Council for International Organizations of Medical Sciences

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

26-27 January 2026, Barcelona, Spain, hybrid meeting

Minutes

Summary

The CIOMS Working Group (WG) XVI on Development Safety Update Report (DSUR) held its fourth meeting in Barcelona, Spain, on 26-27 January 2026 with participants joining both in person and virtually. The meeting focused on reviewing progress made by the subgroups since the previous meeting and advancing the development of the draft report. Subgroups presented updates on their respective sections, outlining progress achieved and key issues identified. The WG discussed the overall structure of the document, alignment between sections, and the process for consolidating subgroup contributions into a single evolving draft. Members agreed on the next steps for further development of the document, including continued drafting, cross-review between subgroups, and integration of revisions. The next virtual WG meeting will be held 23 April 2026, followed by an in-person meeting in Geneva in September.

Minutes of discussion

Day 1

Opening and welcome

- Lembit Rägo, CIOMS Secretary General, welcomed the participants to the WG fourth meeting and provided an update on recent CIOMS news noting that several CIOMS Working Group reports had been published during the previous year:
    - WG report on Severe Cutaneous Adverse Reactions (SCAR)
    - WG XII report on Benefit-Risk Balance for Medicinal Products;
    - WG XIV on Artificial Intelligence in Pharmacovigilance. There are several ongoing CIOMS WGs (more information at https://cioms.ch/).
- A new CIOMS WG XVII on Long-term safety of medicinal products has been initiated.
- Exploratory plans for a potential future topic on the repurposing of medicines were noted, including increasing public-private interest, particular relevance for rare diseases, and the emerging use of artificial intelligence to identify new potential indications for existing medicines.
- CIOMS organises webinars related to WG reports, including the WG XIV report, across multiple time zones to ensure global accessibility, and increasingly uses them as a routine dissemination step to highlight key updates and practical implications following publication.
- *Tour de table* was conducted. For a list of participants see Annex 1.
- Agenda was adopted.
- Kateriina was rapporteur.

Roundtable: relevant external initiatives and developments

- The participants were invited to share any relevant external initiatives, consultations, or conferences that could inform the WG's ongoing work or highlight emerging expectations.
- It was reported that an update to the EU Clinical Trials Regulation (CTR) Questions and Answers (Q&A) document was underway and included content relevant to Development Safety Update Report (DSUR)-related expectations, with some updates potentially important for the WG to consider.
- An additional European Commission initiative was described concerning combined submissions**,** intended to enable a clinical trial to be conducted together with a clinical investigation/performance study or related study types under a coordinated framework (https://health.ec.europa.eu/medical-devices-topics-interest/combine-programme_en#documents) .

  A pilot submission combining an Investigational Medicinal Product (IMP) application with an associated performance study component had been initiated with a large pharmaceutical company, and validation was underway at the time of the meeting.

  A second workstream in this area aims to develop a sponsor guidance for safety reporting in combined studies, with input gathered from multiple organisations and expected finalisation within the coming months.

- Participants agreed that keeping sight of these parallel developments was important for ensuring that the WG's output remains compatible with evolving regulatory and operational realities.
- It was noted that the public consultation phase may also provide a pathway for valuable input from organisations not formally represented within the WG.

Subgroup updates

Subgroup 1 – Signal detection

- Subgroup 1 presented its progress and reasoning on how "signals" should be addressed in the Development Safety Update Report (DSUR).
- The subgroup explained that it examined whether post-marketing signal concepts can be applied directly to investigational products and concluded that terminology and processes cannot be transferred unchanged, as the clinical development context involves smaller datasets and evolving evidence.
- It was emphasised that DSUR guidance should clarify what signal detection or safety surveillance means during development and how it should be described consistently.
- A proposed working definition of an investigational-use signal was presented, describing information suggesting a new potentially causal association, or a new aspect of a known association, between an investigational product and an adverse event that warrants further evaluation or action to protect participant safety.
- The subgroup noted that investigational signal detection may draw on multiple sources beyond individual case safety reports, including trial data, laboratory information, literature and external data, and highlighted guidance supporting prospective safety surveillance plans during trials.
- A risk-based approach was supported, with review methods and frequency varying depending on development phase rather than replicating post-marketing signal detection approaches.
- The subgroup also discussed what information may be useful to include in the DSUR when presenting a signal (e.g., source, evaluation methods, analysis, results and actions taken) and identified further topics requiring discussion, including signal reporting in complex development settings such as combination products and innovative modalities.

