

# Protecting People

## Making safety decisions with NAMs

**Carl Westmoreland**

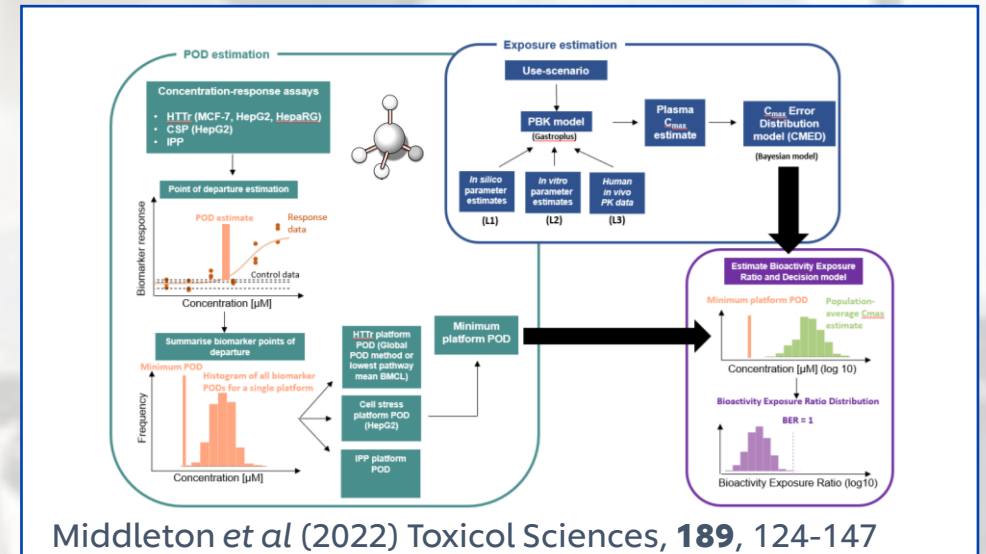
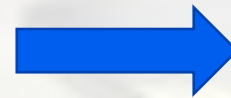
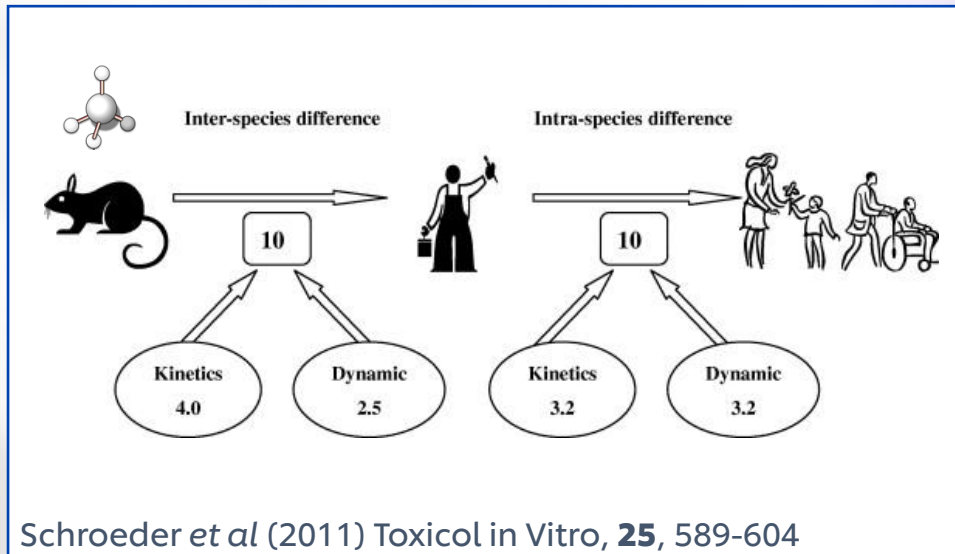
**15<sup>th</sup> November 2022**

