COMPLETE GUIDE

How to Use This Guide

Use the guide as a learning resource, a writing reference, or a pre-submission review aid.

A Development Safety Update Report is not simply a yearly collection of serious adverse events. ICH E2F frames it as an integrated annual evaluation of the evolving safety profile of an investigational drug. The most useful DSURs connect validated data, clinical context, cumulative evidence, signal evaluation, safety actions and benefit-risk interpretation. This guide turns that principle into a practical workflow.

- Pharmacovigilance teams can use Chapters 2 and 3 to map safety data and signal-management inputs to the correct report sections.
- Medical writers can use the structure maps, source matrix and workback plan to coordinate contributors before the data lock point.
- Clinical and data teams can use the exposure, trial-inventory and reconciliation guidance to prepare reliable outputs.
- Regulatory teams can use the regional snapshot and submission-readiness questions to confirm local expectations.
- Job seekers can use the worked example and terminology pages to prepare for DSUR, aggregate reporting and clinical-safety interviews.

> **The guide follows ICH E2F as the core technical framework. Regional examples are included for the United States, European Union/EEA and United Kingdom, but local law and current authority instructions take precedence.**

Seven tables and seven visual diagrams are included. They are designed to be reusable learning aids: one compares DSUR and PBRER, one maps the E2F sections, one organises source data, one assigns cross-functional ownership, and one provides a final QC checklist. The figures show the safety-evidence ecosystem, DIBD/DLP timeline, data workflow, evidence layers, signal-management logic, 60-day workback plan and a worked safety example.

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Four chapters move from regulatory foundations to practical submission readiness.

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> **Tip: If you are preparing an actual DSUR, start with pages 7–8 for timing, pages 11–17 for content, pages 18–24 for workflow, and pages 25–29 for execution and final review.**

CHAPTER 1

DSUR Foundations

Understand the purpose, scope, timing and responsibilities before writing begins.

The quality of a DSUR depends on decisions made before the reporting period closes. Teams need a common interpretation of the investigational drug, the reporting cycle, the applicable reference safety information, the studies and data sources in scope, the regional recipients and the people responsible for producing the report.

ICH E2F recommends a single DSUR for an active substance wherever feasible, covering all dosage forms, strengths, indications and patient populations under the sponsor's development programme. This supports a cumulative view of safety rather than a study-by-study snapshot. When information cannot be consolidated, the report should explain the limitation and the rationale for the approach used.

- Core purpose: evaluate the evolving safety profile of the investigational drug.
- Core period: one year, anchored to the Development International Birth Date (DIBD).
- Core deadline: no later than 60 calendar days after the DSUR data lock point under ICH E2F.
- Core accountability: the clinical-trial sponsor remains responsible for report preparation, content and submission, even when tasks are delegated.

> **A DSUR should describe important safety issues discovered during the period, but it is not the first channel for communicating an urgent new safety issue. Expedited and urgent safety-reporting obligations continue separately.**

What the DSUR Does — and How It Differs From PBRER

Both are aggregate reports, but they answer different lifecycle questions.

The DSUR focuses on clinical development and the safety of participants exposed to an investigational drug. A PBRER/PSUR focuses on the post-authorisation benefit-risk profile of a marketed medicine. When development continues after marketing approval, relevant post-marketing information may feed into the DSUR, and clinical-trial findings may also matter to the PBRER. The documents can overlap without becoming interchangeable.

Table 1. DSUR vs PBRER/PSUR

Aspect	DSUR	PBRER / PSUR
Lifecycle focus	Clinical development; investigational drug	Post-authorisation; marketed medicine
Core guideline	ICH E2F	ICH E2C(R2) / regional PV rules
Main question	What changed in the evolving development safety profile?	Does the marketed benefit-risk profile remain favourable?
Typical anchor date	DIBD and DSUR DLP	International Birth Date / EURD or regional schedule
Key evidence	Clinical trials, exposure, SARs/SAEs, signals, nonclinical data, literature, relevant marketing data	Spontaneous and solicited reports, studies, exposure, signals, effectiveness/benefit information, risk minimisation
Primary recipients	Clinical-trial regulatory authorities; other recipients as required locally	Regulatory authorities responsible for post-marketing pharmacovigilance

> **Practical rule: do not copy a marketed-product narrative into the DSUR without explaining its relevance to the development programme and trial-subject safety.**

Scope: Build a Complete Safety-Evidence Picture

The report is anchored in clinical trials, but the safety assessment reaches beyond the clinical database.

