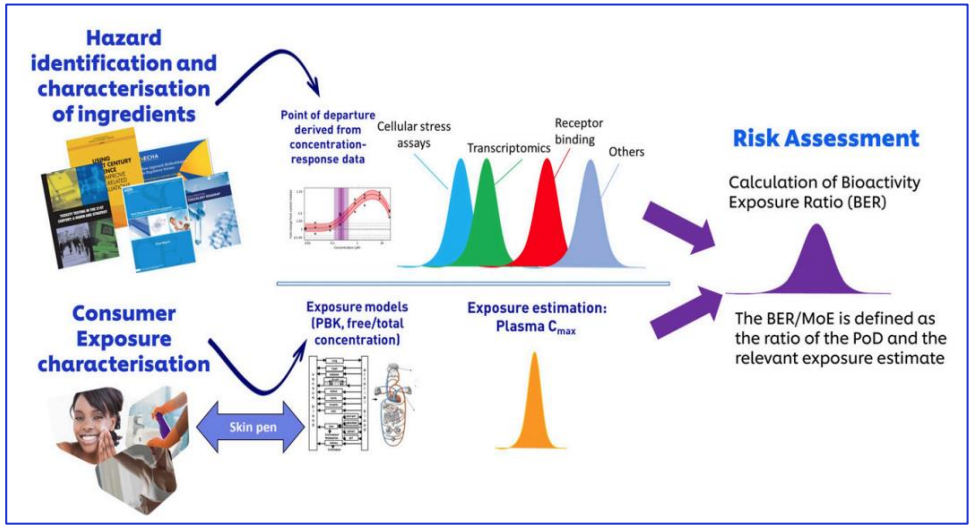
Ramya Rajagopal, Maria T. Baltazar, Paul L. Carmichael, Matthew P. Dent, Julia Head, Hequn Li, Iris Muller, Joe Reynolds, Kritika Sadh, Wendy Simpson, Sandrine Spriggs, Andrew White and Predrag Kukic*

Unilever Safety and Environmental Assurance Centre, Colworth Science Park, Shambrook, United Kingdom



Concluding remarks

- NGRA is a framework of non-standard, bespoke data-generation, driven by the risk assessment questions
  - ✓ Exposure led
  - ✓ Human relevant
  - ✓ Non-animal tools and approaches
  - ✓ Weight-of-evidence



Fentem, J. Altern. Lab. Anim. (ATLA), v. 51, p. 90-101, 2023.

- Bioactivity exposure ratio (BER) is determined by the ratio of human exposure to the point of departure for the most sensitive assay
- Case studies have demonstrated it is possible to integrate exposure estimates and bioactivity points of departure to make a safety decision
- NGRA tools and approaches are available now and research into more frameworks continues

