How to Prepare a PBRER

For PV learners, aggregate-report writers, medical writers and regulatory teams

OUTCOME

What this guide helps you do

The practical problem
PBRER teams often know the definition, but miss timelines, section links, and QC checks.

The practical solution
Use one structure map, one timeline model, and one final checklist before submission.

By the end, you can:

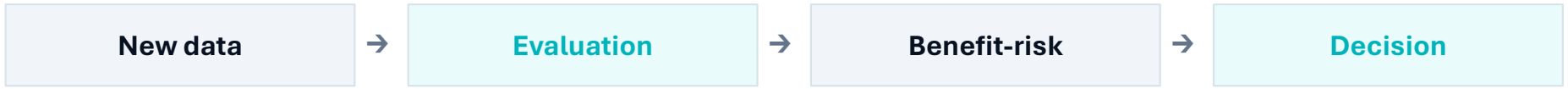
- map all 20 ICH sections
- plan IBD, DLP and due dates
- check signals, risks and benefit-risk logic
- avoid common submission errors

PBRER purpose in the product lifecycle

Main purpose
PBRER evaluates whether new data changes the product benefit-risk balance.

Core scope
It uses interval data and cumulative knowledge across approved uses.

Expected output
It supports labeling, risk minimization, studies, and regulatory actions.



Remember
PBRER should not replace urgent reporting. Teams must escalate urgent safety issues immediately.

GUIDANCE

Regulatory context: ICH E2C(R2)

Common standard
ICH E2C(R2) provides a harmonized format for marketed products.

Cumulative view
The report links interval findings with the full safety history.

Benefit-risk focus
The report moves beyond case lists and asks what changed.

Use the full format
Keep the section numbering. When a section does not apply, explain why it does not apply.

Source basis: ICH E2C(R2), FDA E2C(R2), EMA PSUR/PBRER guidance.

COMPARISON

Historical PSUR versus PBRER

Area	Historical PSUR	PBRER under ICH E2C(R2)
Main focus	Interval safety update	Integrated benefit-risk evaluation
Data style	More case-oriented	Aggregate data and cumulative context
Benefit data	Limited or separate	Built into the evaluation
Final question	Do safety details need updates?	Has the benefit-risk balance changed?

Important note
The EU still uses the term PSUR. However, modern EU PSUR requirements follow a benefit-risk approach.

IBD, DLP and reporting interval

01 International Birth Date
First worldwide marketing approval date for the product.

02 Data Lock Point
Cut-off date for data included in the report.

03 Reporting interval
Time period between two DLPs or from IBD to DLP.

Why these terms matter
They define what data belongs in the report and when the team must submit it.

TIMELINE MODEL

Build the PBRER timeline before writing

IBD	DLP	Day 1–20	Day 21–55	Due date
Anchor global schedule →	Freeze report data →	Collect and reconcile →	Write and review →	Submit final report

Best practice
Start authoring plans before the DLP. Then the team can focus on late data, signal updates, and review quality.

70-day submission timeline

≤ 12 months

Day 0	Day 1–15	Day 16–40	Day 41–60	Day 70
Data Lock Point →	Data extraction →	Draft PBRER →	Medical and QC review →	Submission target

Use case

This timeline usually fits reporting intervals of six months or one year.

DUE DATES

90-day submission timeline

> 12 months

Day 0	Day 1–25	Day 26–60	Day 61–80	Day 90
Data Lock Point →	Collect global data →	Evaluate and write →	Governance review →	Submission target

Use case

This timeline usually fits longer reporting intervals or ad hoc reports.

PROCESS

PBRER preparation workflow

Plan → Collect → Evaluate → Write → Submit

1. Plan
Confirm scope, DLP, products, countries and owners.

2. Collect
Pull exposure, cases, signals, studies, literature and actions.

3. Evaluate
Assess signals, risks, benefits and new safety changes.

4. Write
Build clear evidence, conclusions and action proposals.

5. Submit
Check format, sign-off, publishing package and regional rules.

Key message
A strong PBRER process controls both content quality and submission timing.

Roles and responsibilities

PV lead
Owns timeline, scope and safety strategy

Safety physician
Reviews medical meaning and risk conclusions

Medical writer
Builds the narrative and report structure

Regulatory affairs
Confirms regional rules and submission needs

Epidemiology
Supports exposure, studies and real-world data

Quality reviewer
Checks consistency, traceability and final package

Governance rule
Assign one owner for every late decision. This prevents unclear conclusions.

