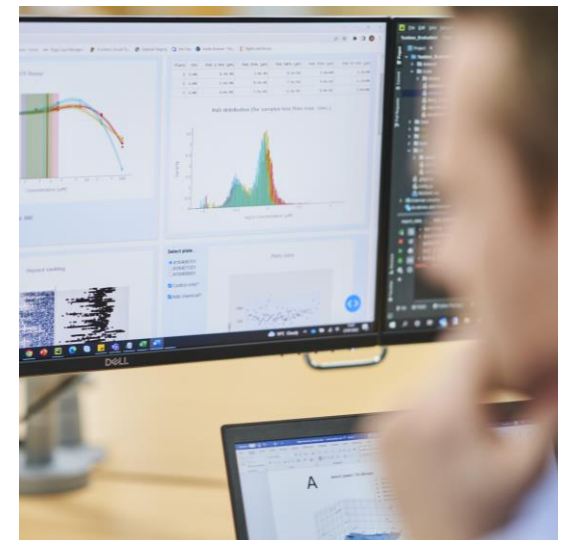


# **A tiered approach to risk assess microbiome perturbations induced by application of beauty and personal care products**

**Aline Métris, Safety and Environmental Assurance Centre (SEAC), Unilever**

# Introduction to **SEAC** and Risk Assessments

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



# 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

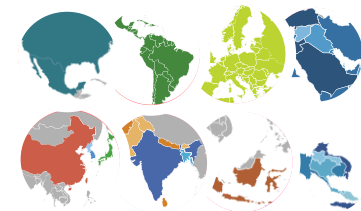


## Business Group R&D

**Global Teams**



**Business Units**



## 'One R&D' Centre

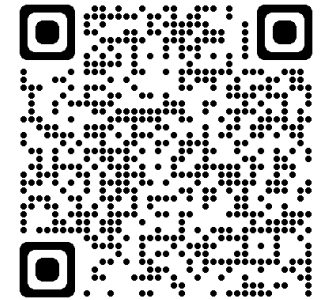
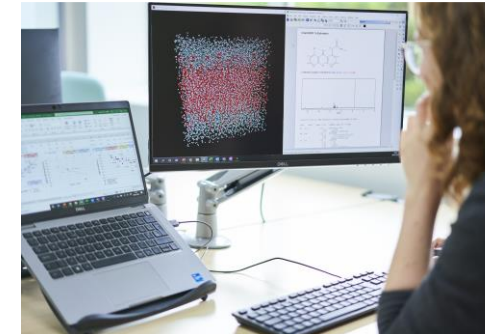
**Safety, Environment & Regulatory**

**Digital & Partnerships**

**Sustainable Packaging**

# Team SEAC's purpose is to **protect people & the environment** by ensuring: Unilever's products & innovations are Safe & Sustainable by Design without animal testing

- Around the world, 3.4 billion people use a Unilever product every day.
- We use **scientific, evidence-based approaches** to ensure that our products and innovations are safe & sustainable without animal testing.



## Responsible Innovation



Unilever conducts responsible, safe and sustainable research and innovation, which fully respects the concerns of our consumers and society. In meeting consumer needs, Unilever's innovations are based on sound science and technology, and reflect high standards and ethical principles.

Unilever has global standards that apply to all research and innovation, including on: the safe and sustainable design of new products, processes and packaging; product and brand development; open innovation collaborations; and publication of our scientific research.

**Musts**

All employees involved in scientific research and innovation activity **must** comply with all standards relevant to their area of work, notably in order to:

- Ensure that risks for consumer safety, occupational safety and the environment are suitably assessed and managed
- Ensure appropriate specifications of raw materials, products and packaging
- Ensure effective management of consumer safety risks from food allergens
- Ensure research on human subjects is conducted to the highest ethical standards

Uphold Unilever's commitment to eliminate animal testing without compromising on consumer safety (see Developing Alternative Approaches to Animal Testing)

- Ensure the integrity, robustness, objectivity and transparency of all scientific research and collaborations with external partners (see Unilever's Position on Science with Objectivity and Integrity)
- Maintain and make accessible records of all research, including study protocols and data, and their interpretation and decisions made
- Raise any concerns about actual or potential non-compliance with this Code Policy with their Business Integrity Officer, Line Manager or their relevant Business Partner in R&D

**Must nots**

Employees **must not**:

- Deliver presentations or publications that have not been approved via internal clearance procedures
- Collaborate with third parties outside a structured and approved contractual framework

Innovation is fundamental to Unilever's business success and a core part of our global strategy. The integrity and objectivity of our Science are a key foundation for our approach to responsible innovation. Safety is non-negotiable.