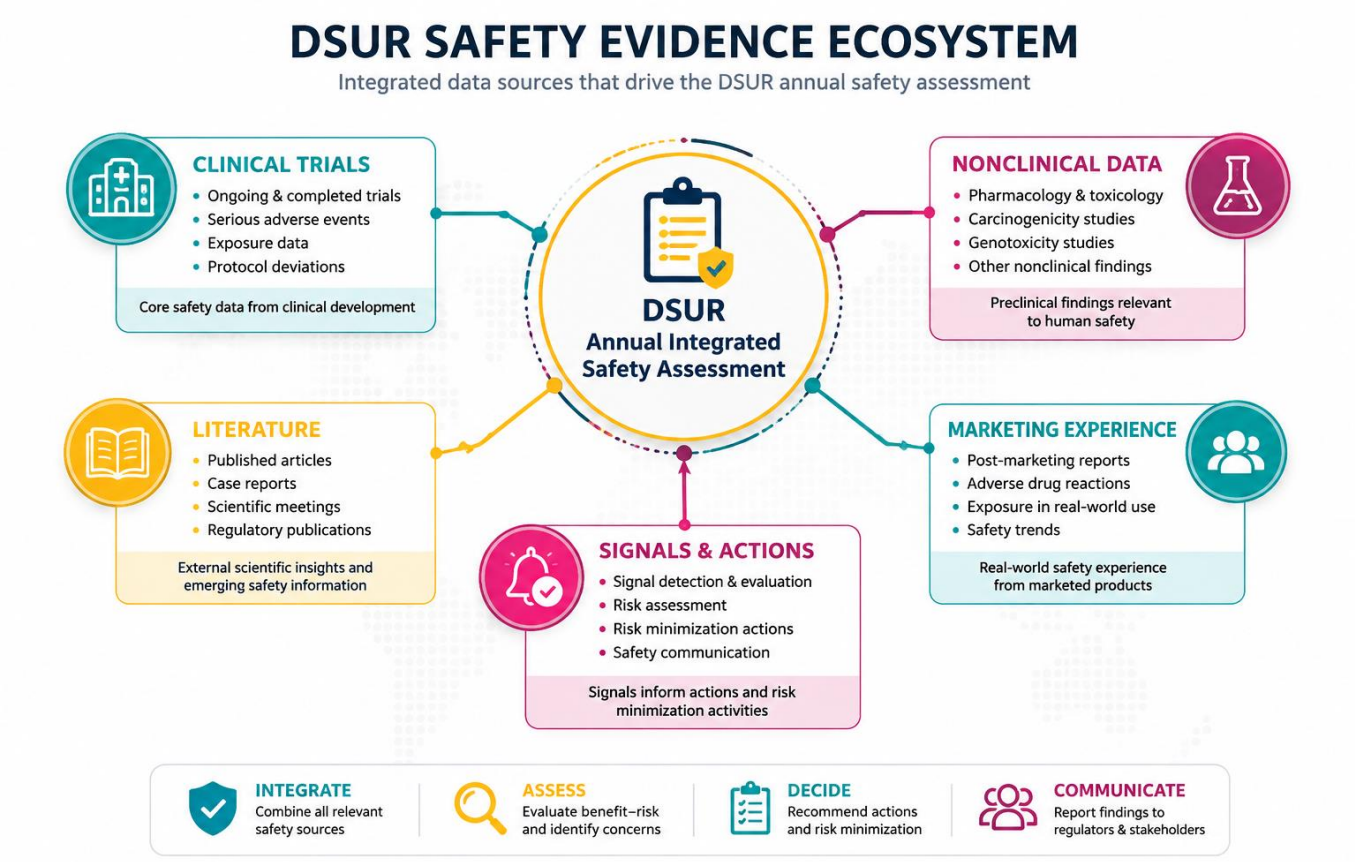

Figure 1. DSUR safety-evidence ecosystem: multiple sources contribute to one integrated annual assessment.

ICH E2F places interventional clinical trials at the centre of the DSUR. However, it also calls for significant information from observational and epidemiological studies, nonclinical studies, related DSURs, manufacturing or microbiological changes, literature, lack-of-efficacy findings that could affect safety, and relevant information from development partners. Where the investigational drug is marketed, important post-marketing safety findings should also be considered.

The practical implication is that the DSUR data-collection plan cannot be owned by the safety database team alone. A high-quality report needs a defined request process across Clinical Operations, Data Management, Biostatistics, Nonclinical/Toxicology, Regulatory Affairs, Medical Writing, Medical/Safety, Manufacturing/CMC when relevant, and partners or licensees.

> **Scope test: ask whether a new fact could change the interpretation of risk, exposure, trial conduct, reference safety information or benefit-risk. If yes, it probably needs to be assessed for DSUR relevance.**

DIBD, Data Lock Point and Reporting Period

Timing errors can undermine an otherwise strong report.

The Development International Birth Date is the sponsor's first authorisation to conduct a clinical trial with the investigational drug in any country. It anchors the start of the annual reporting cycle. The DSUR data lock point is normally the last day of the one-year reporting period. ICH E2F also allows an administrative convention in which the DLP is the last day of the month before the DIBD month, provided the resulting reporting period is appropriately managed.

Table 2. Key DSUR timing terms

Term	Meaning	Operational control
DIBD	First authorisation to conduct a clinical trial with the investigational drug anywhere in the world.	Maintain as controlled master data; do not reset when a later country starts development.
Reporting period	The one-year interval covered by the DSUR.	Define exact start/end dates in the authoring plan and data requests.
DLP	Cut-off date for data included in the annual report.	Freeze listings and outputs against a documented cut-off; manage late-breaking data separately.
Submission deadline	ICH E2F: no later than 60 calendar days after the DLP.	Build an internal deadline earlier than Day 60 and reserve publishing/submission time.
Final DSUR	Last annual report where a country/region no longer requires further annual reporting.	State that it is final for that jurisdiction and whether development continues elsewhere.

Do not confuse the DIBD with a local trial start date, first-patient-in date, IND effective date, marketing International Birth Date, or the date a later indication enters development.

The DSUR Calendar in Practice

Turn the regulatory dates into an operating calendar before the DLP.

Figure 2. The DSUR annual cycle is anchored to the DIBD, closes at the DLP and proceeds to submission within the applicable deadline.

The strongest DSUR teams work backwards from the expected submission date. They confirm the DIBD, regional reporting obligations, the exact DLP, the reference safety information version, the study list and the contributors several months before the cut-off. Near the DLP, they freeze data requests, agree how late data will be handled, and lock the document plan.

The 60-day period is not "writing time." It must accommodate data extraction, SAE reconciliation, exposure outputs, medical review, signal assessment, drafting, cross-functional review, quality control, governance approval, publishing and electronic submission. If all activities begin after the DLP, review quality usually suffers.

- Before DLP: confirm scope, sources, owners and templates.
- At DLP: document cut-off rules and extraction dates.
- After DLP: reconcile, analyse and interpret before final prose is written.
- Before submission: perform independent QC against the source package and regional requirements.

Sponsor Responsibility and Reference Safety Information

Two controls shape the integrity of the annual safety assessment: accountability and the correct safety reference.

ICH E2F places responsibility for the DSUR on the sponsor. Preparation can be delegated to a CRO or another third party, but accountability for content and submission remains with the sponsor. In co-development or licensing arrangements, partners should agree data exchange, responsibilities, timelines, access to case information and the approach to a single DSUR wherever feasible.

