98TH ADVISORY FORUM
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MICROBIOMES IN REGULATORY SCIENCE- EMERGING CHALLENGES AND REGULATORY READINESS

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EUROPEAN FOOD SAFETY AUTHORITY

OUTLINE

- **WHY MICROBIOME & WHY NOW? Strategic context & the challenge**
- **ARE WE PREPARED? Taking stock**
- **EFSA'S RESPONSE Addressing the gaps**
- **THE PATH FORWARD Joining Forces**

MICROBIOME-RELEVANT SCIENTIFIC AREAS

Microbiomes relevant to many EFSA domains

Probiotics, health claims

Virulence

Pollutants, plastics

Soil, biological control agents, plant pathogens

Pesticides, pathogens (e.g. bacteria, fungi), biological control agents

Enzymes, emulsifiers, artificial sweeteners

Expected Operational Result 2.1.3

The quality of scientific guidance and methodologies, with the necessary risk assessment capabilities, is improved to address future challenges

KEY ACTIONS

- Ensure forward looking engagement with partners and stakeholders to achieve synergies on Risk Assessment topics of mutual interest and facilitate the development and implementation of harmonised risk assessment methodologies
- Integrate, bioinformatic and cheminformatics approaches, technologies and data into next generation risk assessment
- Consider how microbiomes could be included in risk assessment, and develop tools to enable this
- Keep EFSA's risk assessment processes updated in line with evolving regulatory, policy and quality drivers (TR)

MICROBIOME: A STRATEGIC EU (& INTERNATIONAL) PRIORITY

EU policy Framework

Microbiome-based solutions/innovations promoted by:

- Life Sciences Strategy 2025
- Bioeconomy Strategy
- Food 2030
- Several EU Horizon projects

EU Health Regulation

- **SoHO Regulation** (taking effect in 2027)
- **Microbiome-based live biotherapeutic products** (European Medicines Agency (EMA)) has received first application)

INTERNATIONAL

FAO

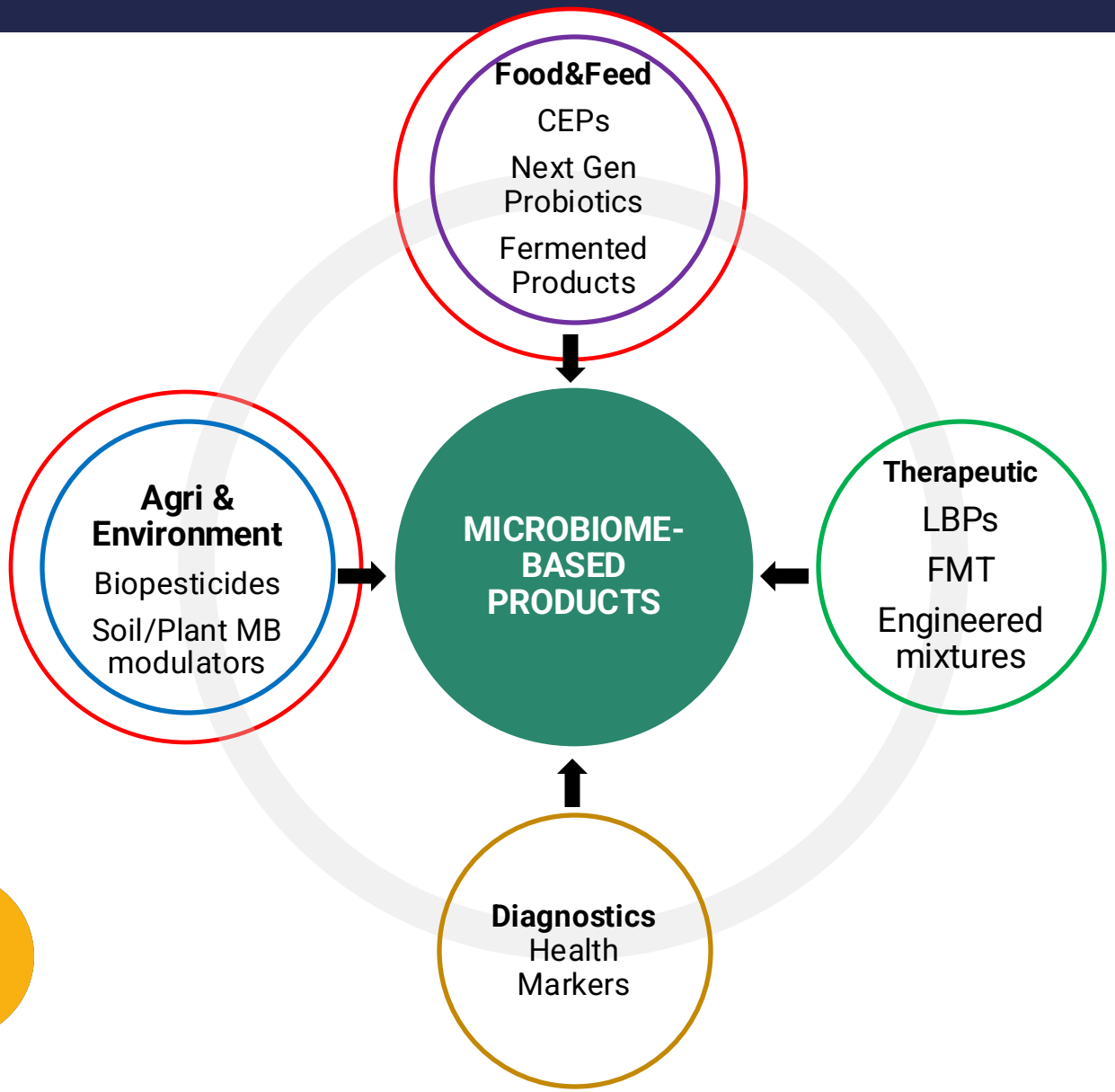
- Microbiome-based solutions for sustainable agrifood & nutrition, food safety, chemical risk assessment