EVIDENCE

Data-source collection map

Safety database
ICSRs, seriousness, outcomes, narratives

Exposure data
Patients, units, regions and indications

Clinical studies
Ongoing and completed trial findings

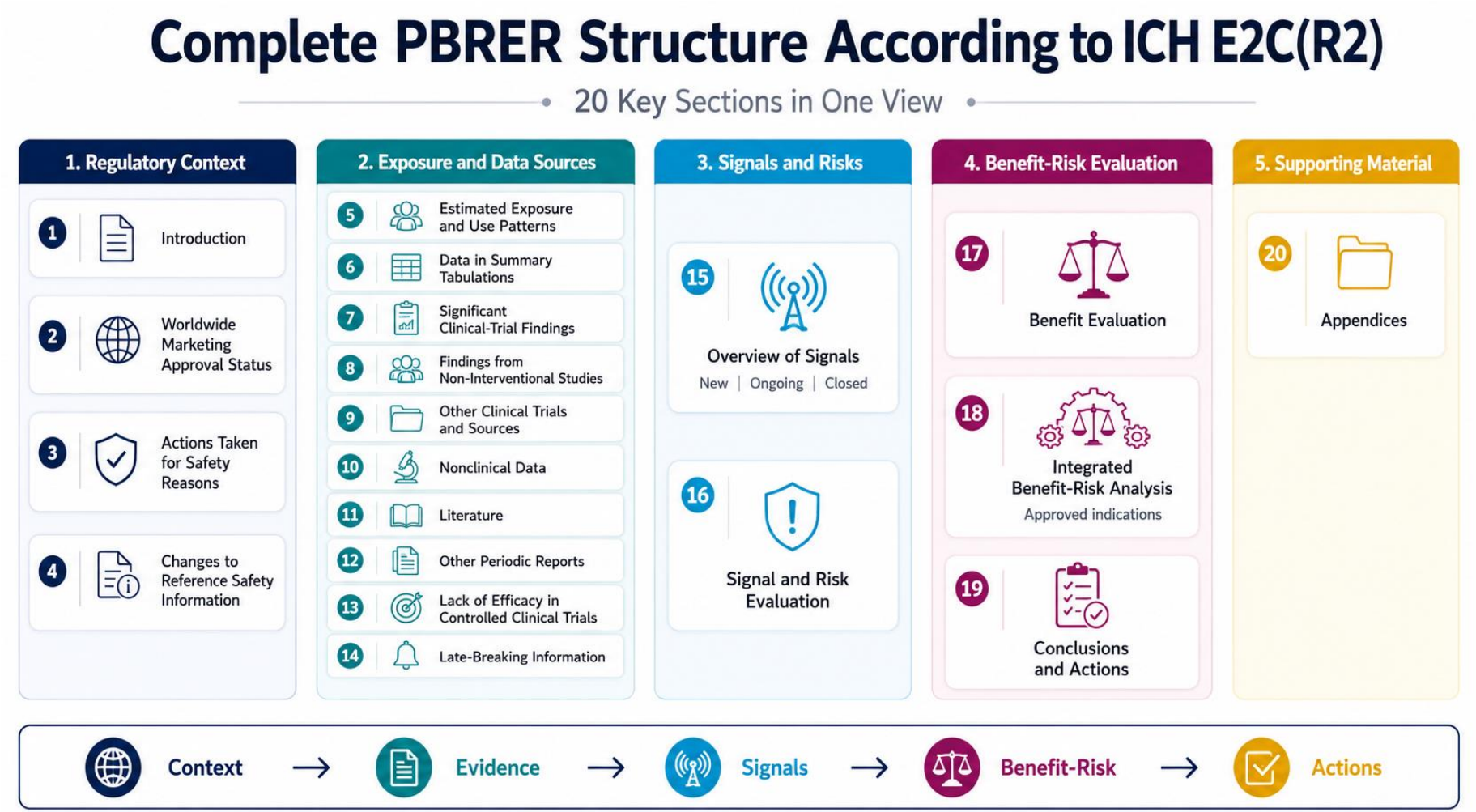
Literature
Relevant published safety and benefit data

Signals/RMP
Open signals, risks and minimization actions

Regulatory actions
Label changes, restrictions and commitments

Data → **Reconciliation** → **Evaluation** → **Report**

All 20 PBRER sections in one view



20 SECTIONS

Sections 1–4: Regulatory context

1 Introduction
Define product, interval, scope and report purpose.

2 Worldwide Marketing Approval Status
Show current marketing authorization landscape.

3 Actions Taken for Safety Reasons
List restrictions, suspensions and safety-driven changes.

4 Changes to Reference Safety Information
Explain RSI updates during the interval.

Sections 5–6: Exposure and tabulations

5 Estimated Exposure and Use Patterns
Show patient exposure and explain data assumptions. Separate interval and cumulative views when needed.