Reference Safety Information (RSI) is equally important. The DSUR should identify the document and version used as the reference for expectedness where required. During development, this is commonly the relevant section of the Investigator's Brochure, although regional requirements and product circumstances can differ. The report should also describe significant safety-related changes to the IB or other RSI during the reporting period.

- Control the effective dates and versions of the IB/RSI.
- Explain material changes such as new warnings, precautions, contraindications or serious adverse reactions.
- Ensure line-listing/tabulation logic uses the correct reference period and expectedness rules.
- Align safety actions in the DSUR with changes already made to the IB, protocol, informed consent or risk controls.

> **A frequent failure mode is to identify an important safety change in narrative text without clearly linking it to the RSI version, implementation date and resulting development action.**

CHAPTER 2

Building the ICH E2F Report

Translate the guideline structure into traceable data, analysis and medical interpretation.

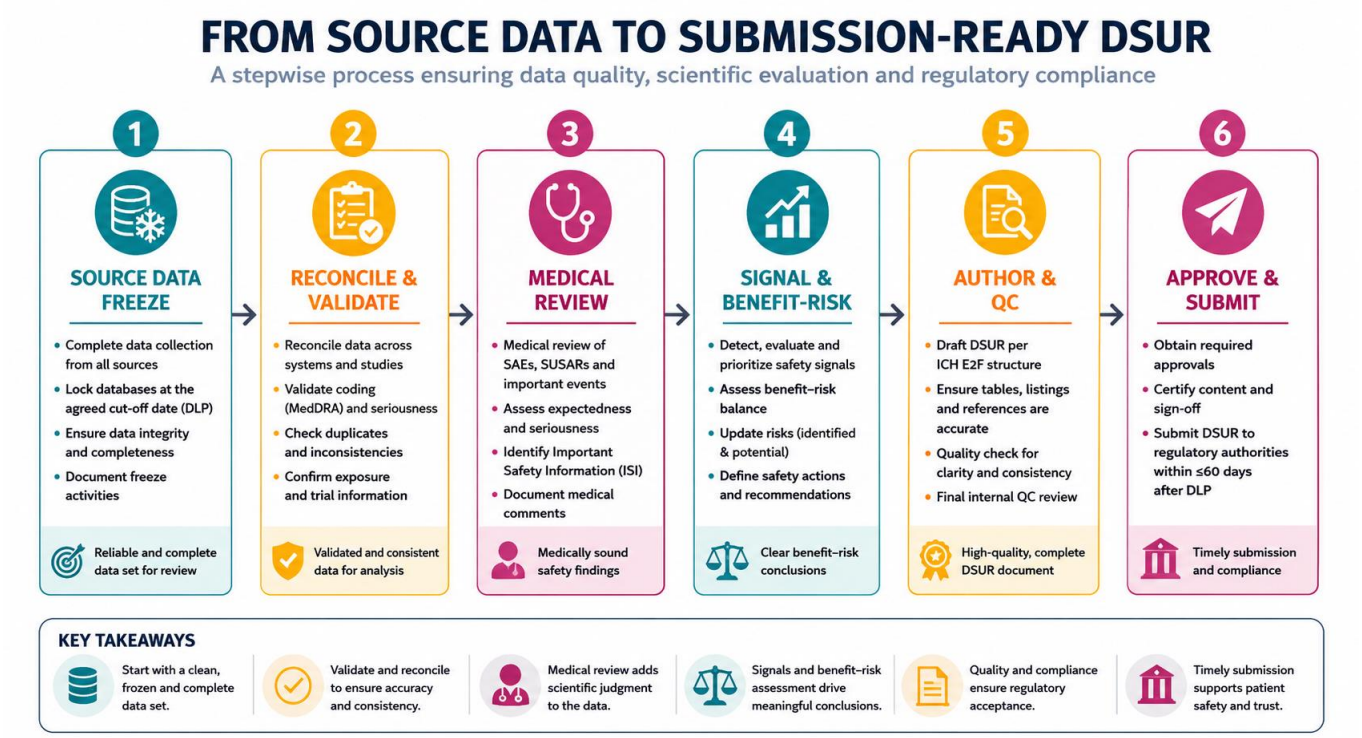

Figure 3. A practical DSUR production flow from source-data freeze to approval and submission.

ICH E2F provides a structured content model for the report, but the value comes from the connections between sections. Trial inventory drives exposure interpretation. Line listings and cumulative tabulations feed signal review. Clinical and nonclinical findings influence the overall safety assessment. Safety actions and RSI changes demonstrate how the sponsor responded to new information.

> **Think of the DSUR as an evidence chain: source → validated output → interpretation → risk decision → action → documented conclusion.**

ICH E2F Content Architecture

Use the section map as the master authoring checklist.

The exact headings and regional additions should be confirmed against the applicable guideline and authority instructions. The following map summarises the major ICH E2F content blocks and the question each block should answer.

Table 3. ICH E2F section map

Content block	What it should establish
Executive Summary / Introduction	Reporting period, product, scope, key changes and the overall safety message.
Worldwide development / marketing status	Where development or marketing status changed and why it matters.
Safety actions + RSI changes	What safety-driven actions occurred and how the reference safety information changed.
Clinical trial inventory + exposure	Which studies were active/completed and how many subjects/patients were exposed.
Line listings + cumulative tabulations	What serious reactions/events occurred and how they aggregate by system/term/treatment.
Significant findings	Clinically important results from completed/ongoing trials, long-term follow-up and therapeutic use.
Other evidence	Non-interventional studies, marketing experience, nonclinical data, literature, other DSURs and other study information.
Late-breaking / lack of efficacy / regional items	Important information emerging after DLP, safety-relevant efficacy concerns and region-specific additions.
Overall safety assessment + benefit-risk	What changed in the safety profile, which risks matter, what is uncertain, and whether development remains justified.
Conclusions + actions	What the sponsor concludes and what risk-management or development actions will follow.

Clinical Trial Inventory: Establish the Development Context

The report needs enough study context for regulators to interpret exposure and safety findings.

