4th meeting of the Advisory Group on Biomarkers of Effect (AGoB)

16 March 2026
09:00-13:00 CET
MEETING MINUTES

Location: Online

Participants:

- AGoB members: Denis Sarigiannis (Chair, EL), Georgieva Tzveta (BG), Ilse Van Overmeire (BE), Ivana Vinković Vrček (HR), Elliott James Price (CZ), Anne Mette Zenner Boisen (DK), Gilles Rivière (FR), Tewes Tralau (DE), Francesco Capozzi (IT), Karolina Žiogelytė (LT), Georges Kass (LU), Marcel Mengelers (NL), Susana Viegas (PT), Milada Syčová (SK), Manca Ahačič (SL), Mariana Fernández (SP), Mattias Öberg (SE)
- Observers: Robert Pasanen-Kase (CH), Frans Verstraete (EC)
- Hearing Experts: Antonio Hernández-Jerez, Eva Cecilie Bonefeld-Jørgensen
- EFSA: Lucian Farcal and Mina Ristovska (MESE), Zainab AL Harraq (FIP), Silvia Valtuena Martinez (NIF), Anna Christodoulidou (FEEDCO), Iris Mangas (PREV)

Apologises were received from Observer Athanasios Raikos (EC).

1. Welcome

The Chair welcomed the participants to the 4th meeting of this group. The new member of the AGoB (Georges Kass, LU) was introduced.

2. Adoption of agenda

The agenda was adopted without changes.

3. Project overview and AGoB's work plan 2026

Presentation by Lucian Farcal (EFSA).

The AGoB members were informed on the transition from the initial EFSA self-task mandate to the newly joint mandate involving EFSA, EMA and ECHA, which formally began in February 2026 and sets the framework for developing harmonised EU guidance on biomarkers of effect (BoEs). They were presented with an overview of the project structure, including the roles of the different WGs co-chaired by the three agencies, and the link to the Advisory Group or other stakeholders group, which will provide scientific input throughout the guidance development process. The guidance is to be developed over three years, with a draft outline expected by January 2027 and final guidance by April 2029.

The first steps under the new mandate include mapping key resources at each agency, harmonising terminologies and identifying different contexts of use and their possible impacts, which will inform the drafting of the guidance outline.

The 2026 work plan was outlined, highlighting the schedule of online and in-person meetings and key tasks such as reviewing draft guidance materials, discussing examples of BoEs, and contributing to knowledge transfer. The group was also encouraged to prepare independent statements or reports to complement the guidance development.

Furthermore, AGoB meetings will continue to serve as a platform for knowledge exchange with external initiatives and projects, facilitating the integration of new research and regulatory developments into the guidance.

Finally, with no further comments, the AGoB 2025 Annual Report was considered endorsed and will proceed for EFSA approval and publication in EFSA Supporting Publications.

4. Regulatory, scientific and technical topics for discussion

4.1 Criteria for the evaluation and selection of BoE: overview and discussion

Presentation by Lucian Farcal (EFSA) and Antonio Hernández-Jerez (Hearing Expert).

During this agenda item, the group was presented with an overview of the draft criteria[1] proposed for evaluating and selecting BoEs, followed by an in-depth discussion. The criteria were structured into four main categories: analytical aspects (e.g. measurability, assay validation, reproducibility), biological aspects (e.g. specificity, sensitivity, mechanistic relevance, human relevance), contextual and regulatory aspects (e.g. clarity of purpose, regulatory applicability, feasibility), and data and ethical standards (e.g. data robustness, ethical considerations, overall quality requirements). A tiered approach was briefly introduced to distinguish BoEs according to their intended use, for screening and prioritisation, for hazard identification and for hazard characterisation, each requiring increasing levels of evidence and validation. Several members provided feedback on improving the clarity of the tier definitions, which will be considered in the next iterations.

Participants discussed the need to incorporate additional aspects, such as confounding factors (e.g. age, sex and lifestyle), and highlighted the importance of omics data and multi-biomarker panels. Challenges such as differentiating between adaptive and adverse effects were also addressed. The importance of linking BoEs to Adverse Outcome Pathways (AOPs) and accounting for mixture assessment considerations was emphasised. Overall, the discussion supported refining the criteria to ensure scientific robustness, practical applicability and adaptability to future developments.

4.2 Proposal for annex on occupational effect-biomonitoring to enable further harmonisation in risk assessment

Presentation by Robert Pasanen-Kase (CH).

