SCIENTIFIC COMMITTEE

14th Working Group meeting on biomarkers of effect

19-20 November 2025
13:00 - 17:00 / 09:00 – 13:00 CET
MINUTES - Agreed on 5 Dec 2025

EUROPEAN FOOD SAFETY AUTHORITY

Location: Webconference

Attendees:

- Working Group Members:
  Antonio Hernández-Jerez (Chair), Susanne Hougaard Bennekou, Hendrik van Loveren, Christina Pieper, Laurentius (Ron) Hoogenboom, Harry McArdle
- EFSA:
  MESE: Lucian FARCAL, Mina RISTOVSKA

  FIP: Zainab AL HARRAQ, Cristina CROERA (Day 1)

  FEEDCO: Anna CHRISTODOULIDOU

  PREV: Iris MANGAS (Day 2)

1. Welcome and apologies for absence

The Chair welcomed the participants.

2. Adoption of agenda

The agenda was adopted without changes.

3. Declarations of Interest of Working Groups members

In accordance with EFSA's Policy on Independence[1] and the Decision of the Executive Director on Competing Interest Management[2], EFSA screened the Annual Declarations of Interest filled out by the Working Group members invited to the present meeting. No conflicts of interest related to the issues discussed in this meeting have been identified during the screening process, and no interests were declared orally by the Working Group members at the beginning of this meeting.

4. Agreement of the previous meeting minutes

The minutes of the 13th WG meeting held on 19 September 2025 (online) were agreed by written procedure on 3 October 2025.

5. Project Management

5.1 Project updates

The WG was updated on the project activities. The status of the planned joint mandate with EMA and ECHA was discussed and the WG members were informed that the agencies have agreed on the terms of reference (ToR), which will be formalised in the coming period.

The WG was also informed and consulted on the agenda for the upcoming Advisory Group on Biomarkers of Effect (AGoB) meeting, scheduled for 2 December 2025 in Denmark. The members of this WG will also participate and act as facilitators, bringing discussion points

[1] https://www.efsa.europa.eu/sites/default/files/corporate_publications/files/independence-policy-2024.pdf
[2] https://www.efsa.europa.eu/sites/default/files/corporate_publications/files/decision-ed-on-competing-interest-management-2024.pdf

forward. The participants at the AGoB event will receive the latest draft guidance at least one week before the meeting.

Additionally, the WG was updated on the EFSA Scientific Committee (SC) plenary on 26–27 November 2025, where the draft guidance (excluding Annexes) will undergo its first reading.

6. Scientific and technical topics

6.1 Guidance development

The discussion focused on the guidance workflow and Annex 1, including an initial version of the criteria for evaluating and selecting biomarkers of effect. Terminology and abbreviations were clarified and agreed (e.g. use of "BoEs" for the plural form).

Several changes were agreed to the workflow for integrating BoEs into risk assessment, shifting from a stepwise approach to a set of elements to be considered. These elements include: establishing the assessment context, identifying candidate BoEs, collecting/generating and analysing data, selecting relevant BoEs, integrating them into the risk assessment framework and documenting outcomes.

Annex 1 will describe supporting principles and criteria, covering analytical, biological, and contextual, regulatory and practical applicability, as well as data quality, ethical standards, and other considerations.

6.2 Examples of BoE

The inventory of examples included in Annex 3 was reviewed, with discussions on adding new examples to cover both acute and chronic effects. Options for visualisation and ways to integrate lessons learned from these examples into the guidance were also considered.

7. Any Other Business

7.1 Actions and next meetings

As a next step, following discussions with the SC and AGoB, the draft guidance will undergo further refinement. Similarly, the annexes will continue to be refined as additional information becomes available and new relevant examples or descriptors are proposed.

The next WG meeting will be held on 23 January 2026, online.

SCIENTIFIC COMMITTEE

13th Working Group meeting on biomarkers of effect

19 September 2025
13:00-17:00
MINUTES - Agreed on 3 October 2025

Location: Webconference

Attendees:

- Working Group Members:
  Antonio Hernández-Jerez (Chair), Susanne Hougaard Bennekou, Hendrik van Loveren, Christina Pieper, Laurentius (Ron) Hoogenboom
- EFSA:
  MESE: Lucian FARCAL, Ana DIGES

  NIF: Silvia VALTUENA MARTINEZ

  FIP: Zainab AL HARRAQ, Cristina CROERA

  FEEDCO: Anna CHRISTODOULIDOU

I. Welcome and apologies for absence

The Chair welcomed the participants. Apologies were received from Harry McArdle.

II. Adoption of agenda

The agenda was adopted without changes.

III. Declarations of Interest of Working Groups members

In accordance with EFSA's Policy on Independence[1] and the Decision of the Executive Director on Competing Interest Management[2], EFSA screened the Annual Declarations of Interest filled out by the Working Group members invited to the present meeting. No conflicts of interest related to the issues discussed in this meeting have been identified during the screening process, and no interests were declared orally by the Working Group members at the beginning of this meeting.

IV. Agreement of the minutes of the 12th Working Group meeting held on 5 June 2025, via web-conference

The minutes of the 12th Working Group meeting were agreed by written procedure on 16 June 2025.

V. Project Management

5.1 Project updates

The WG was updated on the planned interagency mandate, which is now at an advanced stage of discussion.

The group was also briefed on the outcome of the 2nd meeting of the new Advisory Group on Biomarkers (AGoB) that took place on September 18th 2025, noting the nomination of the Chair and the significant opportunities for knowledge exchange brought by the members' expertise and

[1] https://www.efsa.europa.eu/sites/default/files/corporate_publications/files/independence-policy-2024.pdf
[2] https://www.efsa.europa.eu/sites/default/files/corporate_publications/files/decision-ed-on-competing-interest-management-2024.pdf

engagements in key relevant projects. The knowledge exchange with the OECD project and other EU initiatives (e.g. PARC) was also highlighted.

Project timelines regarding guidance development were noted to ensure meeting action points are carried out retroactively planning for the first draft presentation to the EFSA's Scientific Committee during the plenary meeting on 26-27 November 2025.

VI. Scientific and technical topics

6.1 Case studies

The WG members discussed the purpose and expected outcomes of using examples of biomarkers of effect during guidance development. It was clarified that these examples are intended to support the development of the guidance by clarifying complex concepts and informing criteria and descriptors for biomarkers of effect, rather than for testing the workflow under development. The selection of examples, as well as the possibility of including additional ones, was discussed with the aim of maximising knowledge transfer from published scientific opinions or other projects, and ensuring diverse representation of toxicological pathways, including both well-established and emerging biomarkers. Regarding the format of the final outcome, it was agreed that a summary of the examples considered during guidance development would be included.

6.2 Guidance outline

Based on input from the WG and AGoB, the WG reviewed and critically appraised the guidance outline sections developed so far, with particular focus on the logic and scientific content needed to integrate biomarkers of effect into the proposed workflow. Comments on the text were addressed systematically, with actions and follow-up suggestions assigned to group members.

The next revision will address the guidance workflow, illustrating how biomarkers of effect can be integrated into the risk assessment process (e.g. for decision-making or within a weight-of-evidence approach), and will incorporate updates based on WG members' expertise in risk assessment within the EFSA remit.

As a next step, the WG will begin developing the section of the guidance covering the analytical and biological characteristics of biomarkers of effect, as well as the minimum requirements and criteria for selecting biomarkers for use in risk assessment.