The inventory of clinical trials should provide a controlled overview of ongoing and completed studies in the reporting period. ICH E2F recommends detailed information in an appendix, typically including study identifier, phase, status, countries or regions, study design, treatment arms, planned exposure and enrolled subjects as appropriate.

The authoring team should reconcile the trial inventory against clinical-trial management records, regulatory submissions and data outputs. Missing or inconsistent study status can create downstream problems: exposure totals may not reconcile, safety cases may be assigned to the wrong programme, and significant findings may be omitted because a study was not included in the source list.

- Define “ongoing” and “completed” consistently across the sponsor.
- Include relevant trials conducted by co-development partners when information is available under the agreement.
- Separate or stratify information by indication, formulation or population when this improves interpretation.
- Identify studies with long-term follow-up, expanded access or other therapeutic use where safety information continues to accrue.

> **A trial inventory is more than an appendix. It is the index against which exposure, serious events, study findings and regional coverage can be reconciled.**

Build a DSUR Source-Data Matrix

Every major statement should be traceable to a controlled source or approved analysis.

A source-data matrix prevents late requests and makes QC more objective. Create it before the DLP, name the owner of each input, define the cut-off date and identify the DSUR section that will use the information.

Table 4. Source-to-section matrix

Source / owner	Typical DSUR use	Key QC question
Safety database / PV	SAR/SAE line listings, case narratives, cumulative tabulations, signal inputs	Do case counts, coding and cut-off dates reconcile?
Clinical data / Data Management	Exposure, discontinuations, deaths, study status inputs	Is the extract clean enough and aligned with the DLP?
Biostatistics	Integrated tables, treatment-arm summaries, subject-time where relevant	Are denominators and pooling rules documented?
Clinical Operations	Trial inventory, country/site status, protocol changes	Does study status match authoritative trial records?
Medical/Safety	Signal assessments, important risks, benefit-risk interpretation	Is the conclusion supported by cumulative evidence?
Regulatory Affairs	Actions, authority requests, regional requirements, submission status	Are all relevant requests and safety-driven actions represented?
Nonclinical / CMC / Literature	Toxicology findings, manufacturing changes, publications	Could the finding change clinical risk or monitoring?

For each source, capture the owner, version/date, cut-off, file name or system reference, and final QC status. This becomes the audit trail for the report.

From Raw Data to Regulatory Narrative

A DSUR should not reproduce source outputs without interpretation.

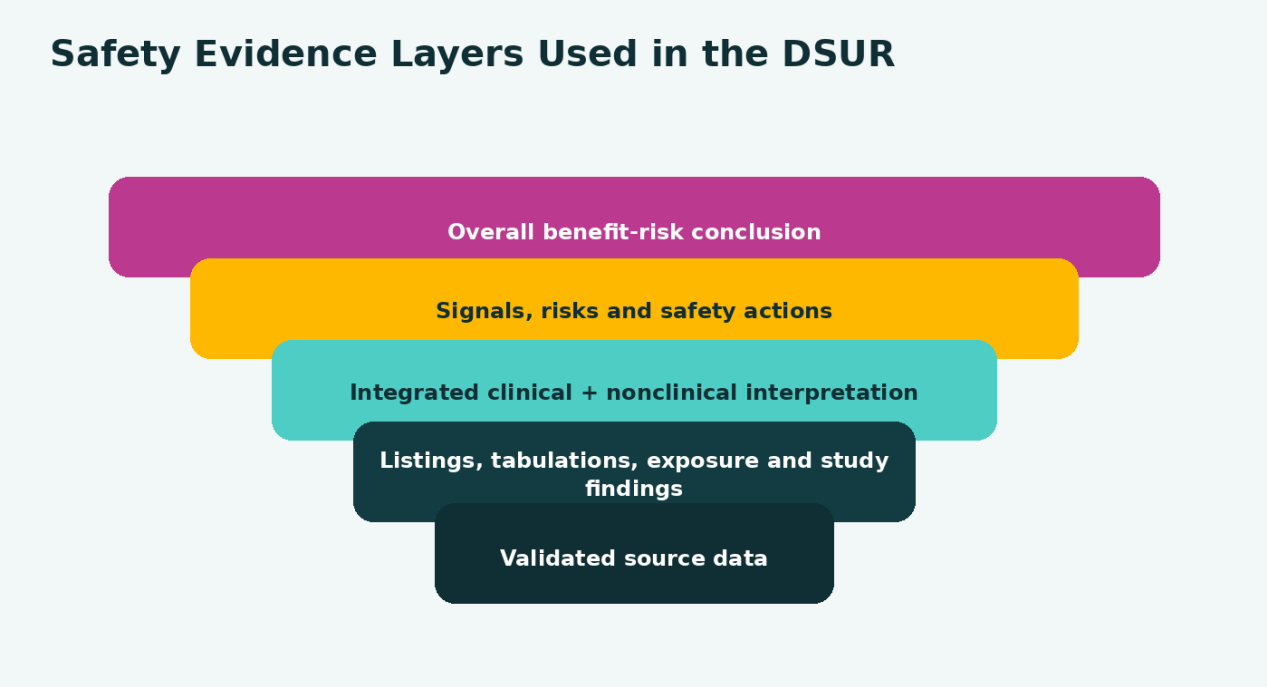

Figure 4. Evidence layers: validated data support integrated interpretation, which supports risk decisions and benefit-risk conclusions.

The first layer is data integrity: correct study scope, clean extracts, coded cases, reconciled serious events and reliable exposure denominators. The second layer is clinical interpretation: what patterns are visible, which findings are new, which known risks have changed and what uncertainties remain. The third layer is risk management: what actions were taken or considered. The final layer is benefit-risk: whether the accumulated information changes the justification for continued development or the way participants should be protected.

Weak reports jump from tables to conclusions. Strong reports show the reasoning between them. They explain whether an apparent increase is attributable to greater exposure, disease severity, a specific population, dose, study design, concomitant therapy or a plausible drug-related effect. They also state when the evidence is insufficient for a firm conclusion.