Unilever | Business Integrity Principles | Countering Corruption | Respecting People | Safeguarding Information | Engaging Externally | Glossary | 13

## Safety and Environmental Science

We want consumers to be confident that our products are safe for them and their families, and better for the environment. The scientists at Unilever's Safety and Environmental Assurance Centre (SEAC) play a key role in ensuring that our products are safe and environmentally sustainable.



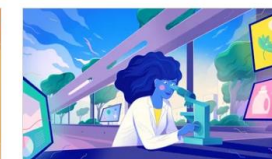
### Leading safety and environmental sustainability sciences

The scientists behind our safe and sustainable products



### Safe and sustainable by design

How we build safety and sustainability into every product innovation.



### Keeping people and the environment safe

The science-based approaches we use to keep our consumers, workers and the environment safe.



### Reducing our environmental impact

How we harness the latest science to minimise our environmental footprint.

<https://www.unilever.com/planet-and-society/responsible-business/product-safety-and-quality/>

<https://www.unilever.com/planet-and-society/safety-and-environment/>

# Introduction: Risk Assessments (RA) approaches

## Microbiology & food

CODEX ALIMENTARIUS  
INTERNATIONAL FOOD STANDARDS



**C O D E X**  
ALIMENTARIUS  
International Food Standards



PRINCIPLES AND GUIDELINES FOR THE CONDUCT OF MICROBIOLOGICAL RISK ASSESSMENT  
CAC/GL 30-1999

Adopted 1999. Amendments 2012, 2014.

### Exposure assessment

Frequency and level at the point of application

e.g. skin/oral microbiome



### Hazard identification & characterisation

hazard=agent capable of causing adverse health effect

Hazard characterisation = Nature/intensity of adverse effect as a function of the dose

NOT AVAILABLE for product-induced changes to the microbiome



### Risk characterisation

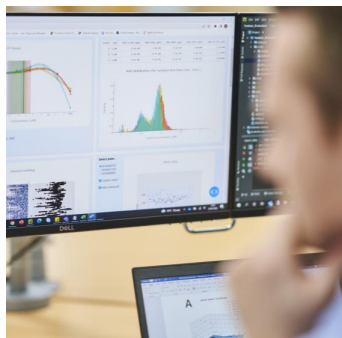
= likelihood X severity of the adverse effect

With uncertainty and variability

## Toxicology

**Next Generation Risk Assessment (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

# The microbiome and risk assessments



The microbiome composition has been correlated to health and disease states (e.g. psoriasis, acne, atopic dermatitis, caries, periodontitis...) however there is no definition nor characterisation of microbiome dysbiosis.

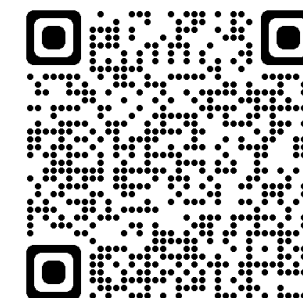
- Need an alternative approach to “traditional” CODEX-type risk assessments
- Experimental data need to be sought at the point of application rather than in products i.e. in clinicals
- Only relative risk assessments can be presently carried out



A tiered approach to risk assess microbiome perturbations induced by application of beauty and personal care products