# Protecting People

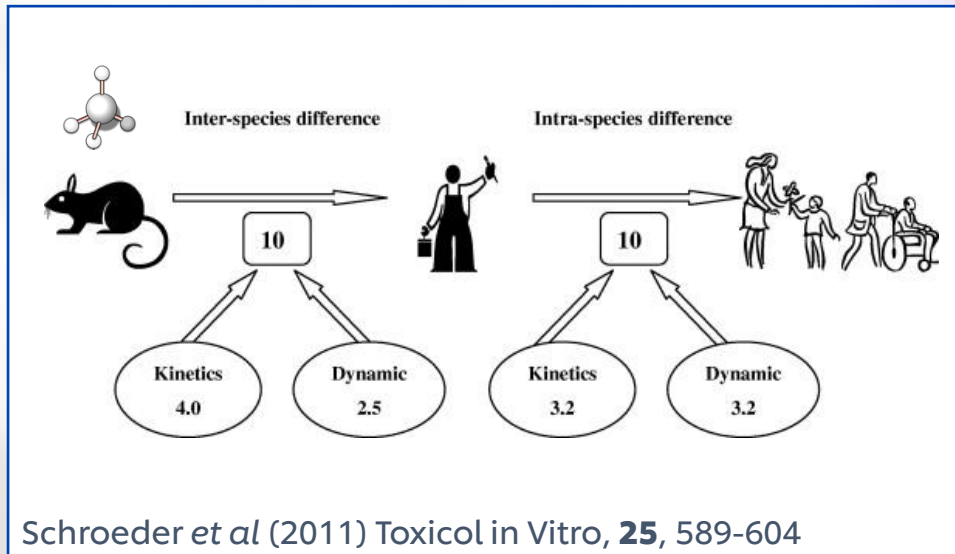


....and ensuring everyone has trust in the safety decisions

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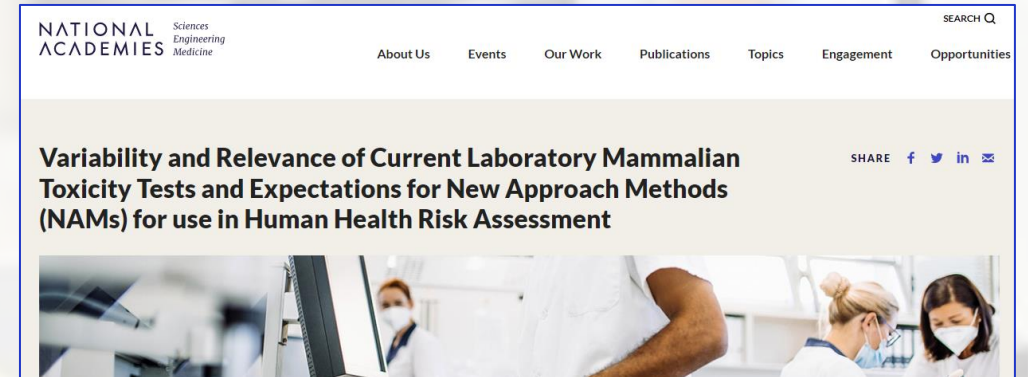
# Protecting People



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 (2022)  
doi.org/10.17226/26496

**EPA**  
United States Environmental Protection Agency

## Grappling With the Issue of Protection vs Prediction

**Limited Qualitative Concordance of Rodent and Human Toxicological Responses**

**Current Risk Assessment Practices Geared Towards Protection Not Prediction**

**Case Studies Demonstrating Application of Bioactivity as a Protective POD**

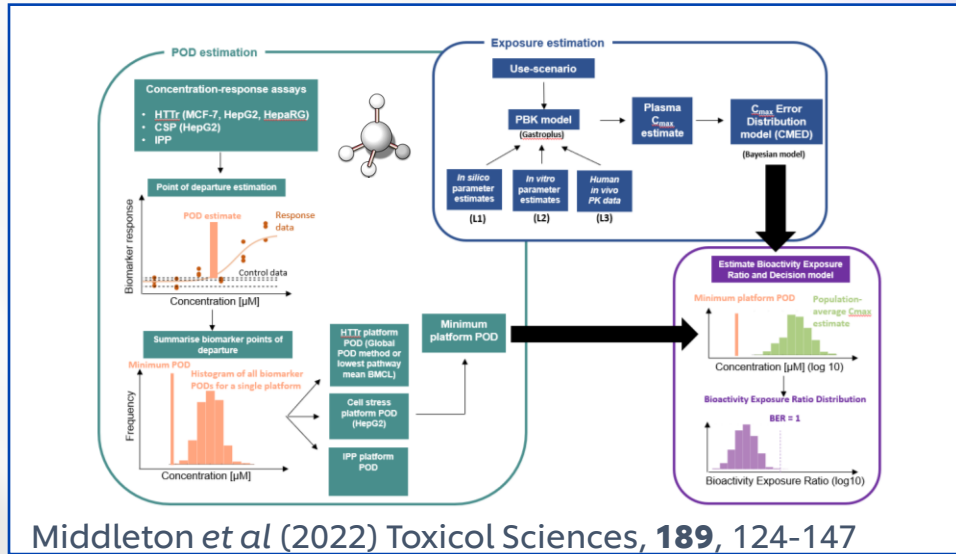
...data compiled from 150 compounds with 221 human toxicity events reported. The results showed the true positive human toxicity concordance rate of 71% for rodent and non-rodent species, with non-rodents alone being predictive for 63% of human toxicity and rodents alone for 43%.