VII. Any Other Business

- **Next steps and actions**

The WG agreed on select tasks for review and refinement of the draft guidance and examples of biomarkers of effect. New work on an annex is also to be started in a separate document, which will be circulated after the meeting. A draft version of the guidance will be shared with the EFSA's Scientific Committee for discussion at the plenary meeting on 26-27 Nov 2025.

VIII. Next meeting

The next WG meeting will be held on 19-20 November 2025, online.

SCIENTIFIC COMMITTEE

12th Working Group meeting on biomarkers of effect

5 June 2025
09:00-13:00
MINUTES - Agreed on 16 June 2025

Location: Webconference

Attendees:

- Working Group Members:
  Antonio Hernández-Jerez (Chair), Susanne Hougaard Bennekou, Hendrik van Loveren, Harry McArdle, Christina Pieper, Laurentius (Ron) Hoogenboom

- EFSA:
MESE: Lucian FARCAL, Ana DIGES
NIF: Silvia VALTUENA MARTINEZ
FIP: Zainab AL HARRAQ
PREV: Iris MANGAS

I. Welcome and apologies for absence

The Chair welcomed the participants.

II. Adoption of agenda

The agenda was adopted without changes.

III. Declarations of Interest of Working Groups members

In accordance with EFSA's Policy on Independence[1] and the Decision of the Executive Director on Competing Interest Management[2,] EFSA screened the Annual Declarations of Interest filled out by the Working Group members invited to the present meeting. No Conflicts of Interest related to the issues discussed in this meeting have been identified during the screening process, and no interests were declared orally by the members at the beginning of this meeting.

IV. Agreement of the minutes of the 11th Working Group meeting held on 11 April 2025 via web-conference

The minutes of the 11th Working Group meeting were agreed by written procedure on 28 April 2025.

V. Status of the project

5.1 Project development updates

WG members were updated on the potential joint mandate by the EC to EFSA, EMA and ECHA for the project's co-creation phase. WG members were also informed about the first meeting of the Advisory Group on Biomarkers of Effect (AGoB) set for 1st July 2025. AGoB, with 16 EU MS representatives, will use this introductory meeting to overview the project and discuss

[1] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/policy_independence.pdf
[2] https://www.efsa.europa.eu/sites/default/files/corporate_publications/files/decision-ed-on-competing-interest-management-2024.pdf

the proposed guidance outline (to be shared prior to the meeting). Participants will be also able to raise specific discussion topics.

VI. Scientific topic(s) for discussion

6.1 Guidance outline

The draft outline of the proposed guidance sections was reviewed by the WG members, featuring initial drafts of the text and methodology. Consensus was reached on prioritising the alignment of terminology and acronyms during the document development process, alongside other scientific and technical discussions. The comments regarding the sections on purpose, scope, objectives, target users, and intended application were reviewed and discussed. One of the issues concerned the inclusion, within the objectives, of aspects related to uncertainty analysis - specifically, the uncertainty factors associated with effect biomarkers and their relevance to the guidance document. Additionally, the WG discussed the general principles, applications and workflow proposed to be included in the guidance outline. The next step is for the WG to review and refine the document and to prepare a draft version for sharing with the AGoB.

6.2 Case studies

The WG reviewed draft versions of two case studies - one on Th17 cells and the other on thyroid hormones - focusing on terminology choices, potential structural and content adaptations of the template based on the specific biomarker of effect. It was reiterated that the primary purpose of these initial case studies and examples of biomarkers of effect is to support the development of the guidance document. They are intended to aid in clarifying complex concepts and assist in selecting appropriate methods, criteria and descriptors throughout the guidance development process.

VII. Any Other Business

7.1 Next steps and actions

WG members will review and refine the draft guidance outline and case studies. The outline (excluding annexes) will be shared with the AGoB ahead of the first meeting.

VIII. Next meetings

The next meeting will be held online in September (the exact date and time to be decided).

SCIENTIFIC COMMITTEE

11th Working Group meeting on biomarkers of effect

11 April 2025
09:00-13:00
MINUTES - Agreed on 29 April 2025

Location: Web conference

Attendees:

- Working Group Members:
  Antonio Hernández-Jerez (Chair), Hendrik van Loveren, Harry Mcardle, Christina Pieper
- EFSA:
  MESE: Lucian FARCAL, Ana DIGES
  NIF: Silvia VALTUENA MARTINEZ
  FEEDCO: Anna CHRISTODOULIDOU
  FIP: Zainab AL HARRAQ
  PREV: Iris MANGAS

I. Welcome and apologies for absence

The Chair welcomed the participants. Apologies were received from Susanne Hougaard Bennekou and Laurentius (Ron) Hoogenboom.

II. Adoption of agenda

The agenda was adopted without changes.

III. Declarations of Interest of Working Groups members

In accordance with EFSA's Policy on Independence[1] and the Decision of the Executive Director on Competing Interest Management[2,] EFSA screened the Annual Declarations of Interest filled out by the Working Group members invited to the present meeting. No Conflicts of Interest related to the issues discussed in this meeting have been identified during the screening process, and no interests were declared orally by the members at the beginning of this meeting.

IV. Agreement of the minutes of the 10th Working Group meeting held on 27 February 2025, in Parma or via web-conference

The minutes of the 10th Working Group meeting were agreed by written procedure on 17 March 2025.

V. Status of the Project

5.1 Project development updates

The WG was informed on the ongoing actions towards establishing the new joint mandate on the guidance development. This included the updates to the Concept Paper to be used as basis for the mandate, bilateral meetings with other EU agencies, as well as the steps towards establishing of a new Advisory Group on biomarkers of effect (AGoB) under the Advisory

[1] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/policy_independence.pdf
[2] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/competing_interest_management_17.pdf

Forum (AF) of EFSA. The group will include experts nominated by the AF members as their representatives for this project and will support EFSA in the context of the guidance development. The WG will be informed on the next steps, in order to prioritise the tasks and prepare draft documents to be shared with the AGoB.
A workshop is scheduled for 2 Dec 2025 (Copenhagen, Denmark), with the participation of all groups and experts involved in this project. Further details will be circulated to the WG in the next period.
It has been noted that until a new mandate will be agreed and established, the WG will develop the guidance under the current self-task mandate of the SC.

VI. Scientific and Technical Topics

6.1 Guidance outline

A draft outline of the proposed guidance sections was reviewed by the WG members for the first time during the meeting, noting content, completeness, structure, and wording edits appropriate to set forth a template supporting a high-level draft guidance.

6.2 Case studies

During the meeting, the principal template, which had been drafted and commented on in previous sessions, was thoroughly reviewed. This led to a provisional path forward regarding the overarching format, with an emphasis on maintaining succinctness. Additionally, specific comments and feedback were addressed concerning one of the proposed case studies on acetylcholinesterase (AChE).

VII. Any Other Business

7.1 Next Steps and actions

WG members will review and provide feedback on the draft guidance outline as well as case studies, to be concluded prior to the next meeting. The draft guidance outline will be also shared with the AGoB in a timely manner for input.
No further issues were brought up by WG members.

VIII. Next meetings

The next meeting will be held online on **5 June 2025**.