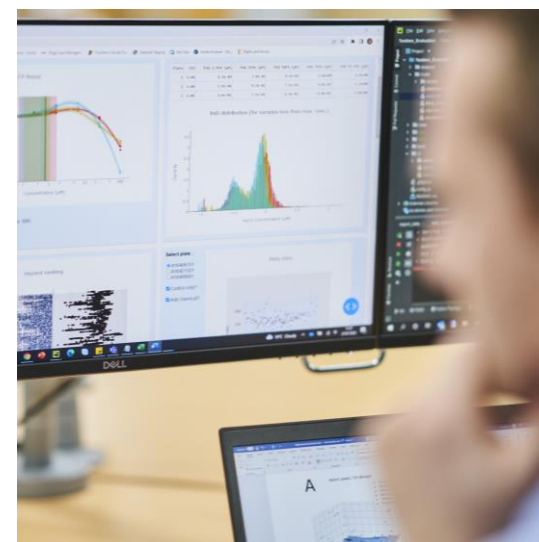
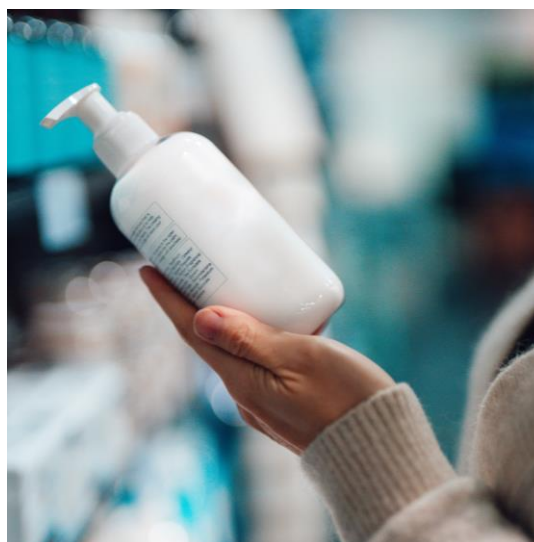
Aline Métris<sup>\*</sup>, Paul Barrett, Laura Price, Silvia Klamert, Judith Fernandez-Piquer

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



<https://doi.org/10.1016/j.mran.2021.100188>

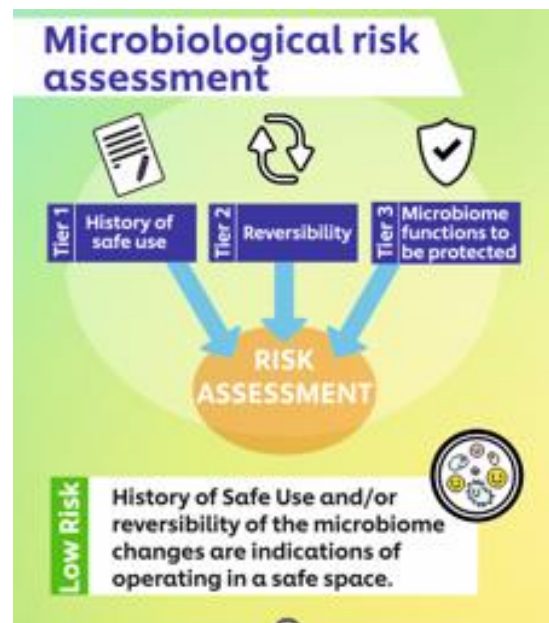
# A tiered framework approach



# A tiered framework to risk assess perturbations induced by the application of beauty and personal care products

## Tier 1 History of Safe Use (HoSU)

Has the technology been on the market long enough without adverse effects at higher or similar levels or does it impact the microbiome less than marketed technologies with a HoSU?



## Tier 2 Reversibility of change

Test with a clinical study whether the technology induces a permanent change in the microbiome

## Tier 3 Microbiome functions to be protected – Research using in silico-in vitro- clinical experiments to characterise endpoints

