Challenges and opportunities for implementing NAMs in a regulatory context: Perspectives from current research initiatives:

An Academic's Viewpoint

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Discussion topics

- General reflection on challenges for academics to contribute to NAMs 'pipeline'
- Focus on 'omics to support grouping/read-across to highlight progress and challenges in the NAMs pipeline
- 3 take-home messages

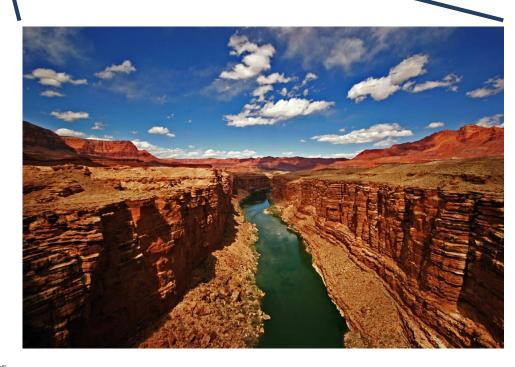




Innovation Applied science

Policy changes

NAMs in legislation







Innovation

Applied science

Policy changes

NAMs in legislation



2003-present

Develop & apply metabolomics to (eco)toxicology

- Academic funders almost exclusively fund innovative research, not applied
- Expected **products** research discoveries, high impact-factor papers (*Nature*, *Science*)
- Personal **motivation** curiosity for blue-skies innovative research
- Academics prefer to ask deeper questions, not provide definitive answers!
- How do some academics genuinely cross that chasm?...







NAMs in legislation

VINIVERSITYOF
BIRMINGHAM
Spin-out company
Spin-out company
Evaluate 'omics approaches in regulatory (eco)toxicology

- Contracts with progressive companies/REACH consortia
- Contracts with regulators e.g. *Services related to metabolomics measurements and multi-omics data interpretation* (2018-2023)



- Message 1: 99% of academics 'locked' in innovation zone (most are happy with that!)
- Illusion (through grant proposals) of considerable academic focus on applied NAM science





Innovation Applied science Policy changes

NAMs in legislation

Challenges and opportunities in application of 'omics to support chemical grouping





'Omics to support chemical grouping: progress in the 'process'

In vivo / in vitro exposures

Sample collection for 'omics analysis

'Omics data generation & processing

Statistical & mechanistic analyses to build chemical categories

- Knowledge exists (fragmented)
- Future: Integrate into *in* vivo, in vitro OECD TGs
- Well established(e.g. biomedical)
- Future: OECD guidance
- Well established;
- New OECD Omics Reporting Framework (OORF)
- OECD GD 194 being updated;
- OORF actively being extended

- Reliability has just been demonstrated



efic LRI C8 - MATCHING

<u>M</u>et<u>A</u>bolomics ring-<u>T</u>rial for <u>CH</u>emical group<u>ING</u>

Five of 6 blinded ring-trial participants derived an identical set of results











Imperial College London





From 'process' to NAMs in legislation

- Challenge arises when we attempt to embed the 'applied science process' into an existing regulatory 'machine'
 - Regulatory machine already has its own processes, outputs, legal timelines
- It's new (NAM), so by definition, insufficient exemplar regulatory case studies
- Remains unclear what adaptations (REACH Annex XI) may be assessed as (in)sufficient
- Lack of transparency but expected for a **new** approach...
- Message 2: We need exemplar case studies
- Message 3 (to 'early adopter' companies/REACH consortia using NAMs): Keep taking risks, your role in advancing NAMs is essential!