> **Interpretation should be proportional to the evidence. Avoid both extremes: merely restating numbers and over-claiming causality from sparse data.**

Significant Findings Across Clinical and Other Evidence

Summarise what changed—not every result that became available.

ICH E2F separates significant findings from completed trials, ongoing trials, long-term follow-up, other therapeutic use and combination-therapy information. The objective is to highlight clinically important findings that support, refute or modify prior safety concerns, including evidence of new safety signals.

Other sections cover non-interventional studies, pooled or meta-analytic findings, marketing experience, nonclinical data and literature. These sources should be included when they are pertinent to the investigational drug's safety profile. A literature citation that confirms a known mechanism may be more relevant than a large volume of publications with no effect on current risk interpretation.

- Completed trials: summarise emerging findings with enough context to understand treatment and population.
- Ongoing trials: include clinically important information learned through interim analyses or appropriate unblinding.
- Non-interventional evidence: capture observational, epidemiological, registry and active-surveillance findings.
- Marketing experience: include key findings that influenced labelling, the IB, informed consent or the risk-management approach.
- Nonclinical evidence: discuss major findings that could have clinical implications.
- Literature: focus on new and significant information, including relevant class effects when appropriate.

Exposure, Line Listings and Cumulative Tabulations

These quantitative sections must be internally consistent and medically interpretable.

Estimated cumulative exposure gives context to the volume and pattern of serious events. Depending on available data, exposure can be summarised by study, treatment arm, dose, age, sex, indication or other clinically meaningful categories. For marketed use, a reasonable estimate of patient exposure may also be included when relevant to development safety.

Table 5. Quantitative-output checks

Output	What to verify	Why it matters
Cumulative subject exposure	Population, treatment assignment, totals, cut-off, unknown/blinded allocation	Provides denominators and context for event interpretation.
Patient exposure from marketing	Estimation method, time period, units and limitations	Connects marketed experience to ongoing development where relevant.
SAR line listings	Inclusion rules, duplicates, case ID, trial, SOC/PT, seriousness, outcome, causality/expectedness fields	Supports transparent review of serious reactions during the period.
Cumulative SAE tabulations	SOC/term grouping, treatment arm, cumulative counts and consistency with study data	Shows the cumulative serious-event profile rather than isolated cases.
Deaths / withdrawals where required	Subject identifiers, treatment, cause/reason and linkage to safety discussion	Ensures clinically important outcomes are not hidden in aggregate counts.

Use MedDRA terminology consistently and document the version used where required by procedure or regional expectation. Ensure coding conventions are stable enough for trend interpretation.

Overall Safety Assessment and Benefit-Risk

This is where the report becomes more than an annual inventory.

The overall safety assessment should integrate information from the reporting period with cumulative knowledge from the development programme. It should discuss new safety issues, changes in known risks, important uncertainties, relevant patterns by dose or population, and the clinical significance of findings. The assessment should distinguish evidence from hypothesis and explain the basis for the sponsor's judgement.

Benefit-risk considerations should reflect the stage of development. Early programmes may have limited evidence of benefit, so the justification may depend on biological plausibility, early efficacy signals, unmet need and the manageability of identified risks. Later programmes can make greater use of controlled efficacy data and more mature exposure. In serious or life-threatening conditions, evidence of lack of efficacy can itself become a safety issue if ineffective treatment exposes participants to avoidable disease risk.

- State important identified and potential risks in language consistent with the development safety strategy.
- Explain new or closed signals and the evidence that changed their status.
- Connect risk interpretation to participant-protection actions such as monitoring, eligibility changes or protocol amendments.
- Describe uncertainty: small exposure, confounding, missing data, unblinding limitations or evolving diagnostic criteria.
- Conclude whether the overall information supports continued development and under what controls.

> **The conclusion should be traceable to evidence presented earlier in the report. A "no change to benefit-risk" statement without supporting reasoning is not a meaningful assessment.**

CHAPTER 3

DSUR Operating Model

Create an operating process that makes quality predictable instead of heroic.

Most DSUR problems are process problems before they become writing problems. Missing inputs, mismatched cut-offs, unclear ownership, late medical review and uncontrolled comment cycles all reduce quality. A robust operating model defines the schedule, data sources, accountable functions, escalation path and quality gates well before the report is due.

Competitor best-practice resources emphasise cross-functional collaboration for the same reason: the medical writer can coordinate the document, but the writer cannot independently generate authoritative exposure data, reconcile safety cases, decide signal status, confirm regulatory actions or approve the medical interpretation. The process must make those dependencies visible.

- Start planning months before the DLP for complex global programmes.
- Use one controlled authoring plan with owners, deliverables and dates.
- Freeze or version-control the source package used for the report.
- Separate content review, medical review, QC and approval into defined gates.
- Track unresolved issues and decisions rather than relying on email threads.

Cross-Functional Roles and RACI

Define who provides data, who interprets it and who owns the final decision.

Table 6. Example DSUR RACI

Activity	PV/Safety	Medical	Clin/Data/Biostats	Regulatory	Medical Writing
Confirm scope and schedule	C	C	C	A/R	R
Safety listings and reconciliation	A/R	C	C	I	C
Exposure and study outputs	C	C	A/R	I	C
Signal and risk assessment	R	A/R	C	C	C
Regulatory actions / regional needs	C	C	I	A/R	C
Draft and integrate sections	C	C	C	C	A/R
Independent QC	R	C	C	C	C
Final approval / submission	C	A/C	I	A/R	I

R = Responsible, A = Accountable, C = Consulted, I = Informed. The exact model depends on sponsor procedures. What matters is that accountability for medical judgement, data generation, regulatory compliance and document control is explicit.

> **For outsourced DSURs, add CRO and partner responsibilities to the RACI and ensure the safety-data exchange agreement supports the reporting timeline.**

Signal Management and Medical Review

The DSUR should make the sponsor’s safety reasoning visible.