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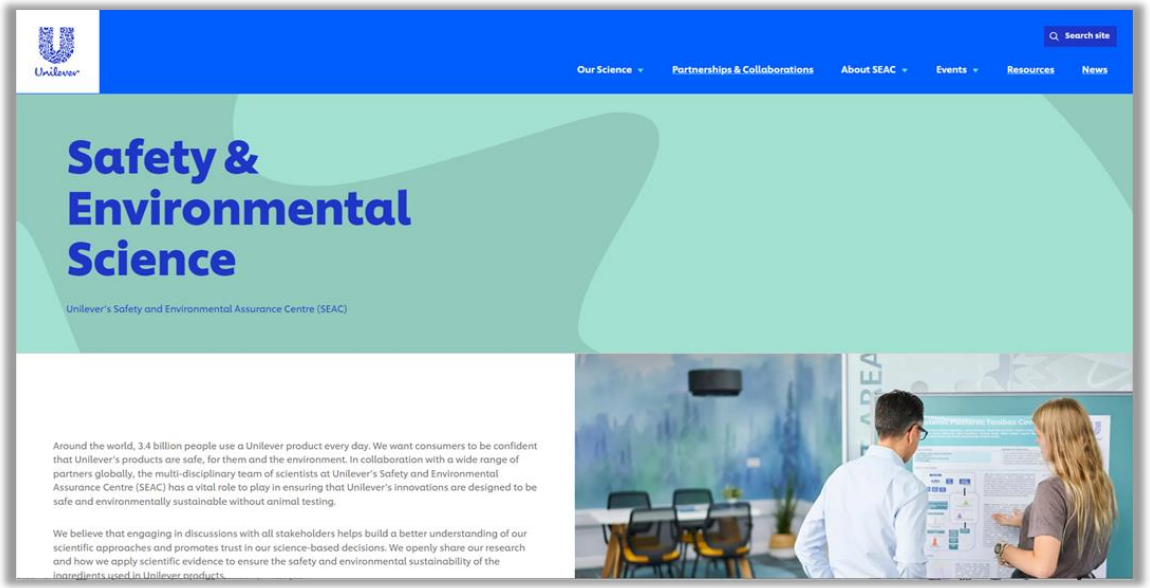
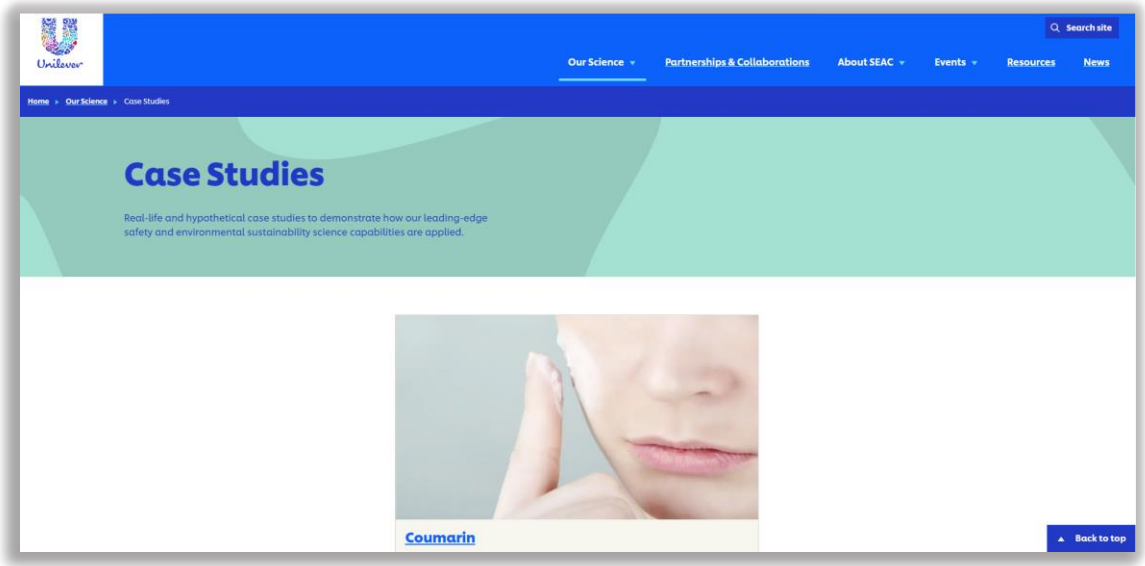
Safety & Environmental Sciences website: https://seac.unilever.com/



- **Microsite covering**:
  - Our Science → **case studies**
  - Partnerships & Collaborations
  - About SEAC
  - Events
  - Resources
  - News

- **Summary of SEAC science capabilities for expert audiences**:
  industry, regulator & academic scientists



https://seac.unilever.com/our-science/case-studies/coumarin/

Série de Webinars em Ciência *In Vitro*

FF FACULDADE DE FARMÁCIA — UFG UNIVERSIDADE FEDERAL DE GOIÁS

https://seac.unilever.com/news/2022/seac-scientists-collaborate-to-launch-latam-in-vitro-science-webinars/

Em português e/ou espanhol!