US FDA

- Establishing regulatory science focus areas for microbiome products

Cross-sectoral momentum signals increasing risk assessment needs across multiple product categories

MICROBIOME PRODUCTS PIPELINES- STRONG PUSH FOR INNOVATION



Microbiome-based products market is growing rapidly (GMI, June 2025)

Multiple types: challenging FWs

- ❑ CEPs: Competitive exclusion Products as Feed additives
- ❑ Fermented Products: Undefined communities
- ❑ Novel foods: multi strains, Akkermansia
- ❑ Biopesticides: microbial consortia

Current Situation

- ❑ Products being/are developed
- ❑ Applications submitted soon?
- ❑ Risk assessment frameworks fit for purpose?

MICROBIOME-BASED PRODUCTS-FOOD & FEED EXAMPLES

Competitive exclusion products (CEPs) as feed additives

- **Composition:** Microbiome material from poultry cecum
- **Benefit** Prevents pathogen colonisation
- **Status:** Already developed

Complex Fermented Products

- **Composition:** Multi Strain complex probiotic drinks, wild fermentation beverages
- **Benefit** Marketed as food supplements with health claims
- **Status;** Already developed

Common challenges

- Undefined microbial communities/composition
- Genome screening (AMR, Pathogen detection, etc)
- Interactions with host microbiome
- Community functional effects and stability unclear

FRAMEWORK NEEDED

- Characterisation methods
- Safety screening methods
- Host interaction assessment
- Functional evaluation tools

WHY CURRENT FRAMEWORKS ARE INSUFFICIENT

Current Frameworks

√ What Works

- Single strain
- Culturable organisms
- Traditional identification methods
- Individual/few strain safety criteria
- Established approaches

VS

Microbiome Products

X What Doesn't Work

- Undefined complex microbial communities
- Non culturable organisms
- Unknown community interactions/effects
- Dynamic ecosystems
- No established frameworks

Regulatory gap highlighted: New EFSA Microbiology Guidance (2025) - Standardised frameworks needed for products containing/produced from complex communities & recipient ecosystems

EFSA PREPARATORY WORK (BUILDING THE FOUNDATION)-ROADMAPS FOR ACTION 2024

HUMAN & ANIMAL GUT MICROBIOME

- Xenobiotics effects on gut microbiome
- Health outcomes assessment
- Critical gaps identified for regulatory science

ENVIRONMENTAL MICROBIOMES

- Soil, water, plants etc microbiomes
- One Health connections
- Food safety implications

BUILDING CAPACITY FOR MICROBIOME-INFORMED RISK ASSESSMENT

Systematic Gap analysis → Coordinated action needed

OMICS TECHNOLOGIES

- Metagenomics and other Omics for microbial characterisation
- Regulaotry application framework

CRITICAL KNOWLEDGE GAPS IDENTIFIED

01

Identity, Functional & Stability Characterisastion

Cannot **identify/characterise** all organisms in complex mixtures/products.