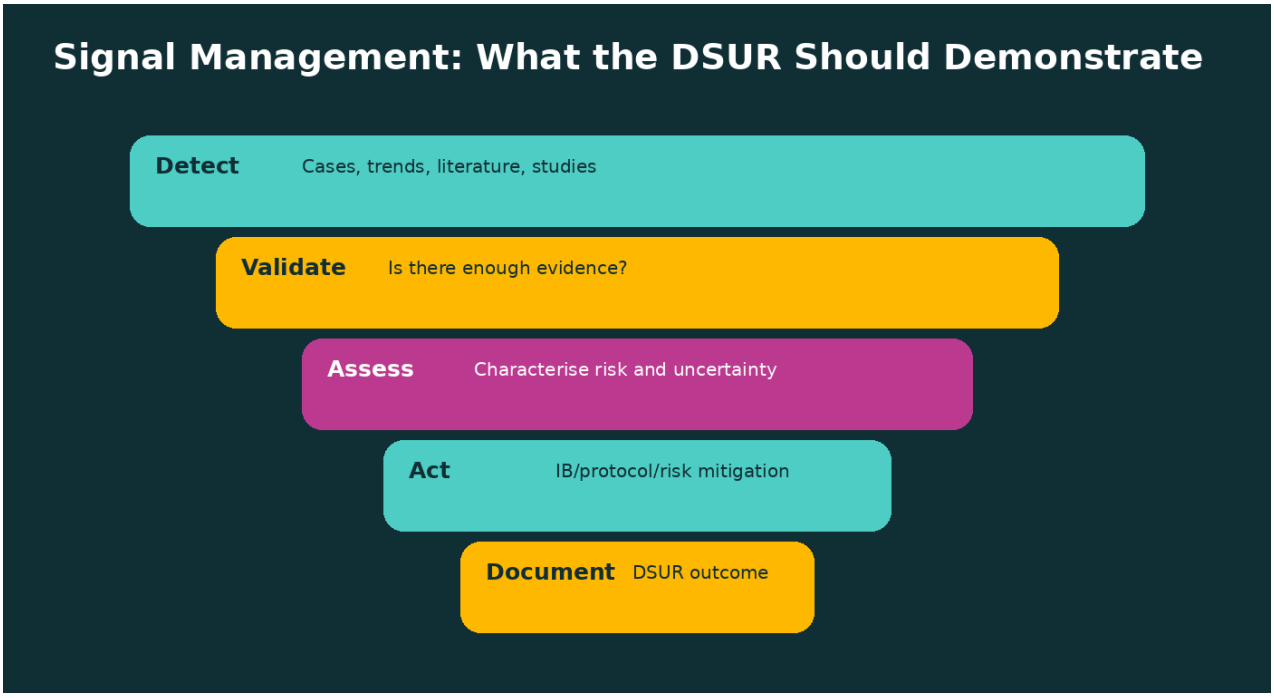

Figure 5. Signal management moves from detection to validation, assessment, action and transparent documentation.

Signal detection occurs continuously, not once per year. The DSUR consolidates the state of knowledge at the reporting cut-off and should explain significant signals assessed during the period, their outcome, and the actions taken. Current UK guidance places particular emphasis on transparent signal-management description and on interpreting new-period data alongside cumulative data from the DIBD.

Medical review should therefore ask more than whether a case is serious or related. Reviewers should examine clustering, dose-response, temporal association, dechallenge/rechallenge information, biological plausibility, confounding, population differences, comparator patterns and changes in exposure. For known risks, the key question is whether frequency, severity, population or preventability has changed.

> **Do not wait for the DSUR to communicate a significant new safety issue. Urgent safety measures, expedited reporting and updates to the IB or other trial documents follow their own timelines.**

Authoring Workflow: Draft From Evidence, Not Memory

Use a controlled source package and a section-level writing plan.

A practical workflow starts with a section shell, prior-year DSUR, current source matrix and list of known changes. Each section should have an identified owner or reviewer and a source reference. Writers can reuse stable background only after confirming that dates, study status, product information and regulatory context remain current.

1. Create a document shell aligned with ICH E2F and applicable regional requirements.
2. Mark sections that require new data, sections that require medical interpretation and sections that may be unchanged.
3. Draft factual sections from validated outputs first: status, actions, RSI changes, study inventory and exposure.
4. Draft safety-evidence sections after listings, tabulations and study findings are reconciled.
5. Draft the overall safety assessment and benefit-risk section only after the evidence package is stable.
6. Complete cross-references, appendices and the executive summary after the report-level conclusions are agreed.

The executive summary should not introduce findings that are absent from the body. It should state the reporting period, product, high-level exposure, major safety findings, meaningful actions and overall conclusion concisely. Readers should be able to understand what changed this year without reading every appendix.

Quality Control: Check Data, Logic and Regulatory Completeness

A spelling review is not DSUR QC.

Effective QC uses a checklist and source comparison. The reviewer should verify numerical consistency, study identifiers, dates, RSI versions, treatment groups, MedDRA terms, signal status, safety actions, cross-references and conclusions. Quantitative discrepancies should be resolved at the source rather than patched in the narrative.

- Reconcile counts between the narrative, line listings, tabulations and study summaries.
- Trace important conclusions to the supporting section or approved signal assessment.
- Check that all significant safety-related actions taken in the period are captured.
- Verify that the report does not use post-DLP information as if it were part of the reporting period; place relevant late-breaking information appropriately.
- Check blinded/unblinded presentation and confidentiality controls.
- Confirm appendices, table titles, abbreviations and report metadata are complete.
- Perform a final regulatory check after content QC because regional submission requirements can change.

> **Separate “content QC” from “medical approval.” QC confirms accuracy and consistency; medical approval confirms that the interpretation and clinical judgement are acceptable.**

Common DSUR Failure Modes — and How to Prevent Them

Most preventable problems can be designed out of the process.

Wrong reporting anchor

The team uses a local date instead of the controlled DIBD, creating misaligned reporting periods. Control the DIBD centrally and confirm it during kick-off.