Plenary

- It was acknowledged that the DSUR is not a standalone signal detection guideline, but participants supported the idea that the DSUR should contain clearer expectations on how signal-related information is presented, particularly for investigational products without marketing authorisation.
- Participants agreed that CIOMS can propose scientifically grounded approaches even where regulation is not explicit, provided the text is framed transparently and does not claim legal status.
- A practical concern was raised that, in current practice, "signal" sections in DSURs sometimes focus on post-marketing signal content, while trial-related emerging safety issues are described elsewhere as actions taken, sometimes creating inconsistency and confusion.
- The subgroup's draft signal definition prompted discussion about whether "study procedure" should be included alongside investigational product, with concerns that this could unintentionally encourage reporting of procedure-related events and add noise to reporting systems.
- It was agreed that the wording needs refinement so that relevant trial contexts are not excluded, while avoiding language that could drive irrelevant reporting or misinterpretation.

- The group emphasised that development-stage signal detection is fundamentally different from post-marketing detection because early-phase DSURs often involve small exposure numbers, where even a single case can be significant.
- Participants discussed expectations for what should appear in a DSUR "signal" section, including: why the sponsor considers something a signal, what was done in response, and whether the signal remains under evaluation.
- The appropriateness of describing signals as "closed" in development was debated, with concern that early-stage uncertainty makes "closure" difficult to justify and may not reflect real monitoring practice.
- Alternative framing was discussed, including describing whether an issue remains under evaluation, has been refuted based on available evidence, or has been "promoted" into an important/potential risk category, with appropriate cross-references to risk sections.
- It was noted that the subgroup's topic is closely linked to other DSUR sections (e.g., benefit–risk, RSI, risk tables), and that consistency and cross-referencing will be needed to avoid duplication.

Subgroup 2 — Reference Safety Information (RSI) and how RSI changes should be reflected in the DSUR

- Subgroup 2 reported that its work focused on how to reflect RSI expectations in DSUR reporting without creating conflict with evolving and highly detailed CTR Q&A materials.
- It was noted that the CTR Q&A (and related national guidance) is extensive and updated over time, and that inspectors and reviewers often expect sponsors to comply with it in practice even when framed as Q&A.
- The subgroup therefore aimed to provide high-level DSUR guidance that supports transparency and traceability, rather than attempting to replace or replicate detailed regional instruction.
- The subgroup proposed that DSURs should clearly identify which RSI version was used for DSUR preparation (including the version in effect at the DSUR data lock point, where applicable), and should summarise changes during the reporting period.
- It was recognised that sponsors may not always be using a single standard "RSI table" format globally, and the subgroup aimed to keep the DSUR guidance workable when RSI is derived from different documents (e.g., IB, label, or other locally accepted RSI sources).
- The subgroup suggested that newly added RSI terms (e.g., new preferred terms) should be listed and linked to the supporting safety evaluation in the DSUR, so that readers can trace why the RSI was updated and what evidence supported the change.
- It was proposed that DSUR content should also indicate whether additional measures were introduced in response to RSI updates, or justify why no additional measures were considered necessary, while avoiding duplication across DSUR sections by using cross-references where appropriate.

Plenary

- A discussion followed on practical challenges related to multiple Reference Safety Information (RSI) and Investigator's Brochure (IB) versions during a reporting period, approval timelines, and the interaction between expedited reporting and Development Safety Update Report (DSUR) expectedness tables.