Tópicos já abordados:

- Sensibilização dérmica
- Irritação ocular e dérmica
- Segurança ambiental
- Processo de validação de métodos alternativos
- Status regulatório no Brasil e América Latina
- Química analítica na avaliação de segurança humana e ambiental

Gravação dos Eventos passados podem ser acessados:

YouTube TOXIN LABORATÓRIO DE ENSINO E PESQUISA EM TOXICOLOGIA IN VITRO

https://www.youtube.com/@laboratoriotoxin5356/playlists

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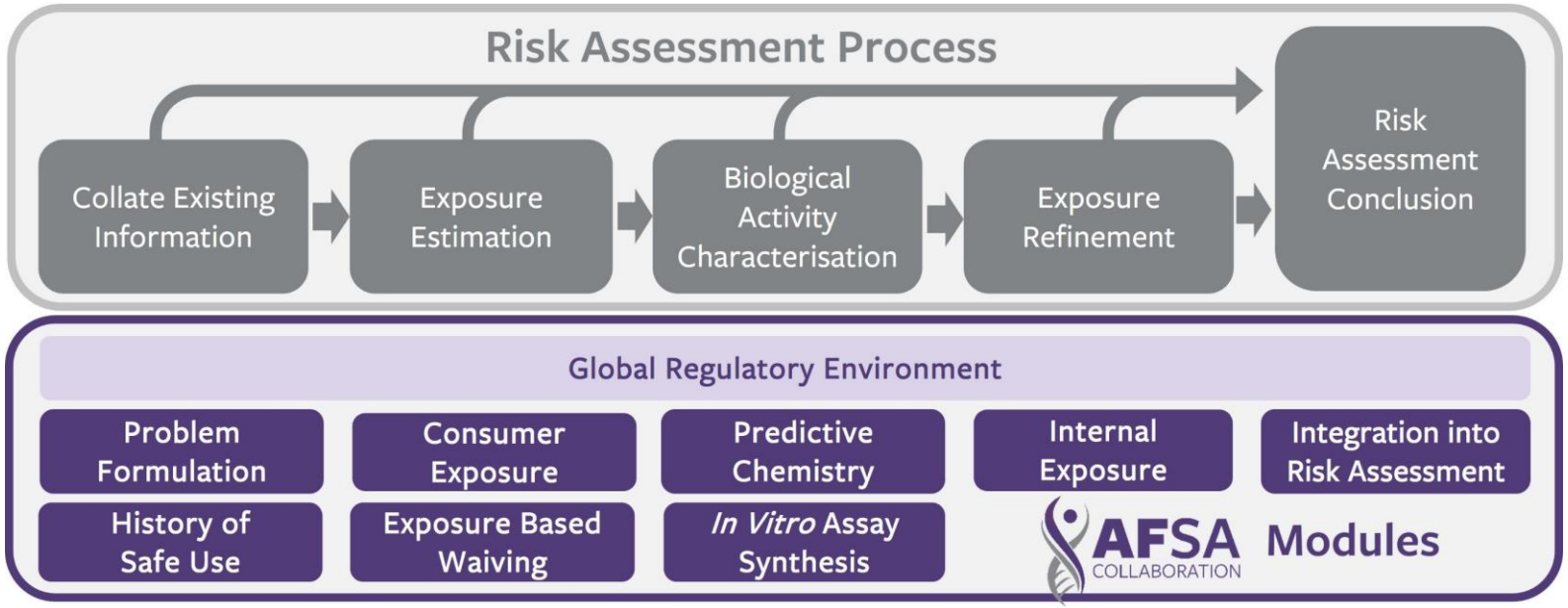
Master Class in Animal-Free Safety Assessment for Cosmetics

- **Covering Risk Assessment from start to finish**

Audience:

- Product and chemical safety assessors and regulators
- Regulatory affairs and compliance specialists
- CRO/GLP laboratories
- Small and medium enterprises
- Graduate students
- Non-governmental organizations

https://www.afsacollaboration.org/masterclass/



New module launched!

Animal-Free Safety Assessment

Module 4B: Safety of Botanicals/History of Safe Use

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Obrigado

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CBMAlt 2023
I Congresso Brasileiro de Métodos Alternativos ao Uso de Animais

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