02

In Vitro Models

No **standardised/validated** systems for testing microbiome products

03

Causality, AOPs & Mechanisms

Cannot establish **cause effect relationships** for microbiome changes

04

Biomarkers

No **validated** markers linking mcirobiome changes to health outcomes

05

Population Baselines

Insufficient **reference data** for “normal” vs “harmful”- microbiome variation

06

Safety Frameworks

No frameworks for **complex mixtures** level safety assessment.

Methodological

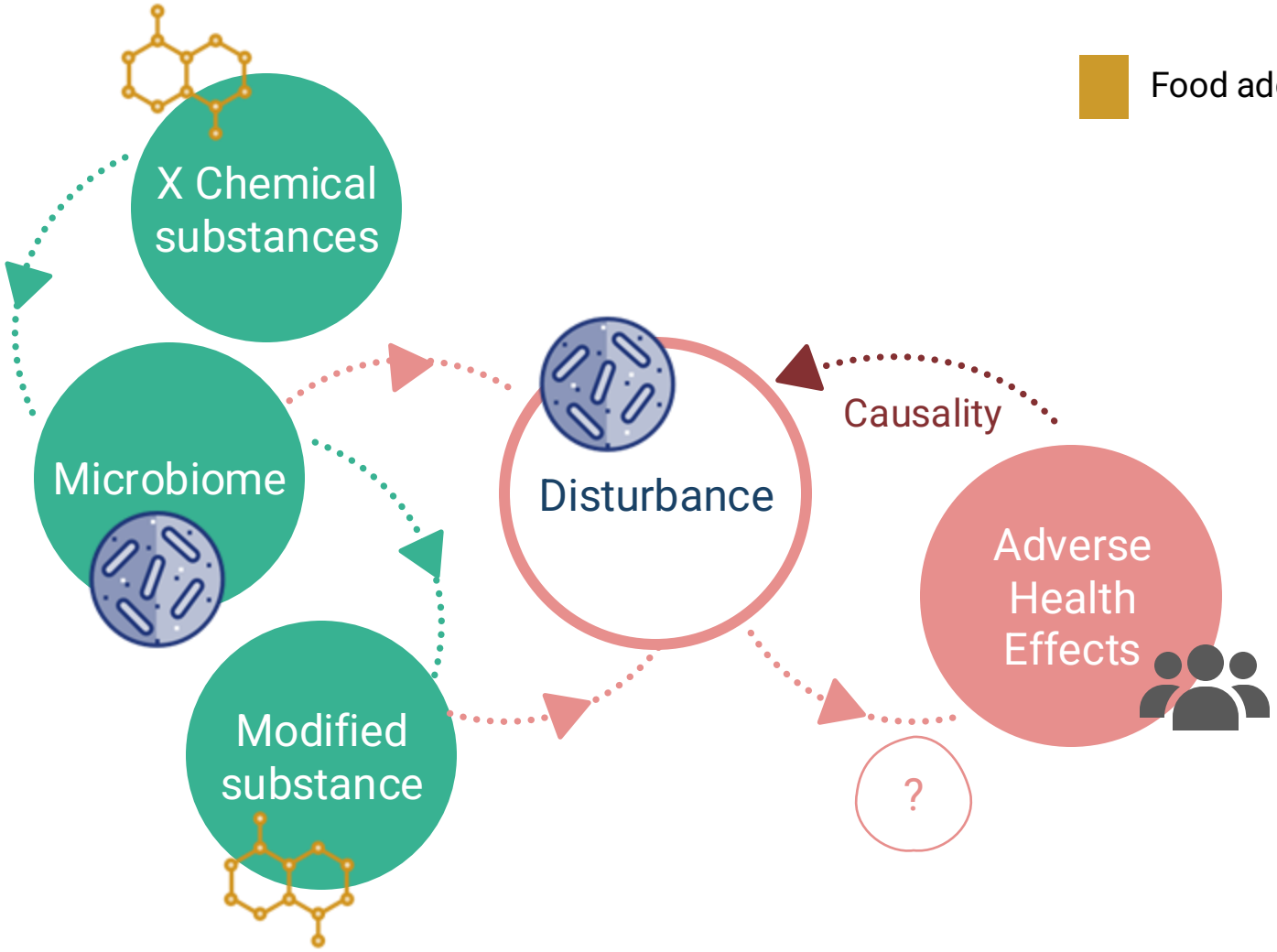
Understanding

Frameworks

Additional important gaps

XENOBIOTICS EXPOSURE–MICROBIOME: ANOTHER IMPORTANT ANGLE

Gut Microbiome roadmap



MEMBER STATES ACTIVITIES/CAPACITY

JOINING FORCES INITIATIVE

- Focal Point Outreach: "What microbiomes-related work is happening in your Country?“
- Bilaterals with member states

14
Member States
With documented activity or interest

4
Supporting EU Framework

5
Regulatory Science Active

Three Levels of Engagement

Tier 1

REGULATORY FRAMEWORKS

- **Italy** –National Framework Proposal
- **Poland** – Long standing experience, Calls for EU FW
- **Germany** – Microbiome data assessment pipeline

Tier 2

ACTIVE PROGRAMS

- **Denmark** - Xenobiotic RA
- **Netherlands** -EU-wide reference database/EU vision
- **Cyprus** – Feed & soil health projects

Tier 3

RA GAP + RESPONSE

- **Lithuania** - Regulatory gap for fermented multi strain products, developing criteria

KEY MS CONTRIBUTIONS & CALLS FOR ACTION

Poland

Specific Recommendations to EFSA:

Standard procedures for microbiome RA

Data/methodology exchange platform

~20 years capacity 3 institutions | Advanced omics

Germany

Automated Pipeline for possible EU-Wide Use:

- Developing microbiome data assessments
- Pathogen detection, virulence, AMR genes
- Microbiome-food interactions

EFSA ADME4NGRA collaboration

Italy

ISS 2025 Report- National FW tailored to EFSA work

- Methodologies for systematic inclusion
- One Health integration across domains

5 active IIZZSS projects | EUPAHW partnership

Lithuania

Request for EU-level Guidance for novel complex microbial products