- Participants noted that expedited reporting must rely on the RSI in effect at the time of the event, while DSUR preparation may involve reassessment using a single RSI version, which can create misalignment.
- It was highlighted that expectedness classification in DSUR tables can support reconciliation with Suspected Unexpected Serious Adverse Reactions (SUSARs) received during the year, although technical and operational constraints may limit full reconciliation.
- Differences between DSUR outputs and SUSAR reports received by regulators may occur due to timing differences between DSUR preparation, RSI updates, and implementation of approved changes.
- Some safety systems allow listings to be re-run using different RSI versions, but this capability is not universally available, and DSUR guidance should avoid requiring functions that many sponsors cannot implement.
- Transparency was considered preferable to attempting perfect reconciliation, with DSURs clearly describing RSI versions used, the approach applied, and any limitations.
- A proposal was discussed to simplify or remove the requirement to retrospectively reassess expectedness using a single RSI, noting that expedited reporting has already applied expectedness classification in real time.
- Under this approach, the DSUR would instead document RSI changes during the reporting period and explain the rationale for updates, supporting traceability without requiring retrospective reclassification.
- Regulators noted that reconciliation remains important but acknowledged that strict retrospective rules may not resolve practical limitations and that clearer explanations may better support regulatory review.
- The group agreed that DSUR template guidance should reflect real-world approval timelines, multiple RSI versions, system constraints, and the goal of practical clarity.
- It was noted that additional points would be incorporated into the written subgroup material and that developments in the Clinical Trials Regulation (CTR) Questions and Answers (Q&A) document would be monitored.
- Subgroup 2 emphasised the need for simplified and implementable DSUR guidance on RSI and expectedness. It was acknowledged that the WG cannot change the CTR Q&A directly but can propose pragmatic DSUR guidance to improve clarity and traceability.
- Participants reiterated that repeated or retrospective expectedness reassessment following RSI changes may be impractical and may add limited value.
- Support was expressed for focusing DSUR content on transparent description of RSI changes rather than attempting strict retrospective reconciliation.
- A regulatory perspective was shared that cases initially reported as SUSARs may later become expected following RSI updates without raising concerns, provided reporting obligations were met at the time.
- It was noted that if a case appears as a SUSAR in DSUR listings but is no longer unexpected under an updated RSI, this should not necessarily be considered problematic.
- The intention is to develop DSUR guidance that is pragmatic, meaningful for safety evaluation, and operationally feasible.

Subgroup 3 – Anticipated benefit and risk

- Subgroup 3 reported that it had agreed development-stage DSURs should avoid implying definitive “benefit” and instead introduce the concept of “anticipated benefit” as a more appropriate framing during clinical development.
- It was noted that the subgroup drafted a working definition of anticipated benefit and had begun implementing revised wording across the document to align with this concept.

- The subgroup explained that the DSUR section should focus on what could affect participant safety and the overall risk–anticipated benefit balance for the investigational product during development.
- The subgroup reported introducing wording and structure that consistently refers to important identified risks and important potential risks, aiming to standardise how these are discussed.
- A structured approach was described, including a table intended to prompt sponsors to inform regulators what happened with important risks during the reporting period and what actions or measures have already been implemented or are being proposed.

Plenary

- Substantial work had already been done to revise wording and further work would be needed to intensify and refine the section.
- It was highlighted that the assessment should not focus only on the product "in general," but also needs to consider the trial context, including the study population, indication, and whether continuation of the trial remains justifiable.
- It was emphasised that the benefit–risk balance of the investigational product may differ across populations (e.g., acceptability of serious risks may be different in oncology compared with other conditions).
- The need for a clear and structured explanation of risk minimisation or risk management measures was discussed, including what has already been done, what is planned, and how these measures relate to the identified or potential risks.
- A concern was raised that "benefit-risk" can mean different things depending on perspective (public health/regulatory perspective versus individual patient clinical decision-making) - what exactly should the DSUR aim to reflect?
- It was argued that DSUR guidance must avoid drifting towards individual clinician-level benefit–risk decisions and instead focus on whether continuation of the clinical trial is justified based on emerging safety information and anticipated benefit in the study context.
- A challenge was raised regarding terminology and escalation: if a risk is truly "important" early in development, it may imply that development or the trial should stop rather than "minimise" the risk, and therefore the document must be careful in how it uses "important risk" language in early phases.
- The WG agreed to keep concepts clearly separated (events vs adverse drug reactions vs risks), and ensure that risk language is used consistently and appropriately for development settings.
- The subgroup clarified that the key question it wants the DSUR to help answer is whether it is justifiable to continue a clinical trial in the presence of a risk of concern, and how that justification should be expressed.
- It was agreed that subgroup discussion should continue to refine the wording so that it remains practical, clear, and aligned with what regulators need to see in decision-making about trial continuation.
- The report must cover all DSUR elements adequately, and that the group should avoid making one section disproportionately complex at the expense of overall coherence and usability.

Template and guidance document approach

- A discussion followed on how subgroup work should be integrated into the evolving DSUR materials, distinguishing between the template itself and a broader guidance document explaining principles and expectations for each section.
- It was observed that some subgroups have been implementing text directly into the main document/template, while others have been developing content externally that still needs to be mapped into the template.