SCIENTIFIC COMMITEE

10th Working Group meeting on Biomarkers of effect

27 February 2025
13:00 – 17:00
MINUTES – Agreed on 17 March 2025

Location: Online (*MTG SEAT 00/M01 for EFSA staff*)

Attendees:

Working Group Members:

Antonio Hernández-Jerez, Hendrik van Loveren, Harry Mcardle, Christina Pieper, Laurentius (Ron) Hoogenboom

EFSA:

MESE: Lucian FARCAL (Chair), Ana DIGES

NIF: Silvia VALTUENA MARTINEZ

FEEDCO: Anna CHRISTODOULIDOU

FIP: Cristina Croera, Zainab AL HARRAQ

PREV: Iris MANGAS

I. Welcome and apologies for absence

The Chair welcomed the participants. Apologies were received from Susanne Hougaard Bennekou.

II. Adoption of agenda

The agenda was adopted without any changes.

III. Declarations of Interest of Working Groups members

In accordance with EFSA's Policy on Independence[1] and the Decision of the Executive Director on Competing Interest Management[2], EFSA screened the Annual Declarations of Interest filled out by the Working Group members invited to the present meeting. No Conflicts of Interest related to the issues discussed in this meeting have been identified during the screening process, and no interests were declared orally by the members at the beginning of this meeting.

IV. Agreement of the minutes of the 9th Working Group meeting held online on 3rd October 2024

The minutes of the 9th Working Group meeting were agreed by written procedure on 14 October 2024.

V. Status of the project and implementation plan for Phase 2

[1] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/policy_independence.pdf
[2] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/competing_interest_management_17.pdf

5.1 Updates on the project process

The WG was informed of the nomination of the new Chair in the person of Antonio Hernández-Jerez, that will take this role starting with the next meeting. The Scientific Committee was also consulted regarding this nomination during the last plenary meeting (19-20 Feb 2025).

The WG was informed on the status of the project, especially on the actions to establish a joint mandate with other EU Agencies (EMA and ECHA) and the mechanism for involving the EU MSs in the guidance development process. A Concept Paper has been discussed with the other Agencies, that will serve to define the Terms of Reference for the new mandate. In addition, the process of establishing an Advisory Group on biomarkers of effect (within the Advisory Forum at EFSA) is in progress. In parallel, the options for developing an OECD guidance are also explored. Several of these aspects were discussed and clarified with the WG members, ensuring that the mechanisms proposed are well understood, before proceeding to the drafting of the guidance.

VI. Scientific and technical topics

6.1 Guidance Outline

In this session, the WG discussed the issues to be prioritised, based on the aspects included in the Concept Paper mentioned above. The WG also reviewed comments on the document, addressing editorial changes and technical considerations.

Based on the discussions, the following items were selected as basis for the guidance outline: purpose and target audience, general principles on the use of biomarkers of effect in risk assessment, criteria for the selection and evaluation of biomarkers of effect, and case studies. It was emphasised that the guidance should be kept clean, simple, and practical.

6.2 Case Studies

The WG reviewed the existing examples of biomarkers of effect from EFSA's published scientific opinions, with a view to selecting relevant case studies that can inform and support the development of the guidance. Several options were explored, considering a range of types (e.g. well established biomarkers, new biomarkers, panel of biomarkers), and categories (e.g. biomarkers of effect that cover the main health outcomes). In addition, the WG reviewed a first version of a template to be used for the case study description. As a next step, the WG will propose a few case studies to be used as starting point, with a preference for less complex examples of biomarkers of effect, boasting sufficient data which are presently used in chemical risk assessment.

VII. Any Other Business

7.1 Next steps and actions

The WG compiled a list of actions for the next period.

VIII. Next meeting

The next meeting is planned for April 11th, 2025.

SCIENTIFIC COMMITEE

9th Working Group meeting on Biomarkers of effect

3 October 2024
09:30 – 17:00
MINUTES – Agreed on 14 Oct 2024

Location: online

Attendees:

Working Group Members:

Antonio Hernández-Jerez, Hendrik van Loveren, Harry Mcardle, Susanne Hougaard Bennekou, Christina Pieper

EFSA:

MESE: Lucian FARCAL (Chair), Ana DIGES, Sara LEVORATO

NIF: Silvia VALTUENA MARTINEZ

FEEDCO: Chantra ESKES, Anna CHRISTODOULIDOU

FIP: Cristina Croera, Zainab AL HARRAQ

PREV: Iris MANGAS

I. Welcome and apologies for absence

The Chair welcomed the participants.

Apologies were received from Laurentius (Ron) Hoogenboom.

II. Adoption of agenda

The agenda was adopted without any changes.

III. Declarations of Interest of Working Groups members

In accordance with EFSA's Policy on Independence[1] and the Decision of the Executive Director on Competing Interest Management[2], EFSA screened the Annual Declarations of Interest filled out by the Working Group members invited to the present meeting. No Conflicts of Interest related to the issues discussed in this meeting have been identified during the screening process, and no interests were declared orally by the members at the beginning of this meeting.

IV. Agreement of the minutes of the 8th Working Group meeting held online on 3rd September 2024

The minutes of the 8th Working Group meeting were agreed by written procedure on 16 Sep 2024.

[1] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/policy_independence.pdf
[2] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/competing_interest_management_17.pdf

V. Collaboration and engagement activities

5.1 Updates on the preparation of Phase 2 of the project

The WG was informed on the feedback received from the SC following the presentation of the project overview during the 120th plenary meeting (11-12 Sep 2024). At the same meeting, the plans for Phase 2 were presented to the SC.

The steps discussed in the previous WG meeting are currently implemented, including further internal discussions on the feasible co-creation mechanisms, as well as initiation of communication with EU agencies (ECHA and EMA) on the proposal for the terms of reference.

The initiation of Phase 2 is expected for Q1 of 2025.

VI. Scientific and technical topics

6.1 Scientific Report (core part)

The WG continued to work on the draft Scientific Report and checked the remaining comments from the Public Consultation (PC). Several editorial and technical aspects were discussed and agreed, for example on the human biomonitoring studies, new approach methodologies, validation of biomarkers of effects, characteristics of biomarkers of effect such as the magnitude of change, further alignment of terminologies used in the document, etc. The changes made to the report aim on one hand to clarify the aspects raised within the PC and, on the other hand, to improve its overall structure and readability. The new section "Conclusions and recommendations" was also revised. The replies to the comments received during the PC are included in Annex 3.3 of the Scientific Report.

6.2 Annexes of the Scientific Report

The following documents were re-checked and discussed by the WG members:

- Annex 1: Template for the description of biomarkers of effect with representative examples
- Annex 2.1: Mapping study report
- Annex 2.2: Inventory of resources
- Annex 3.1: Survey report
- Annex 3.2: Stakeholder workshop report
- Annex 3.3: Public consultation report

Most of the Annexes are finalised, except Annexes 1, 2.1 and 3.3.

The content of Annex 1 was discussed in detailed, especially some of the examples included in the template. Aspects related to the purpose and use of Annex 1 were also discussed, which represents a first version of a draft template to be further developed in the next Phase of the project. The WG checked and completed the examples of biomarkers of effect included in the Annex. These were extracted from Scientific Opinions published by EFSA, representing around 10 well established examples of biomarkers of effect. The structure of the template was also adjusted (e.g. deletion of headings related to the type of biomarkers and the type of effect). The selection criteria for the examples to be used in Phase 2 was briefly discussed. These might include their use , their type

(e.g. early or late biomarkers of effect), well recognised biomarkers versus more innovative and complex examples, etc.