Reference value	Rat		Dog		Piglet	
	$TC_{10}$	$TC_{100}$	$TC_{10}$	$TC_{100}$		
ADL	1.1, 0.9	1.1, 0.9	1.1, 0.9	1.1, 0.9	ND	NA
ADL	1.1, 0.9	1.1, 0.9	P	ND	ND	NA
ADL non-rodent	ND	ND	1.1, 0.9	ND	ND	NA
ADL non-rodent (Rat)	ND	ND	1.1, 0.9	1.1, 0.9	non-specific	NA
ADL non-rodent (Dog)	ND	ND	1.1, 0.9	1.1, 0.9	ND	NA

Center for Computational Toxicology & Exposure

Rusty Thomas, US EPA (2021)

# Protecting People



## Use of human biology to protect people

A large toolbox of NAMs developed over many years

There isn't a lack of 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>

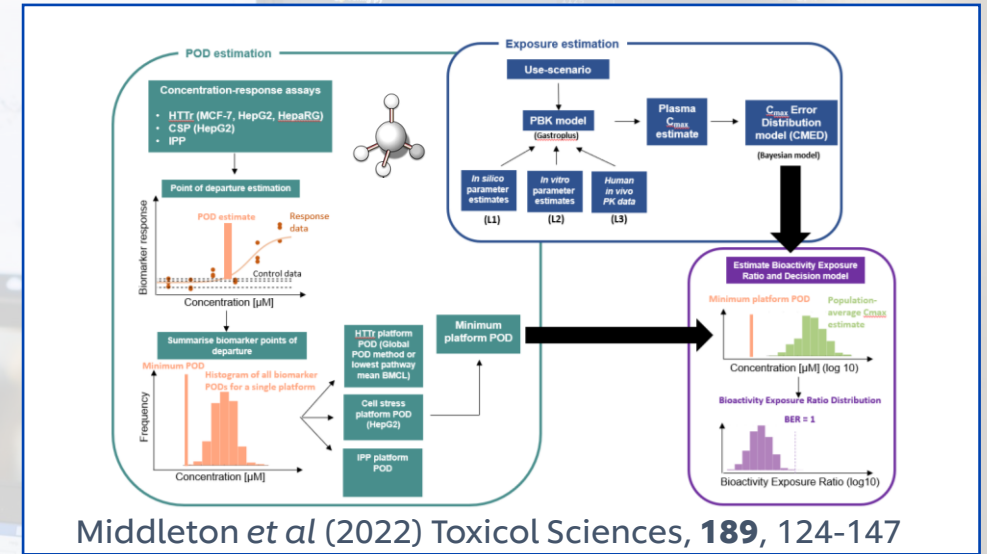
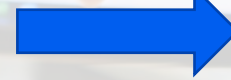
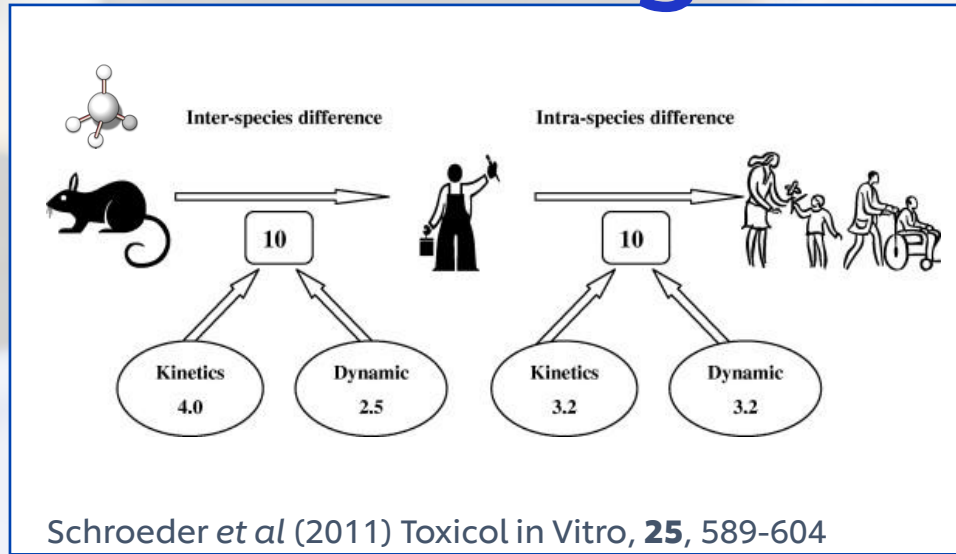
REVIEW ARTICLE