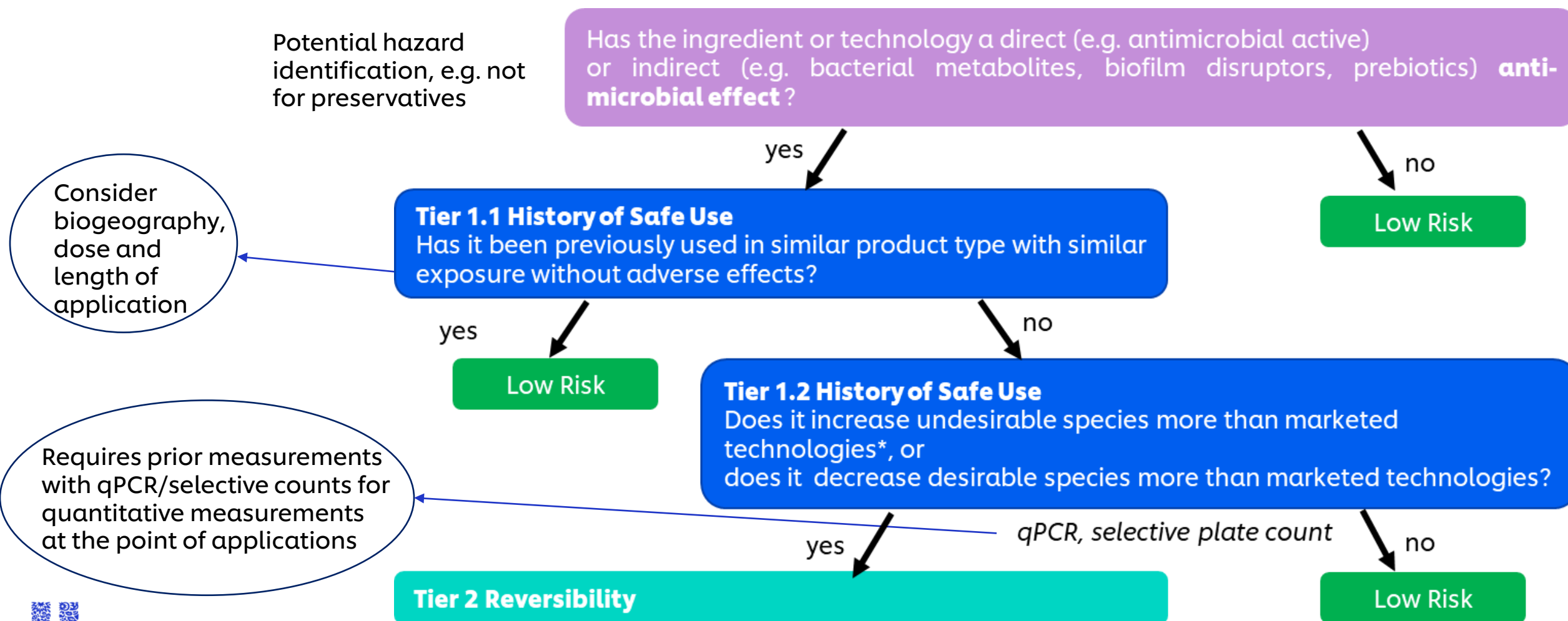
- Protection against pathogen colonisation
- Environmental conditions still conducive to a functional community, e.g. resilience
- Host functions, such as immune response, barrier function or trans-epidermal water loss (TEWL)

*Resilience is the capability of the microbiome to withstand perturbations without becoming dysbiotic. It has been identified as a key factor characterising health but is difficult to assess.*