Annex 2.1 will be finalised after the inclusion of the data generated within the parallel project implemented with the support of an Independent Scientific Advisor (ISA).

Annex 3.3 included the replies to the Public consultation comments and will be finalised in parallel with the revision of the Scientific Report.

6.3 Brainstorming regarding Phase 2

As Phase 1 of the project is closer to its end, the WG members had a brief brainstorming session on the approach to be taken in Phase 2, for the guidance development. Starting from the ideas discussed at the stakeholder workshop (24-25 Jun 2024), several aspects regarding e.g. scope, essential analytical and biological characteristics defining the validity and interpretation of biomarkers of effect, weight and criteria for each characteristic, etc. were further discussed.

The proposal is to start Phase 2 with the development of the guidance outline first, that should be discussed with all organisations involved, before going into more details.

VII. Any Other Business

7.1 Next steps and actions

The WG compiled a list of actions for the next period. The aim is to prepare a new draft version to be discussed and presented at the Scientific Committee plenary on 20-21 Nov 2024. Afterwards, in case of endorsement, the Scientific Report will be submitted for publication to EFSA Journal.

VIII. Next meeting

No WG meetings are planned for 2024. The dates for the meetings in 2025 will be agreed and communicated later.

SCIENTIFIC COMMITEE

8th Working Group meeting on Biomarkers of effect

3 September 2024
09:00 – 13:00
MINUTES – Agreed on 16 Sep 2024

Location: online

Attendees:

Working Group Members:

Antonio Hernández-Jerez, Laurentius (Ron) Hoogenboom, Hendrik van Loveren, Harry Mcardle, Susanne Hougaard Bennekou, Christina Pieper

EFSA:

MESE: Lucian FARCAL (Chair), Georgia BOMPOLA

NIF: Silvia VALTUENA MARTINEZ, Agnès DE SESMAISONS

FIP: Zainab AL HARRAQ, Cristina CROERA

I. Welcome and apologies for absence

The Chair welcomed the participants. No apologies were received.

II. Adoption of agenda

The agenda was adopted without any changes.

III. Declarations of Interest of Working Groups members

In accordance with EFSA's Policy on Independence[1] and the Decision of the Executive Director on Competing Interest Management[2], EFSA screened the Annual Declarations of Interest filled out by the Working Group members invited to the present meeting. No Conflicts of Interest related to the issues discussed in this meeting have been identified during the screening process, and no interests were declared orally by the members at the beginning of this meeting.

IV. Agreement of the minutes of the 7th Working Group (in-person) meeting held on 24th June 2024, in Parma, Italy

The minutes of the 7th Working Group meeting were agreed by written procedure on 5 July 2024.

V. Collaboration and engagement activities

[1] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/policy_independence.pdf
[2] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/competing_interest_management_17.pdf

5.1 Outcome of the engagement activities and next steps

The WG members were informed on the outcomes of the previous collaboration and engagement activities implemented in the context of the Phase 1 of the project.

The **stakeholder workshop** organised on 24-25 Jun 2024 included presentations on scientific and technical challenges and experience from ongoing initiatives, and discussions on the components of the guidance and possible co-creation mechanisms for Phase 2 of the project. Following the event a workshop report (Annex 3.2) was prepared and shared with all participants. It summarises the main aspects discussed during the event, e.g. the importance and the need of guidance in this area, the potential of using biomarkers of effect in risk assessment, the scope of the guidance and further collaboration steps for its development.

In parallel, a **public consultation** on the draft Scientific Report was organised between 19 Jun and 31 Jul 2024. Comments were received from 3 organisations, including suggestions or proposals to amend the scientific concepts/text, requests for clarifications, editorial suggestions, missing references as well as acknowledgement and compliments for the initiative and the report. The outcome of the public consultation will be reflected in Annex 3.3 of the Scientific Report.

Based on the discussions held during Phase 1, a plan for the **co-creation of the guidance** in Phase 2 of the project is currently under development. This refers to mechanisms of collaboration and joint activities with other EU and international organisations. The WG members discussed possible scenarios for developing the guidance, that will be further presented and discussed with the Scientific Committee and EFSA's partners.

VI. Scientific and technical topics

6.1 Updates to the Scientific Report

The WG discussed the comments received during the Public Consultation on the draft Scientific Report, and where necessary the WG proposed changes to the text or actions to be considered for the Phase 2 of the project. The comments included several general statements that need to be considered especially for the guidance development in Phase 2 and also specific suggestions related to the following sections of the report: Interpretation of the Terms of Reference, Context and scope, Definition and application domains of biomarkers, Description of biomarkers, Implications of the use of biomarkers of effect in risk assessment, References, Appendix C and Annex 1. The changes will be reflected in the next version of the report that will be further discussed and agreed.

In addition, the WG members drafted responses to the comments, that will be published in Annex 3.3 of the report.

In the next period, the WG will also refine and finalise the Summary of the report as well as the section on Conclusions and recommendations.

VII. Any Other Business

7.1 Next steps and actions

The WG compiled a list of actions for the next period.

VIII. Next meeting

The next meeting will be held online on **3rd October 2024**.

SCIENTIFIC COMMITEE

7th Working Group meeting on Biomarkers of effect

24 June 2024
10:00 - 13:00
MINUTES – Agreed on 05 Jul 2024

Location: Parma, Italy

Attendees:

Working Group Members:

In person: Antonio Hernández-Jerez, Laurentius (Ron) Hoogenboom, Hendrik van Loveren, Harry Mcardle, Susanne Hougaard Bennekou

EFSA:

MESE: Lucian FARCAL (Chair), Georgia BOMPOLA

FIP: Cristina CROERA, Zainab AL HARRAQ

NIF: Silvia VALTUENA MARTINEZ, Agnès DE SESMAISONS

FEEDCO: Chantra ESKES, Anna CHRISTODOULIDOU

I. Welcome and apologies for absence

The Chair welcomed the participants.

Apologies were received from Tanja Schwerdtle.

II. Adoption of agenda

The agenda was adopted without any changes.

III. Declarations of Interest of Working Groups members

In accordance with EFSA's Policy on Independence[1] and the Decision of the Executive Director on Competing Interest Management[2], EFSA screened the Annual Declarations of Interest filled out by the Working Group members invited to the present meeting. No Conflicts of Interest related to the issues discussed in this meeting have been identified during the screening process, and no interests were declared orally by the members at the beginning of this meeting.

IV. Agreement of the minutes of the 6th Working Group meeting held on 26th April 2024, via web-conference

The minutes of the 6th WG meeting were agreed by written procedure on 15 May 2024.

[1] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/policy_independence.pdf
[2] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/competing_interest_management_17.pdf

V. Collaboration and engagement activities

5.1 Reporting from other relevant activities or meetings

The WG members were informed on the outcome of the **119th plenary meeting of the Scientific Committee**[3], where the updates to the draft report were presented. The presentation and the discussion focused on the actions from the previous plenary meeting e.g. a simplified structure of the report, terminologies and clarifications on different scientific aspects. Following the discussion, the SC endorsed the draft report for public consultation. As such, the **public consultation**[4] was opened on 19 Jun 2024 and it will be closed on 31 Jul 2024. The WG will discuss the feedback received and consider it for the next version of the report.

The WG members were also informed on the participation of EFSA staff to the **ESTIV Congress 2024**[5] (with one oral presentation and one poster), as part of the dissemination activities within the biomarkers of effect project.