A framework for establishing scientific confidence in new approach methodologies

Anna J. van der Zalm<sup>1</sup>, Josjo Barroso<sup>2</sup>, Patience Browne<sup>3</sup>, Warren Casey<sup>4</sup>, John Gordon<sup>5</sup>, Tala R. Henry<sup>6</sup>, Nicole C. Kleinstreuer<sup>7</sup>, Anna B. Lowit<sup>8</sup>, Monique Perron<sup>9</sup>, Amy J. Clippinger<sup>10</sup>



# 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



Principles underpinning the use of new methodologies in the risk assessment of cosmetic ingredients

Scientific Committee on Consumer Safety  
SCCS

THE SCCS NOTES OF GUIDANCE FOR THE TESTING OF COSMETIC INGREDIENTS AND THEIR SAFETY

OECD  
GUIDANCE DOCUMENT  
ENVIRONMENTAL HEALTH AND SAFETY  
ENVIRONMENTAL HEALTH AND SAFETY  
ENVIRONMENTAL HEALTH AND SAFETY

International Cooperation on Cosmetics Regulation (2018)

European Commission: Scientific Committee on Consumer Safety (2021)

OECD (2021)

### Chemicals



Archives of Toxicology (2022) 96:743–766  
<https://doi.org/10.1007/s00204-021-01215-9>

REGULATORY TOXICOLOGY

A framework for chemical safety assessment incorporating new approach methodologies within REACH

Nicholas Ball<sup>1</sup>, Remi Bars<sup>2</sup>, Philip A. Botham<sup>3</sup>, Andreea Cucureanu<sup>4</sup>, Mark T. D. Cronin<sup>5</sup>, John E. Doe<sup>6</sup>, Tatiana Dudzins<sup>7</sup>, Timothy W. Gant<sup>8</sup>, Marcel Letis<sup>9</sup>, Bernard van Ravenzwaay<sup>10</sup>

ecetoc ECETOC (2022)

Regulatory Toxicology and Pharmacology  
Available online 11 September 2022, 105261

ELSEVIER

Use of New Approach Methodologies (NAMs) in regulatory decisions for chemical safety: Report from an EPAA Deep Dive Workshop

Carl Westmoreland<sup>1</sup>, Hans J. Bender<sup>2</sup>, John E. Doe<sup>3</sup>, Miriam N. Jacobs<sup>4</sup>, George E.N. Kass<sup>5</sup>, Federica Madia<sup>6</sup>, Catherine Mahony<sup>7</sup>, Irene Manou<sup>8</sup>, Gavin Maxwell<sup>9</sup>, Pilar Prieto<sup>10</sup>, Rob Roggeband<sup>11</sup>, Tomasz Sobanski<sup>12</sup>, Katrin Schütte<sup>13</sup>, Andrew P. Worth<sup>14</sup>, Zvonimir Zvonar<sup>15</sup>, Mark T.D. Cronin<sup>16</sup>

epaa  
The European Partnership for Alternative Approaches to Animal Testing

EPAA (2022)

# Protecting People without Animal Testing