- It was agreed that the overall deliverable is expected to include both a structured template and accompanying written guidance to explain the rationale, expectations, and how to apply the template.

Subgroup 4 timing

- The fourth subgroup topic (combination products and auxiliary medication) is expected to be addressed after the first three subgroups establish the core approach.
- It was noted that the initial plan was to first clarify the direction of the first three subgroups, as the fourth topic depends on alignment with the foundational sections.

Subgroup work continued

- A proposal was made to use the remaining time before lunch to produce short, concrete summaries from each subgroup capturing: (i) what was achieved, (ii) what the plenary discussion changed or clarified, and (iii) what still remains open or needs further work.
- This approach was supported as a way to make the work more concrete, help participants reflect overnight, and enable a clearer plan for subgroup work in the afternoon.
- Each subgroup should capture its status in a small set of bullet points (potentially a shared slide deck) so the overall direction is visible to all participants in one place.
- For Subgroup 1, it was stated that the subgroup has a written document capturing its thinking but needs to (i) confirm where consensus exists, (ii) identify remaining discussion points, (iii) map conclusions into the actual template, and (iv) address specialised topics such as advanced therapies and other new modalities.
- It was noted that methodology choices remain an open area, including how approaches differ between early-phase and later-phase development.

The subgroups continued their work in subgroups and reconvened for plenary.

Subgroup 1 Progress Report

- Subgroup 1 reported that it had developed a signal concept specific to investigational medicinal products (IMPs) and agreed that updated guidance is needed on signal detection methodology during clinical development.
- The proposed guidance would include background methodological principles, examples of relevant information sources, and a risk-based approach considering factors such as product complexity, trial pace, and product characteristics.
- The subgroup also discussed the need to clarify differences between signal detection for investigational and post-marketing products, including methodological expectations, surveillance frequency, and safety surveillance planning.
- Topics requiring further discussion include non-fixed dose combinations, auxiliary medications, and new therapeutic modalities. The potential future role of artificial intelligence and machine learning in signal detection was also acknowledged, including how early observations that do not yet meet the signal definition may be addressed in the Development Safety Update Report (DSUR).
- The subgroup discussed how signal outcomes should be presented and linked to Reference Safety Information (RSI) and benefit–risk assessment, noting that alignment with the RSI and benefit–risk subgroups will be necessary.
- A working draft describing the proposed general guidance text has been prepared and will be further refined. Two open issues were highlighted: how to translate the principles into concrete DSUR template wording and how to position risk mitigation within the framework.

- It was noted that risk mitigation actions would arise from signal evaluation and feed into the broader benefit–risk evaluation at trial, population, or compound level.
  During discussion with the wider group, it was agreed that the DSUR should focus on important identified or potential risks while ensuring that signals not considered important remain visible in the signal evaluation section. Signal evaluation and benefit–risk sections were considered complementary, with signal evaluation determining importance and only important risks carried forward to the benefit–risk discussion.
- The subgroup confirmed that its draft wording will be circulated to the Working Group for review and alignment with other sections.

Subgroup 2 progress update: Reference Safety Information (RSI)

- Subgroup 2 reported that progress on Reference Safety Information (RSI) drafting depends on ongoing discussions and outputs from European regulators, including the European Medicines Agency (EMA) and Medicines and Healthcare products Regulatory Agency (MHRA) Questions and Answers (Q&A) documents.
- The subgroup proposed that RSI updates should not be restricted to a single annual update linked to the Development Safety Update Report (DSUR), but may occur during the year when important new information becomes available, with the DSUR explaining how RSI evolved over the reporting period.
- Under this approach, the DSUR would describe the RSI version at the start of the reporting period, any updates during the year, and key changes affecting expectedness (including undesirable effects and adverse drug reactions).
- This was considered potentially helpful for improving consistency between Suspected Unexpected Serious Adverse Reaction (SUSAR) reporting and DSUR preparation, particularly where expectedness must be assessed against the RSI version in force when an event occurred.
- Participants noted that this approach could also address reconciliation challenges for some authorities and reduce administrative burden by avoiding retrospective recalculation against a single end-of-period RSI.
- It was clarified that RSI remains part of the Investigator's Brochure (IB) and therefore continues to require appropriate review and approval processes; the group discussed whether the DSUR should explicitly acknowledge that RSI updates may be proposed and subject to approval.
- An external document summarising the problem statement and legislative references related to RSI timing and use was mentioned as potentially useful, and participants agreed it would be helpful to review and incorporate relevant elements where appropriate.
- The WG discussed challenges arising from differing regional interpretations of the RSI at the start of a DSUR reporting period and noted that any proposed solution should aim for clarity and international alignment.
- It was noted that proposed solutions in the external document include using the most conservative RSI (i.e., the version with the fewest expected adverse reactions) when different regional approvals result in divergent RSI versions, or integrating RSI updates within the DSUR process rather than at trial level; these proposals will be considered further by the WG.