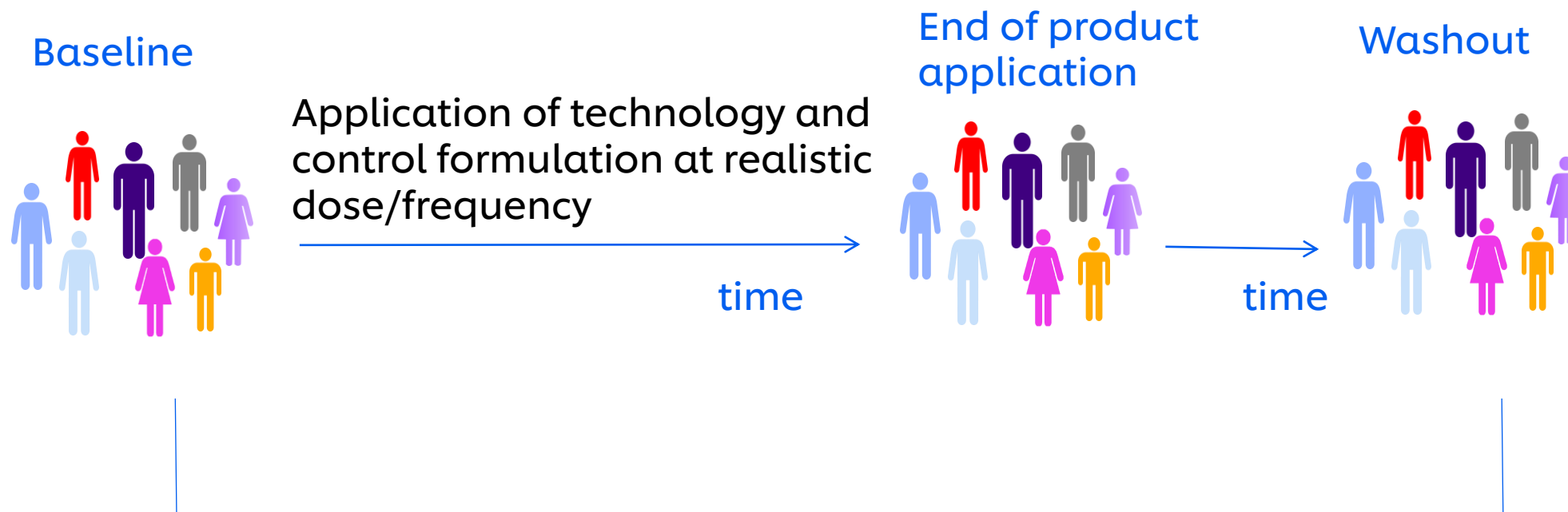
# Tier 1: History of Safe Use

## i.e. comparison to marketed formulations



## Tier 2: Reversibility of change

i.e. the microbiome returning to its initial state after a period of application and washout is evidence of low risk – relative RA.



Comparison of the microbiome composition between baseline and washout

- Including a **control/placebo** to define significant change
- Including qPCR for **quantitative** representation of the microbiome
- Considering **people variability** in the statistics (and control on the same person where possible)

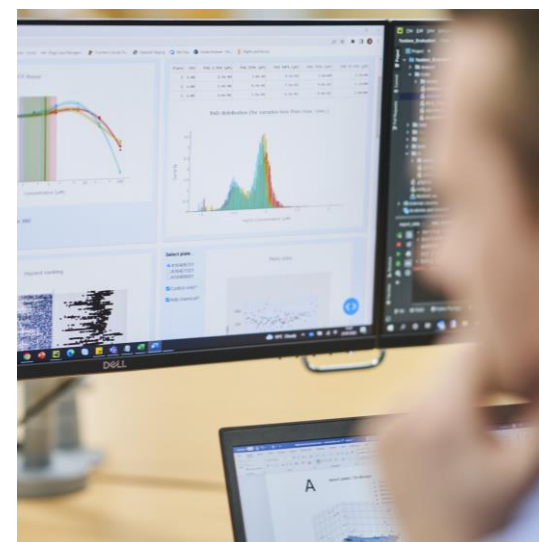
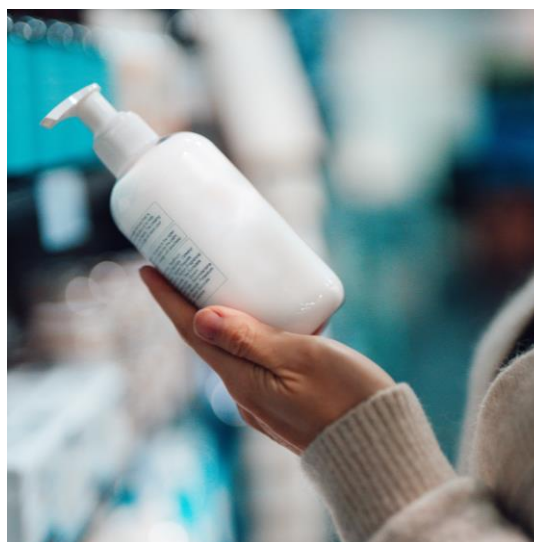
## Tier 3: Some challenges with defining & characterising the functions to be protected for a healthy microbiome