5.2 Preparation of stakeholder workshop

The WG discussed several aspects regarding the **stakeholder workshop** organised by EFSA on 24-25 Jun ("Biomarkers of effect: from principles to a cross-sectoral guidance on the use in regulatory risk assessment of chemicals"). The main focus of the discussion was on the break-out session design, where the WG members will be involved as facilitators or rapporteurs. The session has been further refined, especially regarding the possible components of the future guidance that will be discussed with the workshop participants. The WG members concluded on the final format that was used in the workshop.

VI. Any Other Business

7.1 Next steps and actions

The next steps refer to the outcomes of the stakeholder workshop and the public consultation, that need to be further considered within the next iterations of the project and to update the Scientific Report.

VII. Next meeting

The next meeting will be held online on **3rd September 2024**.

[3] https://www.efsa.europa.eu/en/events/119th-plenary-meeting-scientific-committee
[4] https://connect.efsa.europa.eu/RM/s/consultations/publicconsultation2/a0lTk000001FW5R/pc1003
[5] https://www.estiv.org/congress2024/

SCIENTIFIC COMMITEE

6th Working Group meeting on Biomarkers of effect

26 April 2024
09:30 – 17:00
MINUTES – Agreed on 13 May 2024

Location: Online

Attendees:

Working Group Members:

Antonio Hernández-Jerez, Laurentius (Ron) Hoogenboom, Hendrik van Loveren, Harry Mcardle, Tanja Schwerdtle

EFSA:

MESE: Lucian FARCAL (Chair), Sara LEVORATO, Alicia PAINI

NIF: Silvia VALTUENA MARTINEZ

FEEDCO: Chantra ESKES, Anna CHRISTODOULIDOU

I. Welcome and apologies for absence

The Chair welcomed the participants.

Apologies were received from Susanne Hougaard Bennekou.

II. Adoption of agenda

The agenda was adopted without any changes.

III. Declarations of Interest of Working Groups members

In accordance with EFSA's Policy on Independence[1] and the Decision of the Executive Director on Competing Interest Management[2,] EFSA screened the Annual Declarations of Interest filled out by the Working Group members invited to the present meeting. No Conflicts of Interest related to the issues discussed in this meeting have been identified during the screening process, and no interests were declared orally by the members at the beginning of this meeting.

IV. Agreement of the minutes of the 5th Working Group meeting held on 26th March 2024, via web-conference

The minutes of the 5th Working Group meeting were agreed by written procedure on 12 April 2024.

[1] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/policy_independence.pdf
[2] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/competing_interest_management_17.pdf

V. Collaboration and engagement activities

5.1 Reporting from other relevant activities or meetings

The WG was informed on the feedback received during the 118th plenary meeting of the Scientific Committee (SC) (10-11 Apr 2024). During that meeting, the SC was provided with an update on the ongoing activities on biomarkers of effect and the development of the Scientific Report, made available to the SC for the first reading and discussion. The suggestions (e.g. related to the structure and length of the report, further clarification on the context and scope of the report, characteristics of the biomarkers of effect) were discussed and considered by the WG. The detailed comments included directly in the report, were discussed under Item 6.1.

5.2 Preparation of stakeholder workshop

The WG discussed the overall agenda and description of the stakeholder workshop to be organised on 24-25 Jun 2024, with a focus on the break-out session that aims to discuss an initial workflow including the core aspects/principles to be considered in the development of the guidance, and that can be further exploited and implemented in the next phase. In the workshop, the WG members will play an active role (e.g. facilitators, rapporteurs) in order to guide the participants during the discussion. Ideas related to the break-out session were discussed and recorded and will be used as a starting point for the session design.

VI. Scientific and technical topics

6.1 Scientific report

The WG discussed and updated all sections of the report based on previous comments and new text added to the working document. During the meeting, WG responded to some of the comments and agreed on improving the report structure and its readability, reduction of repetitions and further clarified on different technical or scientific aspects. For each section, a list of immediate actions was compiled. The next version of the report will be shared again with the SC for endorsement, during the next plenary meeting (29-30 May 2024).

VII. Any Other Business

7.1 Next steps and actions

The WG compiled a list of actions for the next period.

VIII. Next meeting

The next meeting will be held in person (Parma, Italy) on **24th June 2024**.

SCIENTIFIC COMMITEE

5th Working Group meeting on Biomarkers of effect

26 March 2024
09:30 – 17:00
MINUTES – Agreed on 12 Apr 2024

Location: Online

Attendees:

Working Group Members:

Antonio Hernández-Jerez, Laurentius (Ron) Hoogenboom, Hendrik van Loveren, Harry Mcardle, Susanne Hougaard Bennekou

EFSA:

MESE: Lucian FARCAL (Chair), Georgia BOMPOLA, Sara LEVORATO

NIF: Silvia VALTUENA MARTINEZ

FEEDCO: Chantra ESKES

Hearing expert:

US FDA: William B. Mattes[1]

I. Welcome and apologies for absence

The Chair welcomed the participants.

Apologies were received from Tanja Schwerdtle.

II. Adoption of agenda

The agenda was adopted without any changes.

III. Declarations of Interest of Working Groups members

In accordance with EFSA's Policy on Independence[2] and the Decision of the Executive Director on Competing Interest Management[3,] EFSA screened the Annual Declarations of Interest filled out by the Working Group members invited to the present meeting. No Conflicts of Interest related to the issues discussed in this meeting have been identified during the screening process, and no interests were declared orally by the members at the beginning of this meeting.

IV. Agreement of the minutes of the 4th Working Group meeting held on 26th February 2024, via web-conference

[1] For Agenda item 6.2
[2] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/policy_independence.pdf
[3] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/competing_interest_management_17.pdf

The minutes of the 3rd Working Group meeting were agreed by written procedure on 8 March 2024.

V. Collaboration and engagement activities

5.1 Reporting from other relevant activities or meetings

The WG was informed on the presentation given by the WG coordinator at the 146th Plenary meeting of the NDA Panel (29 Feb 2024) followed by discussion with the panel members around the concepts included in the report, as well as on the future plans and relevancy for the assessments performed by the NDA Panel. Within this context, examples of biomarkers of effect used in previous assessments done by NDA Panel were already included in the working documents to support the discussions of the WG (see Item 6.1).

Finally, the colleagues that participated in the "International Symposium: Risk Assessment of Genotoxic Compounds – Challenges and Future Perspectives" (26-28 Feb 2024) reported also on this relevant event.

5.2 Dissemination plan

The WG was informed on other dissemination activities, in addition to those reported above. For the ongoing survey, a reminder was sent recently to stakeholders (the survey will be closed on 30 Apr 2024). A poster abstract was submitted to ESTIV Congress (3-6 Jun 2024), in addition to the oral presentation already accepted.

The project will be presented also at the next PPR Panel (18 April 2024), as part of the interactions and information exchange between the WG and the scientific Panels.

The WG was informed on the stakeholder workshop to be organised on 24-25 Jun 2024 and the proposed agenda, objectives and expected outcomes were discussed. More details will be shared with the WG members in order to contribute to the program.