During this agenda item, the group was presented with an overview of recent OECD activities related to effect biomarkers. The presentation summarised outcomes from work aimed at harmonising principles for using effect biomarkers in mixture risk assessment, including guidance on occupational biomonitoring and the derivation of effect-based trigger values. Two OECD guiding principles were highlighted: Mixture threshold derivation from effect biomarkers and Advancing occupational mixture risk assessment with effect biomarkers. A harmonised concept for assessing effect biomarkers and mixtures was presented, supported by case studies using different biomarkers across four toxicity domains, demonstrating its practical feasibility. The concept clarifies existing assessment knowledge levels and guides the transition from scientific use to regulatory application. It is compatible with Occupational Biomonitoring Levels and HBM Guidance Values developed under PARC and can be combined with NAMs and omics approaches. The framework also supports environmental and

[1] *The document represents an early draft developed by the EFSA WG during a previous phase of the project under the self-task mandate M-2023-00097. Therefore, the content reflects only the initial views of the EFSA WG at that earlier stage and does not incorporate input from the partners involved in the new joint mandate.*

occupational mixture assessments and was recommended as a useful contribution to the One Health approach.

The presenter proposed incorporating this harmonised OECD approach as an annex to the future EU guidance, ensuring flexibility of the core document while providing practical recommendations. The group discussed the process for developing such annexes, including consultations at the AGoB level and subsequent evaluation by the coordination and drafting WG. Overall, the proposal aims to enhance consistency, transparency and cross-sectoral alignment in applying effect biomarkers to occupational and mixture risk assessment.

4.3 Exploratory review – methodologies using BoE in chemical risk assessment

Presentation by Mina Ristovska (MESE).

An overview of the exploratory literature review on methodologies for applying biomarkers of effect in chemical risk assessment was presented. The review examined recent studies with a focus on AOP integration and quantitative modelling approaches. A structured Scopus search (2020–2025) identified 133 studies, of which 54 met predefined criteria, including measurable biomarkers, AOP linkage, derivation of reference points and applicability for in vitro to in vivo extrapolation. The selected studies covered a wide range of biomarker types (e.g. omics, in vitro, in vivo) and addressed various toxicity domains such as genotoxicity, hepatotoxicity and neurotoxicity, using methods such as benchmark dose (BMD) and PBK modelling.

The discussion on the preliminary data highlighted challenges in identifying studies that effectively translate in vitro results to in vivo outcomes, as well as the need for strong AOP links and consideration of both early and apical effects. The group agreed that the review methodology is appropriate for identifying and compiling relevant scientific articles into an internal database and for continuing to extract methodological elements for potential inclusion in the guidance.

4.4 Examples of biomarkers of effect used for the identification of acute and chronic nephrotoxicity in humans

Presentation by Marcel Mengelers (NL).

An overview was provided on the use of biomarkers for assessing acute and chronic kidney effects, illustrating current clinical practice, the role of AOPs and barriers to adopting new effect biomarkers. Clinical assessment of acute and chronic kidney conditions relies on established markers such as creatinine, cystatin C, and the albumin/creatinine ratio, with an increasing use of multi-biomarker panels.

Recent developments include the emergence of new biomarkers and the integration of multi-omics and artificial intelligence, although further validation and standardisation are still required. Key barriers remain heterogeneity in biomarker performance, limited standardisation, lack of regulatory acceptance and cost-effectiveness considerations.

It was noted that a broad range of (pre)clinical effect biomarkers exists, many still requiring confirmation of their clinical relevance, though some may be more applicable in toxicological contexts. Progress is ongoing through the use of multi-biomarker panels and early AI-assisted approaches. Within the PARC project, HBM toxicological values based on effect biomarkers have already been derived for metal(loid)s, demonstrating potential regulatory application. The discussion highlighted that while AOPs help identify key events, they do not always lead directly to practical biomarkers, and quantitative dose-response data remain essential yet

often lacking. The examples underscored the need for quantitative cut-off values and the potential usefulness of semi-quantitative risk classes in regulatory settings.

4.5 Knowledge exchange with the Partnership for the Assessment of Risks from Chemicals (PARC)

Presentation by Eva Cecilie Bonefeld-Jørgensen (Hearing Expert).

An overview was provided on ongoing activities within the PARC Effect Marker Group (Task 5.3.2), which focused on identifying and validating effect biomarkers across endocrine, immune, metabolic, neurotoxic and epigenetic domains.

The work relies on AOP-based approaches to identify and evaluate biomarkers relevant to mammalian pathways, supporting both epidemiological and experimental applications. For each domain, relevant AOPs, promising effect markers and existing gaps in clinical biomarkers have been identified, with several reviews published or under preparation. Ongoing efforts include validation and integration of new findings. Future plans include expanding the inventory of AOPs, identifying additional effect biomarkers, incorporating clinical and experimental datasets. Once available, the relevant publications describing these methodologies will be shared with the AGoB to support their possible inclusion in the EU guidance framework.

5. Any Other Business

The outcomes of the meeting were summarised, confirming the process for publishing the 2025 annual report and outlining the iterative procedure for submitting proposals, annexes and other input to the guidance development process.

The next AGoB meeting will be held online on 27 May 2026 from 09:00 to 13:00 CET.

Further information on the AGoB activities is available on EFSA's dedicated webpage: https://www.efsa.europa.eu/en/advisory-group-on-biomarkers-of-effect.