Subgroup 3 progress update: Benefit–risk assessment

- Subgroup 3 reported that its drafting approach focuses the Development Safety Update Report (DSUR) benefit–risk discussion on important identified risks and important potential risks, to support meaningful decision-making and avoid exhaustive lists that do not drive conclusions.
- Benefits during clinical development should be described as anticipated benefits, with sponsors transparently explaining how anticipated benefit is weighed against risks.

- Sponsors would be expected to identify newly recognised important risks or new information on existing important risks during the reporting period, describe actions taken and risk mitigation measures (including population-specific measures where relevant), and provide a clear conclusion explaining why development may continue, with or without modifications.
- Benefit–risk assessment should consider both periodic and cumulative data, with explanations provided where reporting-period trends differ from cumulative understanding.
- Risks not considered important should remain visible through the signal evaluation section to maintain transparency, while the benefit–risk conclusion should focus on risks that materially influence programme-level decisions.
- Participants noted that non-important risks may still be mentioned where relevant (e.g., where RSI updates are expected to be managed through routine clinical practice), with careful wording to avoid confusion between categories.
- The group also discussed how to address situations sometimes referred to as "lack of efficacy," agreeing that wording should instead reflect whether anticipated benefit is no longer supported in a given population or trial context and how this affects development decisions.
- Subgroup 3 confirmed that the proposed table would allow explanation of risk reclassification over time (e.g., important potential risk downgraded to potential risk), with supporting rationale provided for transparency.

Consideration of a potential fourth topic area and "special cases"

- Participants revisited the earlier idea of forming a small additional group or workstream to address "special cases," including non-fixed dose combinations, auxiliary medications and non-investigational medicinal products used within trials, as well as emerging complexities such as drug–diagnostic combinations.
- It was noted that some expectations related to auxiliary products appear to be primarily regional and may differ across jurisdictions; therefore, such content may need to be framed explicitly as regional where global alignment is not feasible.
- Participants referred to European Union (EU) guidance and Questions and Answers (Q&A) documents (including treatment of Suspected Unexpected Serious Adverse Reactions (SUSARs) related to non-authorised auxiliary medicinal products) and noted the importance of clearly specifying how such cases should be presented (e.g., line listings versus summary tabulations) to avoid confusion.

Placement of "additional safety information" and scope of DSUR content

- A proposal was made to retain the current DSUR template section on "additional safety information," potentially repositioning it so that information not falling under "important risks" can still be presented transparently.
- The group discussed whether this section should be placed under signal evaluation (as a flexible space for special issues) or remain under broader risk evaluation, to avoid implying that all content represents a signal.
- Participants agreed that the shift toward focusing on "important risks" may require adjustments to headings and structure to maintain a clear distinction between: important risks that drive benefit–risk conclusions, and other safety information that warrants documentation but does not materially affect programme-level benefit–risk assessment.

Purpose of the DSUR and regulatory expectations

- A broader discussion took place on the primary purpose of the DSUR from a regulatory perspective. Participants emphasised that the DSUR should provide assurance that sponsors are maintaining appropriate safety oversight of the development programme, identifying new findings, taking necessary actions, and documenting the rationale transparently.