### Tier 3 Microbiome functions to be protected

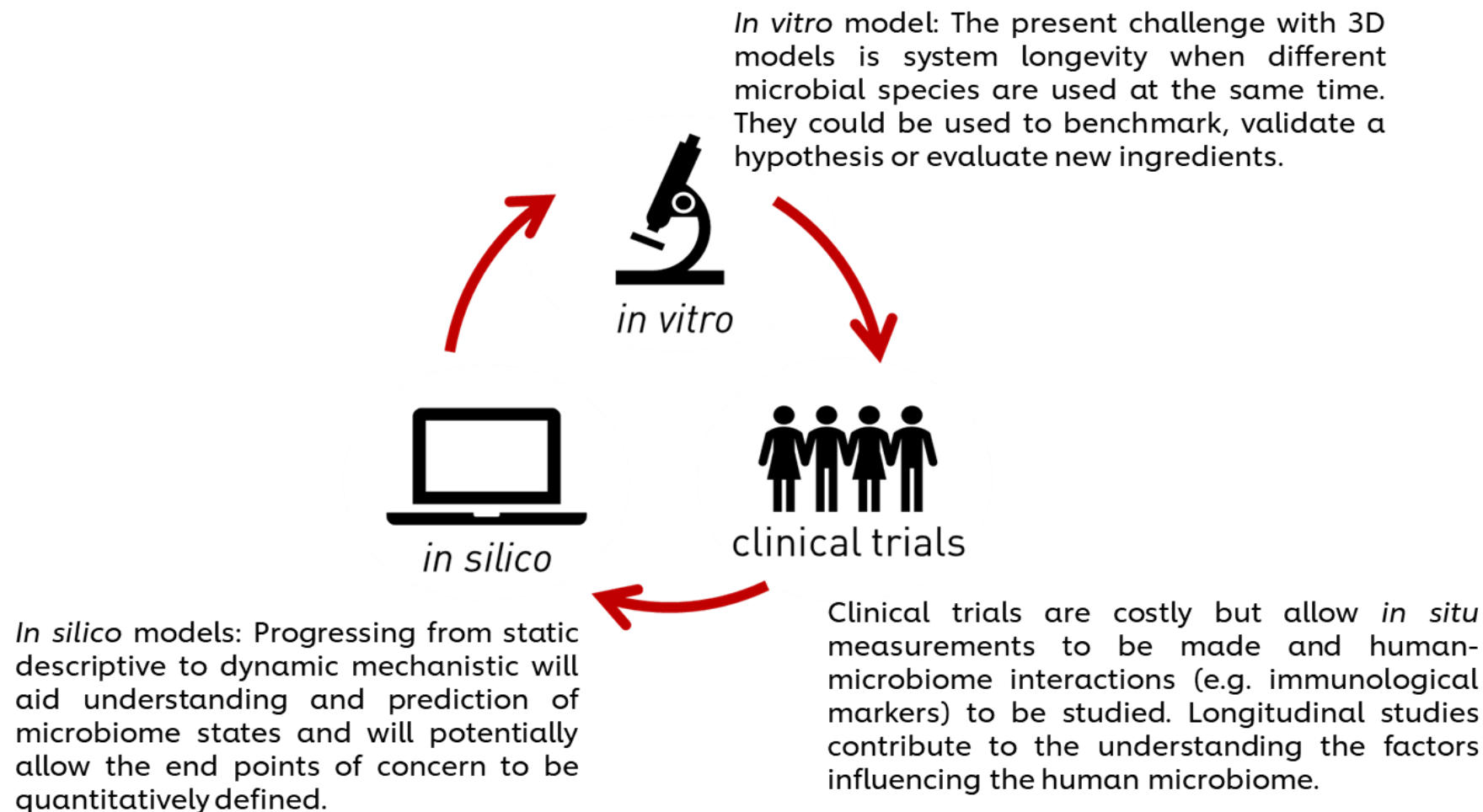
- Protection against pathogen colonisation
- Environmental conditions still conducive to a functional community, e.g. resilience
- Host functions, such as immune response, barrier function or trans-epidermal water loss (TEWL)

- Defining the factors influencing resistance to colonisation .
- Resilience is a “complex” notion involving time evolution with no agreed definition.
- How host functions are affected by the microbiome such as barrier function/immune response is not fully established and is context dependant (e.g. in population at risk).
- Defining meaningful functions rather than taxa based on -omics data; e.g. which -omics, their integration, definitions of pathways/functions and their interpretation?
- Microbiome data bias (Western countries) and limited metadata in the public domain, no embedded “control” for batch effects, power needed because of people variability.

# Towards mechanistic insights



## Towards mechanistic insights: combining *in silico*, *in vitro* and clinical experimental approaches



<https://doi.org/10.1016/j.mran.2021.100188>

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