VI. Scientific and technical topics

6.1 Feasibility study (Scientific Report)

Within this agenda item, the WG members further elaborated on the scientific report, with the aim to prepare a version of the document to be shared and presented at the next plenary meeting of the Scientific Committee (10-11 Apr 2024). The discussions addressed: 1) the title of the report, 2) the sub-types of biomarkers and their groping based on the area of application, 3) the application of biomarkers, 4) definitions, with a focus on clarifications related to early versus late biomarkers of effect, the link to the AOPs and the KER quantitative understanding, described in the AOP framework, and 5) characteristics of biomarkers of effect. In addition, the description of biomarkers of effects (examples related to novel foods area) were discussed and refined by the WG members.

6.2 Food and Biomarkers: Finding the Right Recipe

This session was dedicated to a presentation given by William B. Mattes (invited as Hearing Expert) and discussion on the ongoing activities of the WG on biomarkers at US FDA, especially related to food safety. These included aspects related to biomarkers' definitions, characteristics of "ideal" biomarkers, different models or criteria used for their characterisation, translational biomarkers, AOPs, biological processes, adaptative processes. The outcome of the discussion will be further used by the WG at EFSA in the context of the Scientific Report development and beyond.

VII. Any Other Business

7.1 Next steps and actions

The WG compiled a list of actions for the next period. The focus will be on preparing a version of the Report to be discussed with the Scientific Committee, addressing the feedback received at the next plenary meeting and refining the report based on the existing comments in the document and previous discussions.

VIII. Next meeting

The next meeting will be held online on **26 April 2024**.

SCIENTIFIC COMMITEE

4th Working Group meeting on Biomarkers of effect

26 February 2024
13:00 – 17:00
MINUTES – Agreed on 8 March 2024

Location: Telemeeting

Attendees:

Working Group Members:

Antonio Hernández-Jerez, Laurentius (Ron) Hoogenboom, Hendrik van Loveren, Harry Mcardle, Susanne Hougaard Bennekou

EFSA:

MESE: Lucian FARCAL (Chair), Georgia BOMPOLA, Sara LEVORATO, Alicia PAINI

NIF: Silvia VALTUENA MARTINEZ

FEEDCO: Anna CHRISTODOULIDOU, Chantra ESKES, Paola MANINI

I. Welcome and apologies for absence

The Chair welcomed the participants.

Apologies were received from Tanja Schwerdtle.

II. Adoption of agenda

The agenda was adopted without any changes.

III. Declarations of Interest of Working Groups members

In accordance with EFSA's Policy on Independence[1] and the Decision of the Executive Director on Competing Interest Management[2,] EFSA screened the Annual Declarations of Interest filled out by the Working Group members invited to the present meeting. No Conflicts of Interest related to the issues discussed in this meeting have been identified during the screening process, and no interests were declared orally by the members at the beginning of this meeting.

IV. Agreement of the minutes of the 3rd Working Group meeting held on 24th January 2024, via web-conference

The minutes of the 3rd Working Group meeting were agreed by written procedure on 9 February 2024.

[1] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/policy_independence.pdf
[2] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/competing_interest_management_17.pdf

V. Collaboration and engagement activities

The WG was briefed on the presentation given by the WG coordinator at the 117th Scientific Committee plenary meeting on 5th Feb 2024 and feedback received. On that occasion, the SC was provided with an update on the ongoing activities of the biomarkers of effect project, underlying the main goal of the 1st phase of the project implemented as a descriptive approach that will create the base for the future guidance. The suggestions and comments received from the SC were summarised, as well as the actions taken (e.g. clarifications on terminology, elaborate on the main characteristics of biomarkers, challenges).

The WG was informed that a draft version of the report will be presented and discussed at the next SC plenary meeting on 10-11 April 2024.

In addition, the WG members were informed on the survey status and the dissemination plan.

VI. Scientific and technical topics

6.1 Description of biomarkers of effect

The WG initiated the discussion from a set of characteristics of 'ideal biomarkers' described in case of clinical use. The extrapolation of these characteristics to the risk assessment was then addressed in detail. First the grouping in analytical and biological characteristics was agreed, that correspond also to the aspects included within the validity evaluation of biomarkers.

The discussion was then focused on the biological characteristics, such as the predictivity, sensitivity and specificity, including their definitions and other clarifications regarding their importance in this context. Other aspects discussed refer to the biological plausibility, irreversibility and the 'point-of-no-return', quantifiability, magnitude of change versus normal variability, human relevance, etc.

Further, the template developed for the biomarker's description (including representative examples extracted from published Scientific Opinions of EFSA) was discussed and refined. The current version of the template includes five groups of descriptors: general identification, adverse outcome description, link to existing AOPs, risk assessment descriptors and references.

VII. Any Other Business

7.1 Next steps and actions

The WG compiled a list of actions for the next period, aiming to achieve a version of the report ready for discussion with the SC at the next plenary meeting (10-11 April 2024).

The focus of the WG members in next period will be on refining the sections of definitions and description (characteristics) of biomarkers of effect.

VIII. Next meeting

The next meeting will be held online on **26 March 2024**.

SCIENTIFIC COMMITEE

3rd Working Group meeting on Biomarkers of effect

24 January 2024
09:30 – 16:50
MINUTES – Agreed on 9 February 2024

Location: Online

Attendees:

Working Group Members:

Antonio Hernández-Jerez, Laurentius (Ron) Hoogenboom, Hendrik van Loveren, Harry Mcardle, Tanja Schwerdtle

Hearing experts:

Robert Pasanen-Kase[1]

EFSA:

MESE: Lucian FARCAL (Chair), Georgia BOMPOLA, Sara LEVORATO, Alicia PAINI

FIP: Cristina CROERA

NIF: Silvia VALTUENA MARTINEZ

FEEDCO: Anna CHRISTODOULIDOU, Chantra ESKES

I. Welcome and apologies for absence

The Chair welcomed the participants.

Apologies were received from Susanne Hougaard Bennekou.

II. Adoption of agenda

The agenda was adopted with small changes in the timing of the sessions.

III. Declarations of Interest of Working Groups members

In accordance with EFSA's Policy on Independence[2] and the Decision of the Executive Director on Competing Interest Management[3,] EFSA screened the Annual Declarations of Interest filled out by the Working Group members invited to the present meeting. No Conflicts of Interest related to the issues discussed in this meeting have been identified during the screening process, and no interests were declared orally by the members at the beginning of this meeting.

IV. Agreement of the minutes of the 2nd Working Group meeting held on 17 November 2023, via web-conference

[1] For Agenda Item 6.1
[2] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/policy_independence.pdf
[3] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/competing_interest_management_17.pdf

The minutes of the 2nd Working Group meeting were agreed by written procedure on 5 December 2023.

V. Collaboration and engagement activities

The WG members were informed on the Survey "Mapping of initiatives, expertise and knowledge around biomarkers of effect" launched in January 2024. The aim of the survey is to create awareness regarding EFSA's initiative and to collect input from stakeholders in its initial phase and that could support further the project development. The survey will be closed on 30 April 2024 and the results will be used for the development of the Scientific Report by the WG members. The survey has been distributed to different EU and international organisations. In addition, the WG members suggested few other organisations that could be contacted, as relevant for this topic. It was also proposed to distribute the survey to EFSA Panels, for information.

5.1 Reporting from other relevant activities or meetings

The WG members were informed regarding several dissemination activities (e.g. presentations at EFSA Scientific Committee and Panels meetings, bilateral meeting with members of PARC), aiming at complementing the collaboration and engagement plan towards the development of the guidance within an international platform/mechanism.