Active National Response:

- National project developing microbiological criteria & advanced methods (e.g. Omics)
- Explicit request for EFSA guidance

Baltic region issue | Metagenomics/metabolomics approach

INTERNATIONAL ACTIVITIES & COORDINATION

Global efforts building microbiome regulatory science capacity

FAO

OH/REGULATORY

Soil & gut microbiome work, xenobiotic assessments (JECFA, JMPR), policy, capacity building

WHO

STANDARDS

International Reference Reagents, methodology harmonisation, quality standards

US FDA

REGULATORY

Standardised methodologies, regulatory science focus areas

Health Canada

TESTING

Testing platforms for microbial mixtures, safety assessment methods

World Microbiome Partnership

COORDINATION

Global platform for research coordination, knowledge exchange

EFSA PROJECT CALL 1: METAGENOMICS FOR COMPLEX MICROBIAL MIXTURES AS REGULATED PRODUCTS

EFSA RESPONSE: KIC Biotechnology led activities to prioritise knowledge gaps and propose **two Projects** to address some key gaps

Project Objective

Develop **fit-for-purpose metagenomics protocols and analytical frameworks** for characterising and assessing safety of complex microbial mixtures as regulated products

Gap addressed:
Traditional microbiological characterisation approaches are primarily designed for single organisms, creating a methodological gap for products with complex multi-species products

Budget
€ 1.25 M

Timeline
1.5 yrs

Case study
CEPs

Call launch
Jan/Feb 2026

KEY DELIVERABLES

- Standardised metagenomics protocols
- Safety screening methods (AMR, virulence, pathogens)
- Technical recommendations for data interpretation

IMPACT

- Facilitates assessment of **Competitive Exclusion Products** (CEPs) as feed additives
- Supports microbiology RA guidance
- Foundation for broader metagenomics adoption in RA

EFSA PROJECT CALL 2: MICROBIOME BIOMARKERS FOR RISK ASSESSMENT

Project Objective

Develop foundational methodological elements for integrating biomarker data into RA frameworks, supporting evaluation of dietary compounds and products effects on gut microbiome and host health