- The DSUR remains valuable as it often provides cumulative, programme-level safety overview for an active substance across trials and regions. Cumulative assessment can reveal patterns not evident from expedited reporting alone and can support decisions on continuation, modification, or cessation of development.
- The importance of DSURs for oversight of non-commercial sponsor trials was also noted, recognising that such sponsors may have more limited systems and access to programme-level information. Participants suggested that the guidance could include supportive elements to help non-commercial sponsors meet expectations.
- Participants also discussed the practical challenge that safety data from non-commercial trials are not always shared with marketing authorisation holders, which can limit the completeness of the DSUR.
- It was suggested that the introduction could more clearly explain the purpose of Development Safety Update Reports (DSURs), their intended objectives, and how the revised approach aims to support a more useful, readable, and decision-relevant document.
- Participants also noted that improvements in structure and narrative context, similar to the transition from Periodic Safety Update Reports (PSURs) to Periodic Benefit-Risk Evaluation Reports (PBRERs), could make DSURs more meaningful and easier to review.
- It was discussed whether the DSUR should document all emerging safety observations during development or only those relevant to regulatory decision-making.
- Several participants noted that historically the DSUR often became a descriptive catalogue of adverse reactions. However, the revised concept is intended to shift the report towards a decision-support document**.**
- The WG generally agreed that:
    - The DSUR should focus on safety information that influences benefit–risk assessment
    - Routine adverse event characterisation belongs primarily in clinical study reports and the Investigator's Brochure
    - The DSUR should describe evaluation rather than merely list observations
- It was emphasised that regulators primarily need information that may change – trial continuation, subject protection measures, risk mitigation, or overall development strategy.

DAY 2

Lembit Rägo welcomed participants back for the second day of the meeting and summarised the key conclusions from Day 1. He invited participants to review what had been achieved so far, identify remaining gaps in the draft, and agree who would take ownership of drafting outstanding sections.

Glossary

- The group discussed the need for DSUR-specific term definitions and confirmed that a short glossary will be prepared, starting from existing glossaries. The Chair noted that both the Glossary of ICH terms and definitions and CIOMS Cumulative Glossary, with a focus on Pharmacovigilance (Version 2.4) are available to support drafting.
- The group agreed that a short glossary would be useful. Elena kindly agreed to take the lead in working with the Glossary, starting from existing glossaries.

Identification of missing content and topics requiring additional drafting

- Participants were invited to identify areas not yet drafted or requiring strengthening.

- A regulator perspective was raised that guidance should cover not only additions to RSI but also situations where items are removed from RSI, as removal decisions often require justification and can trigger questions from authorities.
- It was suggested that the document should more clearly address re-classification over time (e.g., downgrading of risks or signals), including the rationale for why something was initially included and later removed or downgraded.

Complex trials and platform study challenges

- Participants discussed the increasing prevalence of complex clinical trial designs, including platform studies, umbrella trials, and multi-arm studies involving multiple active substances and combinations.
- It was noted that DSURs are typically investigational product-specific, which creates practical challenges when multiple investigational products are tested within a single platform trial.
- A concern was raised that, under certain table structures, investigational products used as comparators may not appear in their own DSURs unless the platform study is mapped into multiple DSURs – an approach described as operationally difficult.
- It was noted that extracting and re-assembling data arm-by-arm across safety, clinical trial, and exposure databases can be operationally complex, particularly where trial arms are not consistently structured for extraction.
- The WG acknowledged that trial-specific DSURs may occur, particularly in academic settings, but were generally viewed as less desirable for commercial sponsors.
- The group agreed that this topic requires further analysis and should be addressed in a subsequent phase of the work, after the core sections (Subgroups 1, 2, and 3) and the main template are sufficiently aligned.
- It was suggested that the WG could begin by mapping relevant scenarios and documenting practical approaches used by different companies, including how data are managed in databases and how this affects reporting feasibility.
- A proposal was made to include examples or scenarios (potentially in an appendix) to illustrate practical approaches for complex trial designs, recognising that a single solution may not be feasible in all situations.

Drug-device combinations and implantation/procedure-related complications

- A question was raised on how to handle safety information when complications relate to implantation procedures or drug–device combination products, including whether events should be described as procedure-related issues or device incidents.
- Participants noted that device–related events should follow applicable device legislation and local requirements; however, if a device failure or incident affects investigational product delivery or participant safety, it may be appropriate to describe it in the DSUR as part of safety oversight.
- The group discussed that there is currently limited DSUR-specific guidance for drug–device combinations during development, although post-marketing frameworks exist.
- Variability across jurisdictions was noted (including device-related reporting expectations in Switzerland), highlighting the need for DSUR guidance that recognises regional requirements.
- A possible approach discussed was that sponsors should comply with relevant local device reporting requirements while including descriptions in the DSUR where device-related incidents have implications for investigational product safety or participant protection.
- Participants agreed that clarification on drug–device combinations would be helpful and could potentially be included in the report text and/or illustrated through examples in appendices.