VI. Scientific and technical topics

6.1 OECD Occupational Exposure and Effect Biomonitoring Activities - Discussion of Knowledge Exchange and Synergies with EFSA Effect-Biomarker WG

Hearing Expert (Robert Pasanen-Kase) presented the OECD project on Occupational Exposure and Effect Biomonitoring activities and facilitated the discussions of knowledge exchange and synergies with EFSA WG Biomarkers of effect. OECD project pursues synergies with relevant initiatives on biomarkers (e.g. PARC, EFSA) aiming at the reduction of work duplication and the harmonisation of terminologies and methodologies.

The presentation included aspects related to Occupational Biomonitoring, its challenges and the role of effect-biomarkers in this context, characterisation of biomarkers and the link to the Adverse Outcome Pathways (AOPs) approach. Finally, the case studies included in this project have been briefly described, including the plans for the publication of the project outcomes (e.g. guiding principles).

The discussion with the WG referred to the effect-biomarkers relevance, their interpretation in the risk assessment context, case studies, physiological versus adverse effects and similarities with other risk assessment areas. It was generally agreed that the outcomes from the OECD project represent relevant resources for the WG, to be further reviewed and used by the WG members.

6.2 Deliverable 1 - Feasibility study

In this session, the working draft of the Scientific Report was discussed. Several sections were therefore refined, focusing particularly on the Introduction, Scope and Definitions sections. Members of the WG made additional remarks on the schematic depiction of the scope and its further refinement e.g. including the visualisation of up- and down-stream biomarkers in relation to the critical effect/adverse outcome. As clarifications on terminologies is an important part of the mandate, the WG further discussed on the way forward regarding the terms related to biomarkers of effect used in different contexts.

Further, a new background text on the definitions, classification and application of biomarkers was discussed and reviewed by the WG members and it will be further integrated in the core report.

Part of this session was dedicated to the current format to describe the biomarkers of effect in parallel with several examples extracted from published EFSA Scientific Opinions. As a next step, WG members will complete the description, while the next WG meeting will be dedicated exclusively to the topic.

6.3 Deliverable 2 - Mapping study

The status of the inventory of resources was presented to the WG. Part of this activity will be outsourced starting from 1st Feb 2024 aiming to support the WG with the identification and reviewing of additional resources related to this topic. The outcome will be part of the Scientific Report.

VII. Any Other Business

7.1 Next steps and actions

The WG compiled a list of actions for the next period, with the aim of achieving a draft report ready for discussion by the Scientific Committee in Q2 2024. In addition, several actions regarding the dissemination activities, were added, including further distribution of the survey discussed above.

VIII. Next meeting

The next meeting will be held online on **26 February 2024**.

SCIENTIFIC COMMITEE

2nd Working Group meeting on Biomarkers of effect

17 November 2023
09:30 - 17:00
MINUTES - Agreed on 6 December 2023

Location: Online

Attendees:

***Working Group Members*:**

Susanne Hougaard Bennekou, Laurentius (Ron) Hoogenboom, Hendrik van Loveren, Harry Mcardle, Antonio Hernández-Jerez.

***EFSA*:**

MESE: Lucian FARCAL (Chair), Georgia BOMPOLA, Sara LEVORATO

FIP: Cristina CROERA, Zainab AL HARRAQ

NIF: Agnès DE SESMAISONS

FEEDCO: Anna CHRISTODOULIDOU, Chantra ESKES, Paola MANINI

I. Welcome and apologies for absence

The Chair welcomed the participants.

Apologies were received from Tanja Schwerdtle.

II. Adoption of agenda

The agenda was adopted without changes.

III. Declarations of Interest of Working Groups members

In accordance with EFSA's Policy on Independence[1] and the Decision of the Executive Director on Competing Interest Management[2], EFSA screened the Annual Declarations of Interest filled out by the Working Group members invited to the present meeting. No Conflicts of Interest related to the issues discussed in this meeting have been identified during the screening process, and no interests were declared orally by the members at the beginning of this meeting.

IV. Agreement of the minutes of the 1st Working Group meeting held on 25 October 2025, via web-conference

The minutes of the 1st Working Group meeting were agreed by written procedure on 23 November 2023.

[1] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/policy_independence.pdf
[2] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/competing_interest_management_17.pdf

V. Scientific topics for discussion

5.1 Deliverable 2 - Mapping study

The progress related to Deliverable 2 (mapping study) was presented to the WG. This is developed to fulfill Objective 2 of the project referring to reviewing and mapping the activities, initiatives, knowledge, approaches relevant to the project goal. The outcome will be included as Annex to the Scientific Report resulting from this project. As a first step, the structure of the inventory was created and completed with several resources (relevant projects, databases and publications). The WG discussed further the development of the inventory, information to be included and its use in the context of the feasibility study. As a next step, it was agreed to enhance some of its functionalities, e.g. for tracking new resources added and to include more resources. The project plan for 2024 includes that part of this task will be outsourced.

5.2 Deliverable 1 - Feasibility study

In this session, the WG members were updated regarding the structure of the report (agreed during the 1st meeting) and the status for each section. The focus is currently on developing the introduction (including the scope of the study), definitions, description of biomarkers of effect along with representative examples to support this work. These were further discussed in detail in the next agenda items (5.2 to 5.6).

5.3 Deliverable 1 - Introduction and scope

The WG discussed on the Scope section and the comments received on the initial text. In addition, the WG members worked on a figure that could be used to visualise the elements that are included/excluded from the scope of the study. More specifically, the WG discussed and acknowledged the complexity of addressing together the biomarkers of beneficial and adverse effects, therefore it was proposed that only safety assessment aspects and biomarkers of (adverse) effects should be included within the scope. Aspects related to the beneficial effects / food health claims will be covered and explained in the introduction section. Further, in order to capture all relevant aspects, the WG will create a list of issues that could be considered in the current report or addressed in the next phase of the project.

5.4 Deliverable 1 - Definitions of biomarkers of effect

The WG discussed around an initial proposal regarding definitions, the existing reports referring to biomarkers of effect and related terms considered in the report. The WG looked comparatively at definitions used in previous reports, guidance documents or publications. As a next step, the WG will agree on a general definition for biomarkers of effect to be used. In addition, it will be necessary to work and clarify on other terms (e.g. intermediate events, intermediate and apical endpoints) that are used in this context and compile them in a

glossary. The link with other concepts (e.g. biomarkers of exposure, biomarkers of susceptibility, adverse outcome pathways) will be also considered.

5.5 Deliverable 1 - Examples of biomarkers of effect

The WG discussed around an initial list of examples of biomarkers of effects, used to derive Reference Points for different chemicals and extracted from EFSA's Scientific Opinions. The list includes, for example, biomarkers of effect used for in the assessments of bisphenol A, per- and polyfluoroalkyl substances (PFAS), copper, etc. The WG will work on extending the list and extract useful aspects for the identification and characterisation of biomarkers of effect (see Agenda item 5.6).

5.6 Deliverable 1 - Description of biomarkers of effect

Following the previous discussion (Agenda item 5.5) regarding biomarkers of effect used in a regulatory risk assessment context, the WG agreed to compile a list of key descriptors and aspects for their identification and characterisation. The list will be further refined and harmonised to be useful for the next steps of the project. For each descriptor, the main elements to be reported will be detailed and create the basis for further methodology and guidance development.