Gap Addressed :
Lack of fit for purpose biomarkers and in vitro models to assess dietary effects on microbiome and host health

Budget
€ 1.3 M

Timeline
3 yrs

Case study
Selected xenobiotics

Call launch
Feb/Mar 2026

1

Phase 1 € 300K; 1 year
Systematic Meta-Analysis

- Systematic biomarkers review
- Assess in vitro model capabilities
- Define optimal biomarker-model pairings
- Identify analytical methods

Milestone: Go/No-Go decision for Phase 2 based on findings

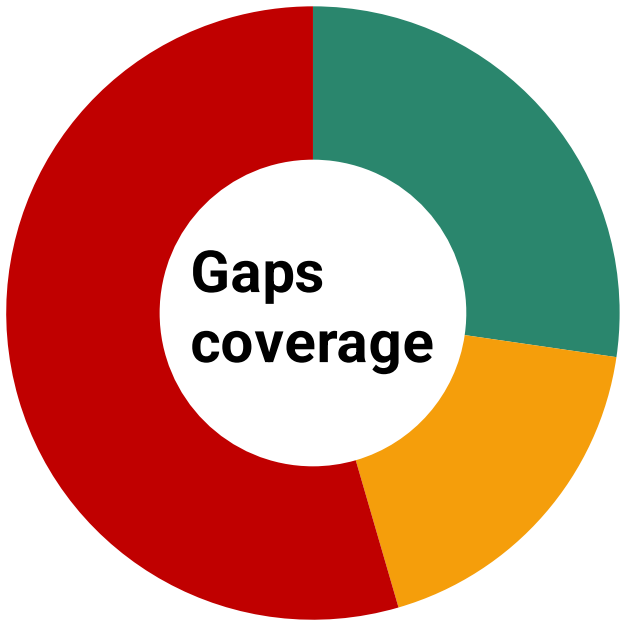
2

Phase 2 € 1M; 2 years
Experimental Testing

- Test prioritised biomarker-model combinations
- Assess microbiome & host responses
- Generate RA relevant data

Outcome: Technical recommendations for RA implementation

KNOWLEDGE GAP COVERAGE: PROGRESS ASSESSMENT



✓ Addressed (3)

Characterisation: Metagenomics protocols (P1)

Biomarkers: Validated endpoints (P2)

In Vitro Models: Model validation (P2)

◐ Partially Addressed (2)

Causality, AOPs & Mechanistic: e.g. dose-response, mechanistic FW remain (P2)

Safety Frameworks: CEPs enabled; broader product frameworks needed (P1)

✗ Not Addressed (6)

Important gaps: Population Baselines & Variability • Data Standards, Harmonisation & Reference DBs • In Vivo Validation • Functional/Efficacy Assessment • Long-term Effects & Persistence • In Silico Predictive Models

POSSIBLE COLLABORATION OPPORTUNITIES

EFSA Project Calls
Apply to metagenomics and biomarkers project Calls

Technical Discussion Group Creation
Expert exchange (e.g. on methodology, data standards. share information on various projects) and coordination

Workshop/Colloquium
Focused meeting on specific technical topics (co-planned/scoped by discussion group

Joint Future Projects
Joint (co-funded?) regulatory science initiatives, share resources

WHAT IS NEXT – POTENTIAL QUESTIONS & TIMELINE

Phase 1 Initiate — Q1-Q2 2026

- EFSA project calls open (Jan-Mar 2026)

1 How can we close the critical gaps together?
What approaches or methodologies could MS contribute?

2 Who addresses what gap based on available MS capabilities/expertise?
Relevant research groups, infrastructure, datasets?

Phase 2 Action — 2026-2027

- Discussion group active
- Colloquium (~Q4 2026 onwards)

3 Interest in EFSA calls or discussion group?
Participation in projects or technical group/discussions?

4 Additional challenges for RA incorporation?
What other gaps or concerns should we address?

Phase 3 Scale — 2027-2030

- Projects deliver results
- Build EU Regulatory capacity
- Develop (phased) harmonised guidelines
- Achieve (phased) EU-wide preparedness

Why Work Together Now?

- Products arriving before frameworks ready
- Critical gaps require MS collaboration
- Shared benefit across EU regulatory system
- International momentum building globally

Thank you

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