Advisory Group on Biomarkers of effect (AGoB)
Minutes of the 3rd meeting

2 December 2025
9:30-17:30 CET
Minutes agreed on 22 December 2025

Location: Copenhagen, Denmark

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), Milada Syčová (SK), Manca Ahačič (SL), Mattias Öberg (SE)
- Observers: Francisca VAN DOESUMWOLTERS (EMA), Mounir BOUHIFD (ECHA)
- Hearing Experts: Antonio Hernández-Jerez, Susanne Hougaard Bennekou, Christina Pieper, Henk van Loveren, Ron Hoogenboom (Members of EFSA's Scientific Committee WG)
- EFSA: Lucian FARCAL (MESE), Zainab AL HARRAQ (FIP)

Apologises were received from AGoB members - Francesco Capozzi (IT), Karolina Žiogelytė (LT), Mark Cassar (MT), Marcel Mengelers (NL), Susana Viegas (PT), Mariana Fernández (SP); Observers - Robert Pasanen-Kase CH), Athanasios Raikos and Frans Verstraete (EC); Hearing Expert - Harry McArdle.

1. Welcome

The Chair welcomed the participants to the first physical meeting of this group.

2. Adoption of agenda

The agenda was adopted without changes.

3. Tour de Table

All participants introduced themselves.

4. Project overview and status of guidance development

An overview of the current progress on the development of the guidance on biomarkers of effect (BoE) was presented, outlining timelines, key milestones and the use of the outcome of Phase 1 of the project. The role of the advisory group was further clarified. The transition from EFSA Scientific Committee's self-task mandate to an anticipated EC joint mandate was explained. The newly established webpage of the AGoB was also announced.

Participants discussed the need for a horizontal guidance built on shared principles and minimum requirements, adaptable across regulatory contexts and agency workflows. Alignment among EU agencies (EFSA, EMA and ECHA) was highlighted as essential, noting differences in validation and acceptance of BoEs across sectors and the potential impact of introducing BoEs into risk assessments workflows. The project is positioned as a pilot within the one-substance-one-assessment approach. The proposed development steps start from an outline and iteratively progress toward more technical elements, including criteria for evaluation and selection, with representative examples. Integration of new approach methodologies (NAMs) and omics, the use of mechanistic evidence, clarity on definitions (e.g. adverse effects), handling uncertainties and benchmark responses (BMRs), and consideration

of quantitative AOPs were identified as core technical areas, along with recognition of current challenges and limitations.

The group discussed on proceeding iteratively, maintain cross-agency alignment and keep the guidance concise and practical with technical detail in annexes. Work will continue consolidating criteria and documenting lessons learned from different examples of BoEs. Updates will be shared with the group for feedback as the project advances.

5. Approaches and case studies from other initiatives

5.1 Introduction and exploration of potential areas and mechanisms for collaboration and knowledge exchange

The discussion focused on identifying opportunities for collaboration and knowledge transfer to strengthen the development and application of BoEs in regulatory contexts. Participants emphasised the importance of data sharing, harmonisation of methods and integration of BoEs into risk assessment frameworks. Existing resources, such as OECD guiding principles, as well as outputs from EU projects like PARC and ASPIS, were highlighted as valuable but underutilised assets. The need for concrete mechanisms beyond previous workshops and surveys was stressed, including joint activities and structured processes for knowledge exchange.

5.2 Opportunities of knowledge exchange with PARC WP5

Ongoing work within PARC WP5 on hazard assessment, innovative testing and AOP development was presented and discussed. The group explored concrete mechanisms to bridge research outputs from PARC and regulatory application, e.g. aiming to accelerate the integration of omics and NAMs into BoE guidance. Several examples of experimental studies were presented that could fit into future development of guidance. Future steps include the intensification of knowledge transfer within joint workshops and/or invitations of relevant PARC experts to AGoB meetings, therefore the group agreed to formalise a collaboration track with PARC WP5, focusing on co-developed workshops, targeted access to relevant datasets and tools.

