Third meeting of the CIOMS Working Group (WG) XVI on the Development Safety Update Report (DSUR)

30 September 2025, virtual meeting

Minutes

Overview:

Summary

The CIOMS Working Group XVI convened its third meeting virtually on 30 September 2025. The main aim of the meeting was to discuss the development and refinement of the newly structured Development Safety Update Report (DSUR) template, focusing on its key components. WG members agreed to hold smaller subgroup meetings to further refine the document in preparation for the upcoming in-person meeting in 26-27 January 2026, in Barcelona, hosted by Bayer.

Minutes of discussion

1. Opening and welcome

- Lembit Rägo, CIOMS Secretary-General, welcomed all participants to the virtual meeting. He noted the group's visible progress and expressed appreciation for the continued engagement of members. (For a list of participants see Annex 1).
- He provided a brief update on recent CIOMS activities and publications:
    - Two CIOMS reports were released earlier in 2025 — the report on Severe Cutaneous Adverse Reactions (SCAR), which received positive feedback, and the Benefit-Risk Balance for Medicinal Products report, which is of broader interest. A webinar on the Benefit-Risk Balance report was recently held, attracting around 900 participants. Due to time zone limitations of the first event, a second session will be organised to better accommodate participants from the Western Pacific and other regions.
    - Upcoming CIOMS webinars include:
        - A second run of the Benefit-Risk Balance webinar on 23 October 2025 (final details to be announced)
        - An additional webinar on MedDRA Labelling Groupings, scheduled for mid-October.
- Lembit emphasised the importance of disseminating WG outputs widely once the DSUR report is completed, including through a dedicated CIOMS webinar to raise awareness and support implementation of the group's recommendations
- Lembit introduced Dr Samvel Azatyan, newly appointed Senior Advisor to CIOMS.
- Agenda was adopted.
- Kateriina was rapporteur.

2. Presentation and Discussion of Revised DSUR Template Proposal

- Tessy and Donald gave a brief overview of progress to date.
- A presentation was shared to illustrate the conceptual framework of the revised DSUR template. Tessy explained that the draft and its table of contents were designed to provide a logical, sequential overview of the product's development and safety profile.
- The new structure ensures that each section builds upon the previous one, beginning with essential background data and progressing through safety analysis to benefit–risk evaluation.
- The framework consists of three main components:

    - Background information: Non-clinical and clinical data, exposure details, non-interventional studies, and other contextual elements outlining the product's development stage.
    - Signal detection and safety monitoring processes: Systems, data sources, and procedures used to identify and assess safety issues.
    - Results and interpretation: Identified signals, risk changes, benefit–risk considerations, and any late-breaking information.

- Tessy noted that placing background information first helps readers understand the development context before reviewing safety findings.
- Donald added that the objective was to create a consolidated template that reduces redundancy while preserving the integrity of required data.
- He explained that several sections of the current DSUR have been merged under signal evaluation, reflecting how safety information is generated and assessed in practice.
- This approach aligns with feedback from regulators and working group members seeking a more efficient, cohesive document.
- Donald concluded that the revised framework provides a practical, user-friendly basis for a DSUR template that reflects current regulatory and industry practices.

Discussion and Reflections on the Proposed Template

- The Working Group expressed appreciation to Tessy and Donald for their work on the revised DSUR template, noting that the proposed structure provides a logical and coherent framework. Members agreed that the draft represents an efficient and well-structured approach that maintains essential safety information while improving overall clarity.

Benefit–risk considerations in development

- Beatrice commended the clarity of the draft and raised whether the proposal marked a shift from a traditional DSUR towards a benefit-risk evaluation for development, similar to the transition from Periodic Safety Update Report (PSUR) toward a Periodic Benefit–Risk Evaluation Report (PBRER).
- Donald clarified that this was not the intent. The DSUR should remain focused on clinical development, where efficacy is still being investigated. The revised structure aims to make the report more relevant by reducing duplication and aligning content with actual developmental processes. Unlike the post-marketing PBRER, the DSUR must reflect the controlled trial environment and provide only data of clear value to regulators.
- Corina noted that benefit-risk considerations remain essential but should be viewed within the context of ongoing clinical trials, where risk-benefit balance may differ between studies.
- Peter suggested keeping an open mind, noting that while the aim was not to create a full benefit–risk document, the group should remain open-minded and allow the work to evolve naturally.
- Andrzej cautioned against adopting a full benefit–risk model, as benefits during development are still hypothetical. Risks can only be balanced against expected or potential benefits. He highlighted the importance of clear definitions for risk, important risk, and potential risk, consistent with post-marketing terminology.