Unclear RSI version

Expectedness or safety-change discussion is based on an incorrect or ambiguously dated IB/RSI. Maintain a version/effective-date record.

Inconsistent denominators

Exposure in one section differs from the dataset used to interpret events. Define pooling rules and the source of truth.

Case-count mismatch

Narrative counts differ from line listings or cumulative tables because extracts were refreshed at different times. Freeze and version the safety package.

Signal narrative without decision

A potential issue is described but the report never says whether it is a signal, what assessment occurred or what action followed. Link finding → evaluation → decision → action.

Late review compression

Medical and regulatory reviewers receive the report too close to Day 60. Build internal gates and escalation dates into the workback plan.

Regional Submission Snapshot: US, EU/EEA and UK

ICH E2F is the common technical foundation, but submission pathways are regional.

United States. FDA states that it accepts the ICH E2F DSUR to meet IND annual-report requirements, supporting global harmonisation. Current 21 CFR 312.33 annual-report obligations remain in force; a 2022 FDA proposal to replace the current IND annual report with an FDA DSUR has not been identified as a final rule in the sources reviewed for this guide. Sponsors should therefore confirm the current regulatory pathway for each IND.

European Union/EEA. Under the Clinical Trials Regulation, sponsors submit annual safety reports through the Clinical Trials Information System (CTIS). EU guidance states that a single annual safety report can be submitted for more than one IMP in a trial in certain circumstances, and SUSAR reporting is handled separately via EudraVigilance. Current CTIS sponsor guidance should be checked at the time of submission.

United Kingdom. Updated clinical-trial safety requirements took effect on 28 April 2026. MHRA guidance states that sponsors should use the DSUR for the comprehensive annual review of pertinent safety information and should interpret new-period data alongside cumulative data from the DIBD. The guidance also emphasises signal management, actions taken for safety concerns, and transparent interpretation.

> **Regional rule: never treat the harmonised ICH format as proof that submission mechanics, fees, recipients, portals or local additions are identical across jurisdictions.**

CHAPTER 4

Practical Tools and Worked Example

Convert the guidance into a repeatable execution plan and a final readiness decision.

Figure 6. Example 60-day DSUR workback plan. Internal deadlines should be earlier than the regulatory deadline.

The following pages provide a practical workback approach, a final QC checklist, a worked safety example and competency questions. Use them as templates, but scale the level of control to the size and risk of the development programme.

> **A "60-day plan" should ideally begin before Day 0. The post-DLP period is for controlled execution, not discovery of basic scope and ownership.**

Example 60-Day Workback Plan

Adjust the dates to your organisation, but preserve the sequence and decision gates.

Pre-DLP readiness

Confirm DIBD/DLP, jurisdictions, RSI version, study inventory, source owners, data specifications, templates, prior-year actions and unresolved signals.

Days 1–10: source package

Run safety extracts, reconcile serious events, produce exposure and study outputs, gather regulatory/nonclinical/literature inputs and document late data.

Days 11–28: first integrated draft

Complete factual sections, incorporate validated tables, draft significant findings and prepare the initial medical interpretation.

Days 29–40: medical and cross-functional review

Resolve signal/risk questions, confirm benefit-risk narrative, verify actions and reconcile review comments against source evidence.

Days 41–52: final QC and approval

Perform independent QC, confirm regional completeness, finalise appendices, obtain governance approvals and freeze the content.

Days 53–60: publishing and submission

Generate the final submission package, complete technical validation, submit through the required portal/pathway and archive acknowledgements.

> **Escalation trigger examples: missing exposure output, unresolved case reconciliation, late signal assessment, pending IB change, partner data gap, or a new safety issue emerging after DLP.**

Final DSUR Submission-Readiness Checklist

Use this as the last structured review before content freeze.

Table 7. Final submission QC checklist

Check	Ready when...
Dates and scope	DIBD, DLP, reporting period, product scope and jurisdictions are confirmed.
RSI / IB	Correct version is identified; significant changes and effective dates are described.
Trial inventory	All in-scope studies and therapeutic-use programmes are reconciled.
Exposure	Cumulative exposure totals and methods are consistent across sections.
Listings / tabulations	SAR line listings and cumulative SAE outputs reconcile to source data.
Evidence	Important clinical, nonclinical, literature and marketing findings are assessed.
Signals / risks	New, ongoing and closed signals are reflected consistently with approved assessments.
Safety actions	Risk-mitigation, protocol, consent, IB and regulatory actions are captured.
Benefit-risk	Conclusion is supported by the cumulative evidence and states key uncertainty.
Late-breaking information	Post-DLP information is handled in the correct section and does not distort the reporting-period dataset.
QC / approvals	Independent QC, medical approval and regulatory approval are documented.
Submission package	Required format, portal, fee/process, cover documents and acknowledgement plan are confirmed.

Worked Example: Hepatic Safety Finding

A simplified example shows how one finding should connect data, assessment and action.