5.3 Omics for regulatory applications

The session provided an overview of ongoing initiatives at the European Chemicals Agency (ECHA) to integrate omics and NAMs into regulatory science. The role and opportunities of using omics in modernising regulatory science and reduce reliance on animal testing was underlined. Such techniques can be integrated into current frameworks to link molecular data with adverse effects, identify modes of action and support the development of AOPs. Success depends on involving key stakeholders and embedding routine omics measurements into toxicity studies to ensure confidence and effective regulatory implementation. The discussion highlighted the potential of omics for advancing animal-free hazard assessment, while recognising the technical and interpretive challenges that remain.

5.4 Group discussion and conclusion on the collaboration opportunities

Several mechanisms for collaboration were proposed, such as joint workshops, and improved access to ongoing project outputs. Participants agreed that harmonisation and consistency should be prioritised to avoid duplication of efforts. The group debated whether the guidance should include a fixed list of BoEs or focus on criteria for evaluation; consensus leaned towards establishing robust criteria rather than exhaustive lists, given the dynamic nature of scientific progress. The discussion also addressed the complexity of defining adversity and adverse effects. Involvement of additional stakeholders, including the medical community and industry, should be considered to ensure relevance and facilitate translation from science to policy.

The group agreed to integrate existing methodologies and principles into the guidance, identify gaps that require further research and explore collaborative mechanisms with external initiatives such as PARC, ASPIS, OECD or other relevant projects, with a focus on transferring knowledge (e.g. data, tools, methodologies).

Additionally, it was proposed to develop use cases to demonstrate the application of guidance, once criteria and other elements of the methodology are established.

6. Working session to discuss, comment and refine the draft guidance and its examples

6.1 Draft guidance

The session focused on the draft guidance that aims to establish a harmonised framework for the use of BoEs in risk assessment. Its scope includes hazard identification and characterisation (including the identification of Reference Points (RPs)), using data from in vitro, in vivo and in silico approaches. The current draft of the guidance outlines the BoEs lifecycle, from identification, evaluation, selection and integration in risk assessment, supported by principles such as biological relevance, specificity, sensitivity, temporal concordance, quantification, etc. It was underlined that the guidance will not reinvent validation or qualification criteria but reference existing frameworks.

It was further discussed on the guidance aims to cover different applications of BoEs in risk assessment, the process for their use, and principles for evaluation and selection. Other key challenges discussed include handling complex datasets like transcriptomics, which require bioinformatic filtering and pathway analysis and defining BMRs for BMD analysis. The integration of quantitative AOPs was highlighted as essential. The uncertainty and the need of uncertainty factors were also discussed.

6.2 Examples of biomarkers of effect

An overview of BoEs examples was presented to illustrate their role in clarifying complex concepts, guiding method selection and enhancing the practical relevance of the guidance. An inventory and a lessons-learned annex are under development to document descriptors, classification schemes and critical discussions.

Key points included the need to expand examples beyond animal studies to include clinical BoEs and human applicability, as well as coverage of multiple exposure routes. The group discussed early versus late biomarkers, noting that definitions require clarification, and highlighted the importance of distinguishing individual-level from population-level relevance. Suggestions were made to include common BoEs across toxicity domains and non-invasive clinical biomarkers.

The inventory will use structured descriptors (e.g. biological matrix, assay, target organ, linkage to AOPs) and group BoEs by toxicity area, effect type and applicability. Lessons learned will be compiled in a dedicated annex to support harmonised documentation and regulatory use. Collaboration with other initiatives will help fill gaps and broaden the scope of examples.

7. Conclusions, AGoB work plan 2026, actions list and next steps

In conclusion, the group agreed to further explore and implement mechanisms for knowledge transfer, identify opportunities for EU projects to contribute their results to guidance development and establish direct contact with relevant initiatives, including inviting presentations at future AGoB meetings.

Regarding guidance development, the current draft will be refined based on the feedback received and the technical annexes will be made available in the coming period once the Scientific Committee's WG has finalised the first draft. In addition, the list of examples will be further extended, including the list of descriptors, as new examples will be identified along with the guidance development.

The AGoB work plan for 2026 will focus on providing advice on draft guidance, contributing to BoE examples, supporting knowledge transfer of methodologies and tools, and advising on the overall guidance development process.

Deliverables include regular input to EFSA on documents and processes, meeting minutes, progress updates at Advisory Forum meetings, and the Annual Report 2025.

Four meetings are planned in 2026, three virtual and one physical.