Safety reporting in public health emergencies

- The group discussed whether and how DSUR guidance should address safety reporting in public health emergencies, drawing on experiences during COVID-19.
- Participants noted that DSURs may have limited utility in rapidly evolving emergency situations where safety oversight requires real-time coordination, frequent updates, and ad hoc reporting arrangements.
- Examples were shared in which emergency contexts involved weekly or monthly safety reporting formats agreed with authorities, as well as intensive ongoing safety reviews and cross-regulatory coordination.
- The WG agreed that it may be useful to include clarifying text on:
    - The limitations of DSURs in emergency contexts
    - How safety oversight may be managed through alternative, higher-frequency processes
    - How such arrangements relate to the scope of the DSUR (e.g., in introductory text and/or an appendix describing lessons learned or best practices)

DSUR for marketed products with ongoing clinical development

- A point was raised that for products already marketed, DSURs may overlap substantially with Periodic Benefit-Risk Evaluation Reports (PBRERs), potentially creating duplicative workload if DSUR templates become more extensive.
- Participants reiterated that the WG's direction is to keep the DSUR focused primarily on clinical trials and the development programme, rather than duplicating post-marketing benefit–risk assessment.
- A possible approach discussed was whether DSUR expectations could be simplified for marketed products used in low-intervention trials or where the safety profile is stable, potentially relying more on current label information for cumulative post-marketing context while focusing DSUR content on new clinical trial data.
- The WG agreed that this idea warrants further consideration during review of the proposed template, to support proportionality and avoid unnecessary duplication.

Discussion on AI in DSUR preparation and assessment

- Participants discussed potential roles for artificial intelligence (AI) and automation in DSUR preparation and regulatory review, particularly for operational tasks such as compilation, formatting, and quality checks.
- Both potential benefits and risks were noted, including the need for human oversight and the possibility that AI-generated errors may be difficult to detect due to plausible outputs.
- Examples were shared of AI-assisted triage tools used during COVID-19 to manage large volumes of safety reports, highlighting the importance of controlled implementation and performance evaluation.
- Industry participants noted that adoption remains variable and that efficiency gains may currently be limited due to oversight and validation requirements.
- The group agreed that the report could reference existing principles for responsible AI use and emphasise the need for appropriate governance and oversight.

Work in subgroups followed, after which the WG reconvened in plenary to review the proposed DSUR template and to discuss the intended overall approach of the revised report. The purpose of the discussion was not only to review proposed textual changes but also to clarify the fundamental role and scope of the DSUR. The main discussion points are summarised below.

Important risks as the organising principle

- The WG confirmed alignment around a central principle: Benefit–risk evaluation in the DSUR should be driven by important identified and important potential risks. Based on this concept:
    - Not every adverse drug reaction needs inclusion
    - Newly observed events only enter the DSUR once evaluated through the signal process
    - Non-important risks do not require a dedicated evaluation section
- Participants recognised that some sections present in the current DSUR format were historically introduced to compensate for the absence of structured signal evaluation. With the new approach, these sections may no longer be necessary.
- The WG therefore considered removing or consolidating sections describing:
    - "new risks not considered important"
    - general safety observations not linked to signal assessment
- The consensus was that these would become redundant once the signal evaluation framework is clearly described.

Signal evaluation versus Adverse Drug Reaction (ADR) identification

- The relationship between signal detection and adverse drug reaction (ADR) identification was discussed. Examples were raised where clinical development teams identify ADRs based on aggregate analyses (e.g. frequency differences versus placebo) without conducting a formal signal evaluation report.
- The WG clarified the conceptual distinction:
    - Many clinical observations become ADRs in the label but do not represent signals requiring regulatory action
    - The DSUR should capture safety issues relevant to ongoing development oversight
    - The DSUR is not intended to replicate the clinical study report safety analysis
- It was agreed that:
    - ADR identification alone does not automatically justify DSUR inclusion
    - Only safety issues relevant to ongoing benefit–risk evaluation should be discussed
    - The threshold for DSUR discussion should be defined in the sponsor's signal detection methodology
- Participants emphasised that sponsors must describe their signal detection framework transparently, including decision thresholds and responsible functions. Regulators can then assess adequacy of the approach rather than requiring exhaustive event reporting.