Signal definition and assessment

- Elena noted the challenge of defining a signal during development, as thresholds vary by trial phase. A single case may be relevant in early trials but not in later ones. She suggested that further discussion on this topic take place in the signal subgroup or breakout session.

Regulatory perspective on risk assessment and mitigation

- From a regulatory viewpoint, the key question is whether participant risk in a trial is acceptable, and that this question should be clearly reflected in the DSUR.

- Antonella stressed the importance of identifying, minimising, and monitoring potential risks, even where efficacy data are limited. She recommended including a table summarising risk mitigation measures, and their effectiveness to support regulatory evaluation.
- Andrzej agreed, recalling earlier initiatives on developmental risk management plans, and suggested aligning developmental risk concepts with established post-marketing practices to ensure consistent terminology.

Clarifications on Swissmedic progress reports

- Anita raised a practical point regarding recent Swissmedic requirements for progress reports in both combined and standard clinical studies. She noted that companies handle these reports differently: some submit them separately, others include them as appendices and proposed maintaining flexibility.
- Donald clarified that Swissmedic progress reports are study-specific and distinct from the DSUR, which summarises all studies under a development programme. This can create confusion since both documents are often submitted together.
- It was agreed that progress reports should remain separate from the DSUR, as combining them would be operationally difficult due to differing timelines and formats.

Presentation of the DSUR roadmap and section mapping

- Tessy and Donald presented a roadmap illustrating the evolution of the proposed DSUR structure from the current International Council for Harmonisation (ICH) E2F: Development Safety Update Report (DSUR), intended to make the transition clearer and easier to follow. The roadmap also serves as an audit trail, mapping each section of the existing DSUR template to its corresponding place in the proposed version. This allows users to see how sections have been consolidated, relocated, or removed, and to understand the reasoning behind these changes.
- The mapping includes an overview of regional appendices, following earlier discussions on the importance of tracking regional requirements and assessing whether some could be harmonised with global content to improve consistency.
- It was noted that regional appendices remain a practical challenge because country-specific requirements change more frequently than updates to ICH E2F can accommodate. The WG will therefore need to consider how best to represent regional variations within the future template.
- Maintaining a clear audit trail was recognised as essential for transparency and for explaining the evolution of the DSUR to both regulators and industry stakeholders. The roadmap may also serve as a useful reference in future presentations or training materials.

Discussion on section mapping, signal evaluation, and integration of post-marketing information

Review of redundant sections

- Andrzej asked whether the revised DSUR template had removed redundant sections that added little value to the report.
- It was confirmed that certain sections from the current ICH E2F template had been eliminated, including *worldwide marketing approval status* and *patient exposure from marketing experience*, as these were considered duplicative or not essential for evaluating the investigational medicinal product (IMP).
- The WG noted that all proposed deletions were clearly marked in the roadmap and justified to maintain transparency.

Post-marketing experience and signal evaluation

- Beatrice questioned the removal of the post-marketing experience section, noting that post-marketing data can provide critical safety insights, particularly when few trials remain active.
- It was clarified that relevant post-marketing information would continue to appear under the signal evaluation and safety concerns sections, ensuring coverage without duplication of PBRER content.
- Signal evaluation will be presented as a global appendix, with the main body describing the signal detection process and the appendix summarising identified signals and outcomes.
- Antonella highlighted the importance of explaining whether signals were confirmed or refuted, and why, to improve transparency. The WG agreed that this aspect should be further developed in accompanying guidance.