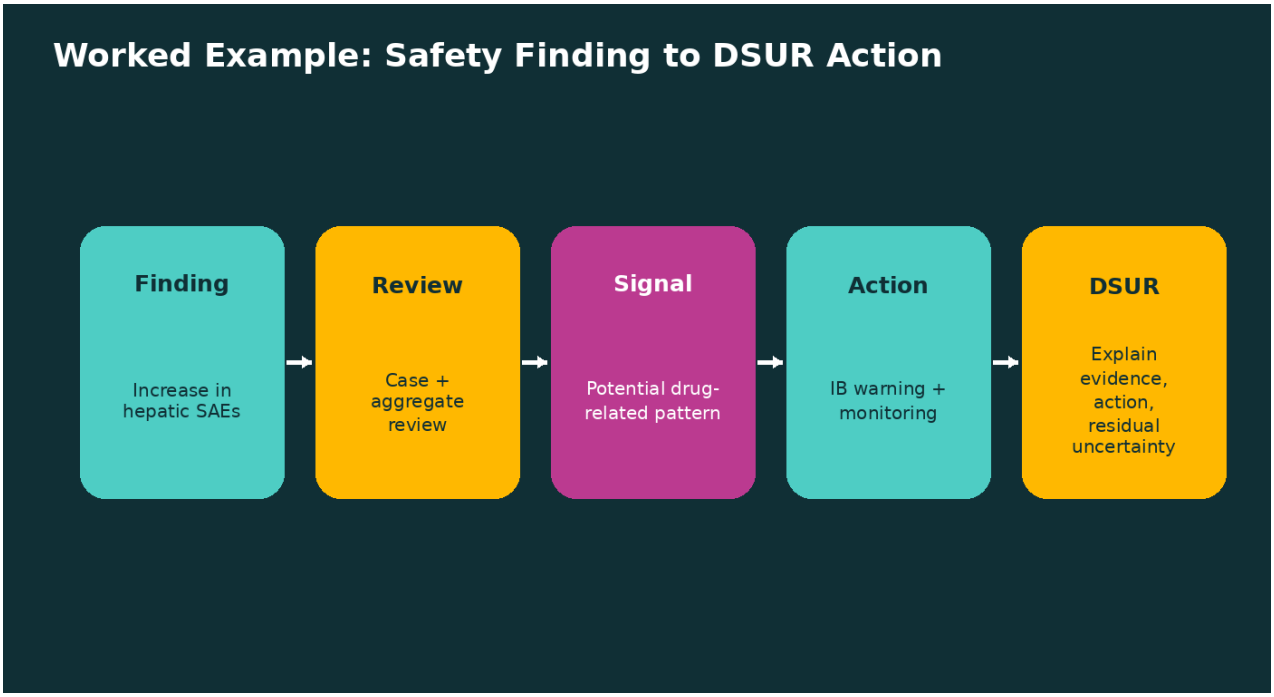

Figure 7. Example evidence chain for an emerging hepatic safety concern.

Scenario. During the reporting year, several serious hepatic events occur across two studies. The crude number is higher than in the previous year, but exposure has also increased substantially. The safety team reconciles the cases, confirms MedDRA coding, reviews baseline liver disease and concomitant medicines, and compares timing with dose and treatment duration.

Assessment. Medical review identifies a subset with a plausible temporal relationship and limited alternative explanations. The pattern does not prove causality, but it is sufficient to treat the issue as a potential safety signal. The sponsor initiates focused monitoring, updates the Investigator's Brochure warning language, modifies laboratory monitoring in active protocols and informs investigators through the appropriate process.

DSUR treatment. The report describes the case pattern and cumulative context in the relevant safety sections, explains the signal assessment in the overall safety evaluation, documents the IB/protocol actions, and states the remaining uncertainty. The benefit-risk conclusion explains why development continues and what controls are intended to reduce participant risk.

DSUR Competency Questions for Teams and Job Seekers

Use these questions to test whether you can explain the process, not just define the acronym.

1. What is the Development International Birth Date, and why should it remain consistent across countries?
2. How does the DSUR data lock point differ from the submission date?
3. Why is the Investigator's Brochure / Reference Safety Information relevant to a DSUR?
4. Which sources beyond interventional clinical trials can materially affect the annual safety assessment?
5. What is the difference between a SAR line listing and a cumulative SAE tabulation?
6. How would you reconcile exposure data when treatment assignment is still blinded?
7. What should happen if a significant new safety issue is identified before the DSUR is finalised?
8. How should an ongoing safety signal be reflected in the DSUR?
9. What is the role of medical review compared with document QC?
10. Why can lack of efficacy become a safety concern in a serious or life-threatening condition?
11. What cross-functional inputs are usually required to prepare a global DSUR?
12. How do DSUR and PBRER/PSUR differ in lifecycle focus?
13. What regional submission mechanics differ between FDA, EU/EEA and MHRA pathways?
14. What would you do if line-listing counts do not match the narrative after the DLP?
15. What evidence should support a "no change to benefit-risk" conclusion?

> **Interview tip: answer with a short process example. Demonstrating how you would validate data, interpret a signal and connect it to action is stronger than reciting the report sections.**

Primary References and Further Reading

Core regulatory sources used to develop this guide. Verify current versions before operational use.

1. ICH E2F — Development Safety Update Report — https://database.ich.org/sites/default/files/E2F_Guideline.pdf

2. EMA — ICH E2F Development Safety Update Report scientific guideline — https://www.ema.europa.eu/en/ich-e2f-development-safety-update-report-scientific-guideline

3. FDA — E2F Development Safety Update Report guidance — https://www.fda.gov/regulatory-information/search-fda-guidance-documents/e2f-development-safety-update-report

4. FDA — IND Application Reporting: Annual Reports — https://www.fda.gov/drugs/investigational-new-drug-ind-application/ind-application-reporting-annual-reports

5. European Commission — Clinical Trials Regulation (EU) No 536/2014 — https://health.ec.europa.eu/medicinal-products/clinical-trials/clinical-trials-regulation-eu-no-5362014_en

6. EMA — Reporting safety information on clinical trials — https://www.ema.europa.eu/en/human-regulatory-overview/research-development/clinical-trials-human-medicines/reporting-safety-information-clinical-trials

7. MHRA — Collection, verification and reporting of safety events — https://www.gov.uk/guidance/clinical-trials-for-medicines-collection-verification-and-reporting-of-safety-events

8. CIOMS Working Group XVI — Development Safety Update Report — https://cioms.ch/working_groups/working-group-xvi-dsur/

9. Precision for Medicine — Best practices to streamline DSUR development — https://www.precisionformedicine.com/blog/best-practices-to-streamline-development-of-safety-update-reports-dsurs

10. Pharmuni — DSUR in Pharmacovigilance: 2026 Guide — https://pharmuni.com/2025/11/26/dsur-in-pharmacovigilance-complete-guide-for-year-ich-e2f-explained/

> **Regulatory note: ICH E2F remains the primary harmonised DSUR guideline. Regional law, authority guidance and submission systems can change. Always confirm current requirements for the specific jurisdiction and development programme.**

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