

Protecting People

Making safety decisions with NAMs

Carl Westmoreland

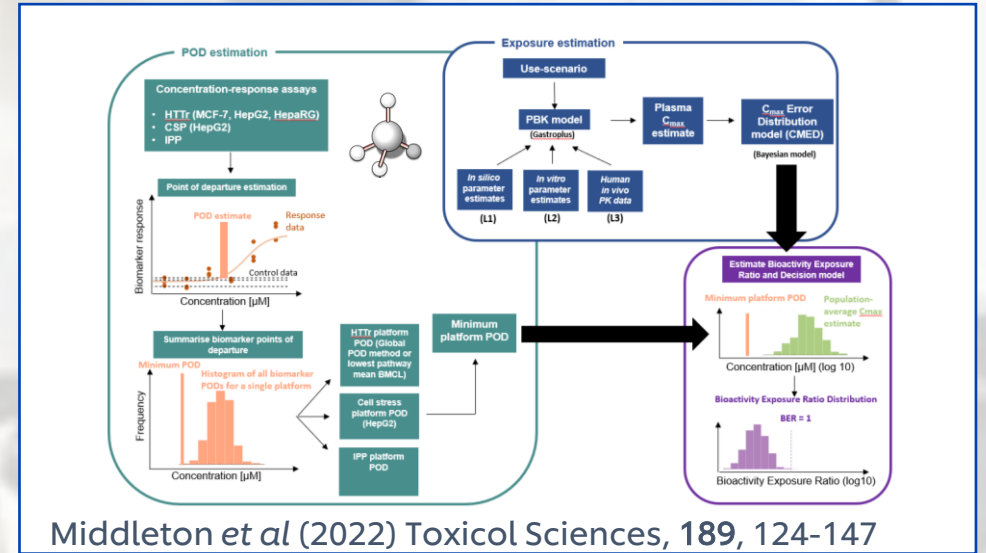
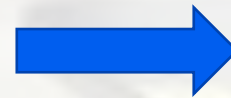
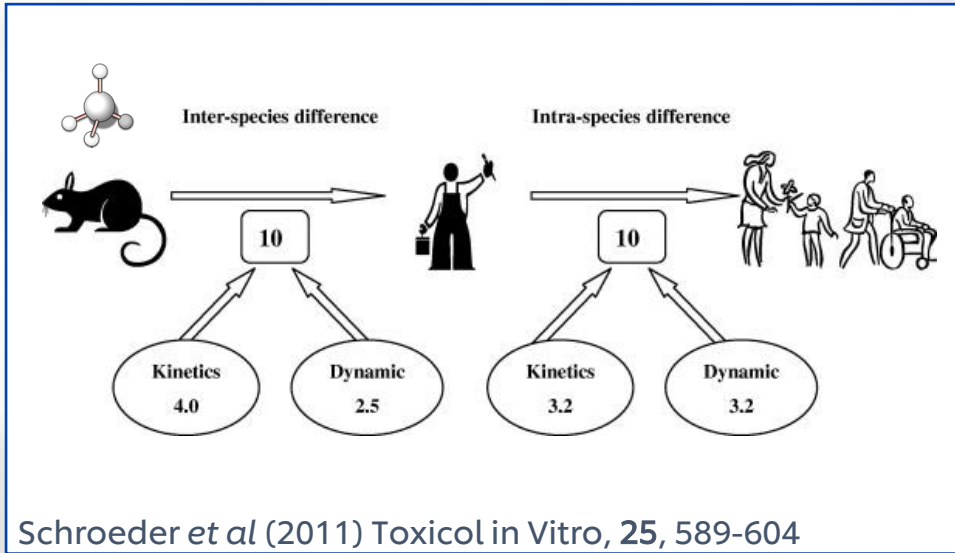
15th November 2022

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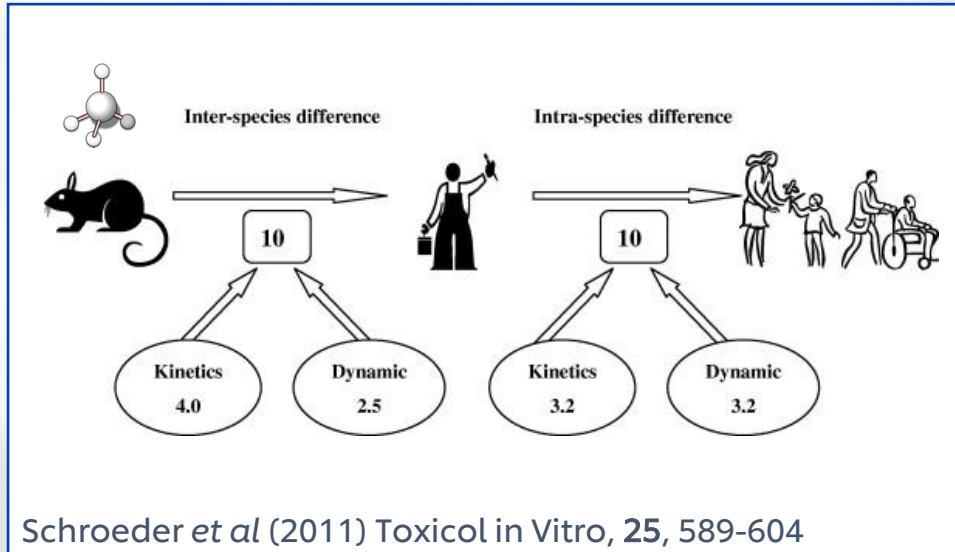


....and ensuring everyone has trust in the safety decisions

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Tests at high doses in rodents
The gold standard for protecting people?