VI. Any Other Business

6.1 Collaboration and engagement activities

The WG was informed on the collaboration and engagement plan and ongoing actions. As a short/medium-term activity, a stakeholders' survey is in preparation, with the plan to be launched in Q1 2024. This should create awareness on EFSA's initiative, support the collection of input on existing initiatives, expertise and other scientific aspects. Overall, it should complete the feasibility study and help in identifying the mechanism for co-creation of the guidance (in Phase 2 of the project) within an international partnership. The WG will be consulted further regarding the content of the survey.

6.2 Next steps and actions

A list of immediate actions was compiled and discussed. The focus in the next period will be on clarifications regarding the scope of the self-task mandate, definitions and description, starting from the examples of biomarkers of effect used in a regulatory risk assessment context.

VII. Next meeting

The next meeting will be held online on 24 January 2024.

SCIENTIFIC COMMITEE

1st Working Group meeting on Biomarkers of effect

25 October 2023
09:30 - 17:00
MINUTES - Agreed on 23 November 2023

Location: Online

Attendees:

***Working Group Members*:**

Susanne Hougaard Bennekou, Laurentius (Ron) Hoogenboom, Hendrik van Loveren, Harry Mcardle, Tanja Schwerdtle.

***EFSA*:**

MESE: Lucian FARCAL (Chair), Georgia BOMPOLA, Sara LEVORATO

FIP: Cristina CROERA, Zainab AL HARRAQ

NIF: Silvia VALTUENA MARTINEZ

FEEDCO: Anna CHRISTODOULIDOU, Paola MANINI

I. Welcome and apologies for absence

The Chair welcomed the participants.

Apologies were received from Antonio Hernández-Jerez.

Tanja Schwerdtle attended half of the meeting (agenda items 1 to 5.4).

II. Adoption of agenda

The agenda was adopted without changes.

III. Declarations of Interest of Working Groups members

In accordance with EFSA's Policy on Independence[1] and the Decision of the Executive Director on Competing Interest Management[2], EFSA screened the Annual Declarations of Interest filled out by the Working Group members invited to the present meeting. No Conflicts of Interest related to the issues discussed in this meeting have been identified during the screening process, and no interests were declared orally by the members at the beginning of this meeting.

IV. Tour de table

The participants in the meeting introduced themselves, their expertise and other relevant activities especially related to EFSA's Panels, WGs or Units.

[1] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/policy_independence.pdf
[2] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/competing_interest_management_17.pdf

V. Scientific topics for discussion

5.1 Terms or reference and project plan

The Scientific Committee requested and received from EFSA the mandate related to the "Guidance on the use of biomarkers of effect in regulatory risk assessment of chemicals" (EFSA-Q-2023-00583[3]). This project will be implemented in two phases: feasibility study (phase 1) and guidance development (phase 2), with the overall goal to work towards guidance on the use of biomarkers of effect to derive Reference Points (RPs) for establishing Health Based Guidance Values (HBGV) or deriving Margins of Exposure (MoE).

The project plan and timelines were presented by the Chair, with a focus on the feasibility study to be performed in the first twelve months of the project. This includes activities related to definitions and description of biomarkers of effect and the overall scope of the guidance. These tasks will be completed by a mapping study, that will compile and review initiatives, approaches and publications relevant to the project. The outcome of phase 1 will include conclusions and recommendations from the WG regarding the feasibility of such guidance.

5.2 Collaboration and engagement activities

The aim of the project is to achieve an internationally agreed guidance by establishing consultation and co-creation mechanisms within EU (e.g. Member States, EU Agencies, European Commission), international (e.g. OECD, WHO) and other national organisations (e.g. US FDA, Health Canada). For this, the feasibility study should identify and recommend a way forward in developing the guidance, jointly with other organisations.

These mechanisms could include consultations on the main outcomes, endorsement of the approaches proposed and/or direct involvement in the process (co-creation). The involvement of relevant organisations from the initial phases of the project is essential for achieving an internationally agreed guidance at a later stage. A collaboration and engagement plan is being developed by EFSA and the WG will be consulted further on these activities.

5.3 Deliverable 1 Report

Within this Agenda item, the plan for Phase 1 and its main outcome was presented by the meeting Chair. The WG will work on a Scientific Report (Deliverable 1 of the project) to be published in EFSA Journal (Q3 2024) and to be used as a base for further development of guidance. The report will define the scope and limitations of the approach, will address several challenges especially related to the definitions of biomarkers of effect and other relevant terms, descriptors for their identification and characterisation and any other scientific concepts needed in this context.

[3] https://open.efsa.europa.eu/questions/EFSA-Q-2023-00583

The work will also include the identification and analysis of representative examples of biomarkers of effect that have been used already by EFSA's Scientific Panels to derive Reference Points and use them along the project implementation. The examples will be included as an Annex to the scientific report.

5.4 General discussion on the project plan and Deliverable 1

Several aspects and challenges were discussed by the WG members, e.g. *i*) clarifications regarding the scope, applicability and limitations of the concepts to be developed, *ii*) a general and broader scope of the project, that would cover the adverse effects, as well as the beneficial effects (addressing toxic substances and also nutrients), versus a more focused scope, *iii*) use of existing examples from EFSA's Scientific Opinions, especially for the definition and description of biomarkers of effect.

The WG discussed on the main challenges, possible solutions and their prioritisation (starting from a previously prepared draft list). It was concluded that Phase 1 should provide a set of recommendations for the further development of the guidance and solutions to the identified challenges.

5.5 Definitions related to biomarkers of effect

The discussion within the WG started from the existing definitions of biomarkers of effect and related terms that should be clarified and used first (e.g. available definitions and concepts developed by other organisations (e.g. WHO, OECD, FDA) and investigate which elements should be used as such or adapted.

As harmonisation of terms is needed, the WG should discuss regarding the link between "biomarker of effect" and related terms that are often used interchangeably (e.g. intermediate events, effects and endpoints, surrogate endpoints, markers of status).

5.6 Description of biomarkers of effect

The WG members discussed the options for the description of biomarkers of effect that could include different type of descriptors, e.g. for the identification, characterisation, classification or measurements of biomarkers of effects. It was discussed that the description should include different aspects, e.g. naming and other identifiers, relevant biological process or level of organisation, measurement methods and matrixes, other mechanistic information.

5.7 Other scientific concepts

The WG considered that the work on the definition and description of biomarkers of effect may also bring clarifications regarding other aspects, e.g. whether the effect in question constitutes an impairment, a disease or rather a change in homeostasis, the specificity of the biomarkers of effect, the predictive power of the biomarkers of effect (e.g. sensitivity and the

magnitude of the response to the stimulus, the correlation of a decrease/increase of a biomarker with the adverse effect), their human/animal relevance, the use of *in vitro* measurements and creation of batteries of biomarkers of effect/multimodal biomarkers, especially in the context of a transitioning towards new approach methodologies (NAMs) to enhance their predictivity in risk assessment, the link to the adverse outcome pathways (AOPs) approach.

VI. Any Other Business

6.1 Distribution of tasks, responsibilities and expectations

Following the presentation of the project plan, the outline of deliverable 1 and discussion, different tasks towards developing the report were distributed to WG members. The first steps will include working on the scope of the report, the definitions of biomarkers of effects and extraction of representative examples of biomarkers of effect from EFSA's Scientific Opinions.

VII. Next meeting

The next meeting will be held online on 17 November 2023.