Signal detection methodology section

- The group reviewed the section requiring sponsors to describe their signal detection process.
- It was agreed that sponsors should explain: review frequency, roles involved, data sources used, and criteria triggering evaluation.
- New technologies, including AI-assisted analysis, may be acknowledged where relevant.
- The DSUR will also include a structured signal overview table containing: new signals, ongoing signals, closed signals, and outcomes and actions.

Auxiliary medicinal product safety reporting

- The WG addressed the EU-specific expectation to report serious adverse reactions related exclusively to unauthorised auxiliary medicinal products used in trials.
- Participants raised operational concerns:
  - safety databases are structured around investigational products,
  - auxiliary products may not exist as identifiable entities in the safety database,
  - sponsors may not be the manufacturer,
  - and such cases may not be technically retrievable.
- It was noted that this situation appears rare and may be difficult to implement consistently across sponsors.
- The WG agreed that before proposing guidance text, feasibility should be investigated and practical industry experience collected. The topic will be handled within the subgroup addressing auxiliary medicinal products and complex study designs.

Finalisation of working template and shared working environment

- The working Word version of the guidance will serve as the master drafting document.
- Subgroups will submit tracked-change contributions, circulate drafts to the full group, and cross-reference related sections.
- Circulation of multiple Word document versions may create challenges with version control and extensive layered commenting. Nevertheless, organisational IT restrictions often prevent all participants from using the same collaborative platform and members confirmed that no single platform appears universally accessible.
- The possibility of small subgroups using a common platform among themselves was mentioned as a partial solution, although not feasible for the entire WG.
- the CIOMS Secretariat proposed using a password-protected section of the WG website to host the latest document versions. While this would not allow simultaneous editing, it would ensure all members can access the current version.
- It was concluded that, although no ideal technical solution is currently available, pragmatic measures should be used to maintain transparency of updates and minimise version conflicts.

Next steps / next meeting

- Subgroups will continue drafting over the coming months and circulate the drafts ahead of the meeting for the WG to review.
- A virtual whole-group meeting will be organised in spring to assess progress. Post-meeting: next virtual WG meeting will be held 23 April 2026.
- An in-person meeting will be held in September to finalise a consultation-ready draft.

Closing remarks

- Lembit thanked Bayer for kindly hosting the meeting and all WG participants for their continuous efforts in progressing their work.

Annex 1: List of participants

Participants

Attending in person

Catherine Berset Kipouros (Swissmedic), Antonella Caselli (Italian Medicines Agency), Andrzej Czarnecki (Eli Lilly), Peter De Veene (MSD), Eun Mi Kim (WHO), Mamiko Konishi (Eisai), Pete Nash (Gilead), Beatrice Panico (Individual expert), Elena Prokofyeva (FAMHP), Indra Purevjal (Bayer), Donald Puccio (Pfizer), Lembit Rägo (CIOMS), Kateriina Rannula (CIOMS), Tessy Ruijgrok (Biogen), Anita Shenoy (AbbVie), Corina Spreitzer (Austrian Medicines Agency), and Ling Tang (National Medical Products Administration).

Attending virtually
Mutsuhiro Ikuma (PMDA)

Apologies
Juliana Dornelles (ANVISA), Carmen Campanile (Swissmedic), Andrea Best (Gilead), Huanhuan Cui (National Medical Products Administration), Maria Grazia Malpezzi * (Italian Medicines Agency), Richard Pendlebury (Novartis), Wang Xiangyu (National Medical Products Administration), and Wang Haixue (National Medical Products Administration).

*Alternate

Subgroups are based on the whiteboard notes recorded during the meeting. Participants are invited to review and suggest any additions or modifications.

I Introduction (purpose, main changes, etc.) (Indra, Antonella, Donald)

II General principles (including future directions)

III Guidance on content

IV Appendices

A Template

B Glossary (Elena)

Subgroups and topics:

Combination products (FDC, NFDC, AUX) – Tessy, Beatrice, Elena, Pete

Complex studies – Tessy, Beatrice, Elena, Pete

Simplified DSUR – Hiro, Tessy, Donald

Devices – Corina, Mamiko, Carmen

Emergency trials (e.g. Covid) – Donald

Artificial Intelligence – Donald