Do rodents predict what might happen in people?

Margins of Safety (MoS) can allow us to protect people

NATIONAL ACADEMIES OF SCIENCES, ENGINEERING AND MEDICINE

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Variability and Relevance of Current Laboratory Mammalian Toxicity Tests and Expectations for New Approach Methods (NAMs) for use in Human Health Risk Assessment

SHARE f t i n

National Academies of Sciences, Engineering and Medicine (2022)
doi.org/10.17226/26496

U.S. EPA Environmental Protection Agency

Grappling With the Issue of Protection vs Prediction

Limited Qualitative Concordance of Rodent and Human Toxicological Responses

...data compiled from 150 compounds with 221 human toxicity events reported. The results showed the true positive human toxicity concordance rate of 71% for rodent and non-rodent species, with non-rodents alone being predictive for 63% of human toxicity and rodents alone for 43%.

Current Risk Assessment Practices Geared Towards Protection Not Prediction

Reference value	TC_1	TC_2	TC_3	TC_4	PPRP ^a
ADD	1.1-3.9	1.1-3.9	1.1-3.9	1.1-3.9	NA
ADDL	1.1-3.9	1.1-3.9	P	ND	NA
ADDL (non-rodent)	ND	ND	1-10	ND	NA
ADDL (rodent)	1.1-3.9	1.1-3.9	1.1-3.9	1.1-3.9	NA
ADDL (MSL)	1.1-3.9	1.1-3.9	1.1-3.9	1.1-3.9	ND

Case Studies Demonstrating Application of Bioactivity as a Protective POD

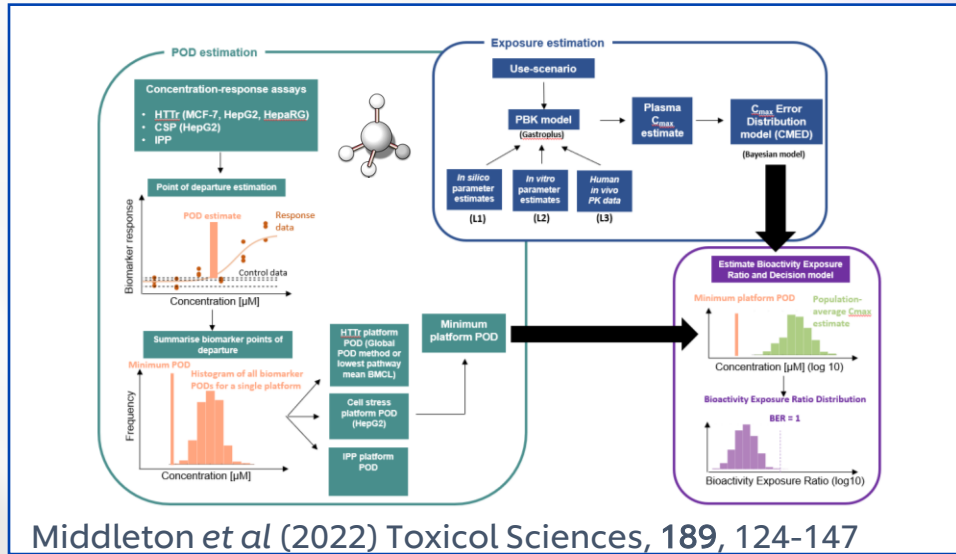
Paul-Friedman *et al.*, 2020

Nyffeler and Harrill, ISMB Poster, 2020

Center for Computational Toxicology & Exposure

Rusty Thomas, US EPA (2021)

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Use of human biology to protect people

A large toolbox of NAMs developed over many years

There isn't a lack tools, just experience with using them to make decisions

Do NAMs predict what might happen in high dose animal studies?

Bioactivity Exposure Ratios (BER) can allow us to protect people



Science Approach Document

Bioactivity Exposure Ratio:
Application in Priority Setting and Risk Assessment

Health Canada

March 2021

APCRA

ACCELERATING THE PACE OF CHEMICAL RISK ASSESSMENT

Archives of Toxicology (2022) 96:2865–2879
https://doi.org/10.1007/s00204-022-03365-4