Template review

- The subgroup on signal evaluation will provide detailed guidance for assessing signals in development-stage products and determine how best to align reporting with post-marketing requirements.
- It was reaffirmed that post-marketing data meeting the signal threshold will be included, while exposure data will be excluded due to the challenges of reliable calculation.
- Tessy noted that once a product is marketed in the EU, safety monitoring follows Module IX guidance. For products still in development, the DSUR should describe the signal detection process**,** including monitored sources and internal procedures.
- Members will provide detailed written comments on the new DSUR template. The current version serves as a blueprint and supporting guidance text will be developed in stages, drawing from existing ICH material and subgroup contributions.
- In response to Corina, Tessy and Donald outlined key challenges during drafting.
  o Tessy noted uncertainty around how to incorporate analysis from line listings**,** leading to the creation of a placeholder section titled Additional safety information reported during the period for findings not meeting signal thresholds.
  o Donald said the process provided an opportunity to view the DSUR from a regulatory assessor's perspective**,** focusing on elements that add real value. He added that alignment improved as the work progressed.
  o Tessy emphasised that the draft aims to help readers identify immediately what is new and where to focus attention.

Causality assessment and international differences

- Beatrice raised the issue of differing causality assessment standards, citing the FDA's Investigational New Drug (IND) Final Safety Reporting Rule, which relies on sponsor assessment, versus other jurisdictions that use investigator causality.
- Peter explained that companies typically submit a global DSUR containing both investigator and sponsor assessments where applicable, without separate reporting for the FDA. Beatrice agreed that guidance clarifying this would be helpful.

Analysis of line listings and risk mitigation

- Antonella recalled that the Clinical Trials Coordination Group (CTCG) Safety Sub-group had recommended adding a short narrative analysis of trends or imbalances in serious adverse events, rather than tables alone.
- Tessy confirmed that this recommendation was integrated into the draft, with such analysis placed under Additional safety information to avoid repetition.

- Corina and Antonella suggested using the same section to summarise risk mitigation measures and their effectiveness, including comparisons across reporting periods to demonstrate impact.
- This section would be further refined in the final guidance, and subgroups will consider these points in their future work.

Commenting the draft template

- Lembit proposed extending the commenting period by two weeks to allow members who had not yet provided input to do so. Tessy and Donald agreed to collate all comments, identify those requiring wider discussion, and prepare a summary for the next meeting.
- It was acknowledged that the draft template represents a working version that will continue to evolve alongside the development of accompanying guidance. Members noted that once the full draft DSUR document takes shape, further revisions may be necessary to ensure internal consistency.

Consideration of non-commercial sponsors

- Corina raised the question of whether the new DSUR template could also be applied to non-commercial sponsors, noting that such organisations often lack the same resources and systems as industry sponsors.
- Lembit agreed that the group could make a recommendation encouraging non-commercial sponsors to follow the same structure, where feasible, while allowing flexibility in implementation.
- Beatrice suggested that the future guidance clarify that certain sections may not apply to single-trial or academic sponsors and that simplifications should be permitted according to the scope of their development programme.
- Andrzej supported this approach, recommending that flexibility be maintained to reflect the diversity of academic and investigator-initiated trials (IITs). He proposed that regulators could play a key role in promoting awareness and consistent use of the DSUR framework across non-commercial settings
- Lembit noted that explanatory notes could be added to the final guidance, outlining how non-commercial sponsors might adapt the DSUR to their context, rather than merely recommending its use. Andrzej further suggested including an example DSUR for a non-commercial sponsor, similar to examples included in the original 2006 ICH E2F guidance.
- Antonella informed the group that a simplified DSUR template for non-commercial sponsors is already used in Europe, based on ICH E2F but allowing omission of certain sections (e.g. post-marketing data, expanded access programmes). She proposed using this as a reference to develop a short guidance note for non-commercial sponsors under the CIOMS framework.
- It was agreed that the European simplified template would be circulated to all members for reference.

3. Subgroup discussions

It was confirmed that subgroup participation was generally well balanced, with final preferences to be clarified following the meeting. The breakout sessions were intended to initiate discussions, with detailed work to continue in subsequent meetings. Each subgroup was asked to identify a lead or co-leads to coordinate ongoing activities and ensure continuity, while Subgroup 4 may reconvene separately if participation remains limited.

Summary of subgroup discussions

Subgroup 1 – Signal management

- Tessy gave an overview of the first subgroup discussions. The group identified a need to clarify terminology and definitions related to signal detection for investigational products.
- Existing guidance provides only limited direction; further work is needed on appropriate methodologies, data sources, and reporting formats during clinical development.
- Discussion highlighted the importance of defining the signal lifecycle in development and ensuring proportional approaches suitable for both large and small sponsors.

Subgroup 2 – Reference Safety Information (RSI)

- Pete gave an overview of the discussion. The subgroup reviewed the Medicines and Healthcare products Regulatory Agency (MHRA) fact sheet and noted alignment with forthcoming Clinical Trials Coordination Group (CTCG), a working group under the Heads of Medicines Agencies (HMA) in Europe, guidance.
- The DSUR could serve as a tool to justify RSI changes by linking updates to signal evaluations and related risk-mitigation actions.
- Further clarification is required on the distinction between reference safety information as a broad concept and the RSI section of the Investigator's Brochure. Placement of RSI-related content within the DSUR structure will be discussed further.

Subgroup 3 – Benefit–risk considerations

- Beatrice gave an overview of the group discussions. The group agreed that benefit in development should refer to anticipated rather than demonstrated benefit, while risk should focus on important identified and potential risks. Definitions will be reviewed against ICH E6(R3) to ensure consistency.
- A new subsection is proposed to describe risk-minimisation measures and their effectiveness, even where no new risks are identified.
- The subgroup emphasised the need for coordination with the signal group to maintain alignment across sections and discussed including clarification on how investigational product safety relates to public-health impact.

4. Next steps / Next meeting / Subgroup work

- It was agreed that the three active subgroups (signals, reference safety information, and benefit–risk considerations) would continue developing their respective sections with the goal of presenting a consolidated draft or overview at the January 2026 face-to-face meeting**.**
- The fourth subgroup will be launched after the January meeting, as its focus areas, such as evolving PV regulations and regional implementation aspects are less critical to the immediate structure of the revised DSUR template.
- The 28 October virtual meeting slot will be used for subgroup sessions rather than a full-group discussion, to allow each subgroup additional time to refine their drafts.
- If possible, subgroup leads will arrange at least one preparatory meeting before the October session to advance work and identify key issues for discussion.
- Beatrice will circulate Subgroup 3 (Benefit–risk considerations) updated draft template as soon as possible to support intersessional progress and subgroup coordination.

- Next in-person meeting is scheduled for 26–27 January 2026 in Barcelona, to be hosted by Bayer.

5. Closing remarks

- Lembit thanked all members for their active engagement and constructive input throughout the meeting.

Annex 1: List of participants

Participants

Antonella Caselli (Italian Medicines Agency), Carmen Campanile (Swissmedic), Andrzej Czarnecki (Eli Lilly), Peter De Veene (MSD), Mutsuhiro Ikuma (PMDA), Eun Mi Kim (WHO), Mamiko Konishi (Eisai), Maria Grazia Malpezzi* (Italian Medicines Agency), Pete Nash (Gilead), Beatrice Panico (Individual expert), Elena Prokofyeva (FAMHP), Donald Puccio (Pfizer), Indra Purevjal (Bayer), Kateriina Rannula (CIOMS), Lembit Rägo (CIOMS), Tessy Ruijgrok (Biogen), Anita Shenoy (AbbVie), Corina Spreitzer (Austrian Medicines Agency), Huanhuan Cui (NMPA), Wang Haixue (NMPA), and Wang Xiangyu (NMPA).

*Alternate

Apologies
Juliana Dornelles (ANVISA) and Richard Pendlebury (Novartis).

Subgroups as per 30 September

1. Signals (for investigational products)

Tessy Ruijgrok, Peter de Veene, Indra Purevjal, Antonella Caselli, Mutsuhiro Ikuma, Elena Prokofyeva, Beatrice Panico, Indra Purevjal, Huanhuan Cui, Anita Shenoy, Huanhuan Cui

2. Reference Safety Information (RSI)

Pete Nash, Carmen Campanile, Elena Prokofyeva, Donald Puccio, Mutsuhiro Ikuma, Anita Shenoy

3. Risk and Benefit

Beatrice Panico, Andrzej Czarnecki, Eun Mi Kim, Indra Purevjal, Antonella Caselli, Peter de Veene, Mamiko Konishi, Samvel Azatyan, Corina Spreitzer, Mutsuhiro Ikuma, Anita Shenoy, Huanhuan Cui

4. 1) Device Combination products; 2) AxMPs. (to start work at a later stage)

Donald Puccio, Corina Spreitzer, Mamiko Konishi, Anita Shenoy