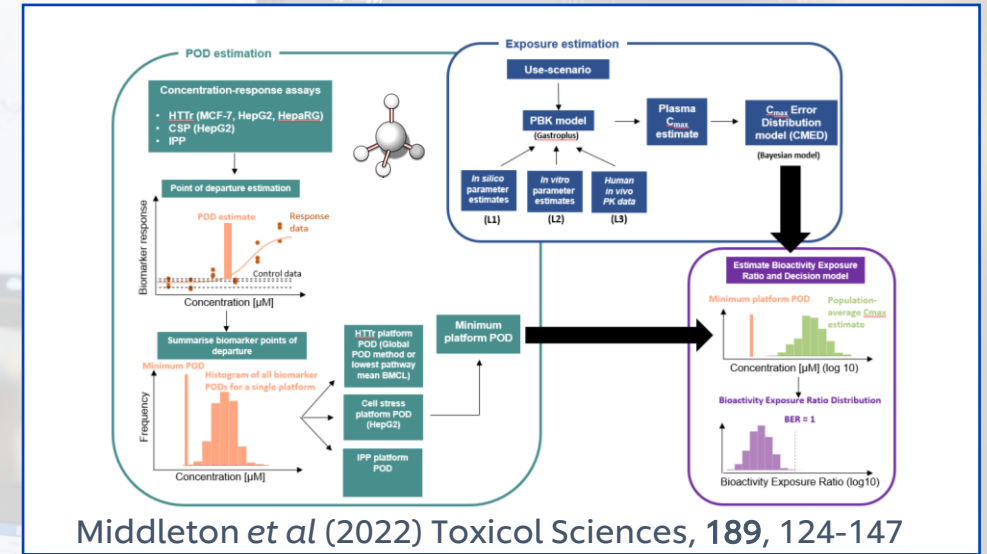
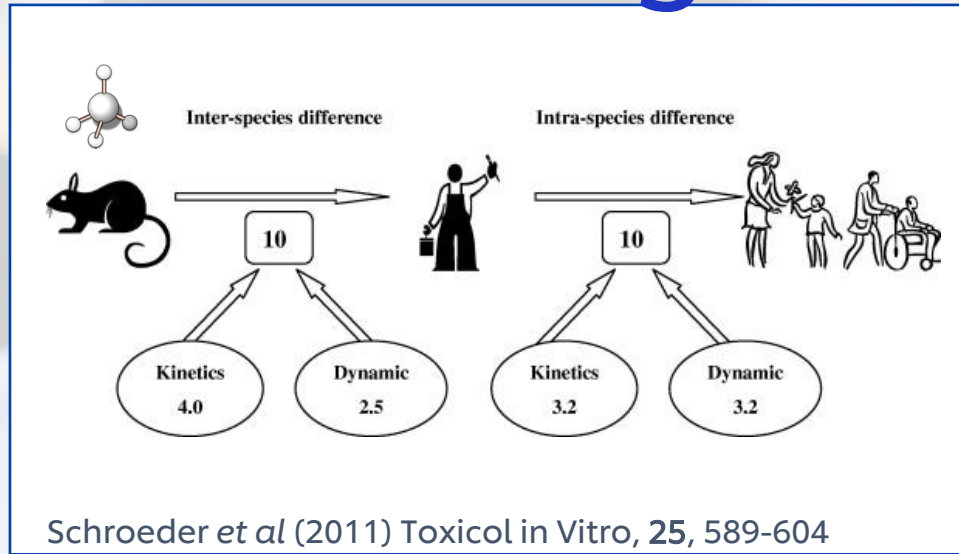
REVIEW ARTICLE

A framework for establishing scientific confidence in new approach methodologies

Anna J. van der Zalm¹ · Josjo Barroso² · Patience Browne³ · Warren Casey⁴ · John Gordon⁵ · Tala R. Henry⁶ · Nicole C. Kleinstreuer⁷ · Anna B. Lowit⁸ · Monique Perron⁶ · Amy J. Clippinger⁹



Protecting People



Animal Technician Statistician

Veterinarian Pathologist

Study Director Clinical Chemist

QA CRO Haematologist

Histologist

Cell Biologist Bayesian Statistician

Bioinformatician Molecular biologist

QA PBK Modeller

Study Director Immunologist

CRO Computational Chemist

Protecting People without Animal Testing

The toolbox of NAMs will keep evolving

Ensuring we continue to use the best new science for protecting people as it emerges

We will keep learning together

Building experience, gaining confidence

Building capability and capacity

Continue sharing and publishing

NAMs in regulations

Guidance on NAMs vs. specific lists of tests

Opportunities to embrace NAMs vs. 'waiving animal tests'

Flexibility and scientific dialogue

Maximising opportunities within Annex XI of REACH

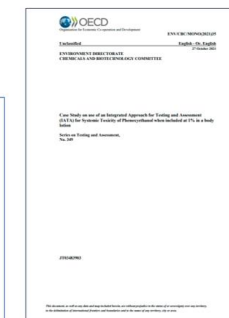
Cosmetics



International Cooperation on Cosmetics Regulation (2018)

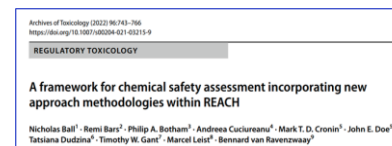


European Commission: Scientific Committee on Consumer Safety (2021)



OECD (2021)

Chemicals



eceioc ECETOC (2022)



EPAA (2022)

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