6 Data in Summary Tabulations
Present summarized safety data. Keep tables consistent with the safety database and narrative.

QC focus
Exposure estimates must match risk conclusions and signal interpretation.

Sections 7–14: Evidence sources

7 Clinical-trial findings

8 Non-interventional studies

9 Other trials and sources

10 Nonclinical data

11 Literature

12 Other periodic reports

13 Lack of efficacy

14 Late-breaking information

Writing rule
Every evidence source should answer one question: does it change safety, benefit or uncertainty?

Sections 15–16: Signals and risks

15 Overview of Signals
Summarize new, ongoing and closed signals during the reporting interval.

16 Signal and Risk Evaluation
Evaluate evidence, uncertainty, impact and required risk actions.

Signal source → **Evidence review** → **Risk meaning** → **Action**

Sections 17–19: Benefit-risk actions

17 Benefit Evaluation
Review current benefit evidence by approved indication.

18 Integrated Benefit-Risk Analysis
Explain how new safety findings affect the benefit-risk balance.

19 Conclusions and Actions
State whether labeling, studies, monitoring or risk minimization must change.

Strong conclusion formula
Evidence → interpretation → benefit-risk impact → proposed action → owner and timing.

Section 20: Appendices

Purpose
Appendices support the report. They should not hide key conclusions.

Typical content
Reference safety information, signal tables, line lists when required, and supporting summaries.

QC check
Every appendix must match the report body, table references and final conclusions.

PRACTICAL FOCUS

Exposure estimation essentials

What to include

- exposure by region
- exposure by indication
- patient-years where suitable
- special populations

What to explain

- data sources
- assumptions
- limitations
- major changes from previous reports

Why it matters

Exposure shapes the interpretation of frequency, seriousness and benefit-risk impact.

PRACTICAL FOCUS

Safety case summary tables

Table check	What to verify
Case counts	Interval and cumulative totals match source data.
Serious cases	Definitions and filters stay consistent.
Fatal cases	Medical review supports interpretation.
Special populations	Age, pregnancy or renal/hepatic data are traceable.

Tip
Do not let a table tell a different story than the risk evaluation.

Signal-status management

New signal
First identified during the reporting interval and requires evaluation.

Ongoing signal
Still under evaluation at the Data Lock Point.

Closed signal
Evaluation ended during the interval with a documented conclusion.

QC focus
Signal status must match the signal tracker, RMP updates and final conclusions.

Risk characterization

Describe the risk
Clarify frequency, seriousness, severity, reversibility and affected groups.

Explain uncertainty
State data gaps, confounding, exposure limits and evidence quality.

Define actions
Connect the risk to labeling, monitoring, studies or minimization.

Evidence → **Risk meaning** → **Population impact** → **Action**

Benefit evaluation

Use approved indications
Evaluate benefit in the context of approved uses and populations.

Use current evidence
Include meaningful efficacy, effectiveness and treatment-context updates.

Keep it balanced
Do not repeat old benefit statements without showing current relevance.

Integrated benefit-risk analysis

Question 1
Did any risk become more important?

Question 2
Did benefit evidence change meaningfully?

Question 3
Do actions need to change now?

Safety → **Benefit** → **Uncertainty** → **Conclusion**

Write the conclusion clearly
The reader should understand what changed, why it matters, and what the MAH will do next.

SECTION 14

Late-breaking information

What it covers
Important new information after the DLP but before finalization.

Why it matters
Late data may change signal evaluation, risk conclusions or proposed actions.

Control point
Define a cut-off rule. Then document what arrived, what changed and who approved it.

REPORT COMPARISON

PBRER versus DSUR, PSUR and PADER

Report	Product stage	Main purpose	Typical owner
PBRER / PSUR	Marketed product	Periodic benefit-risk evaluation	MAH / PV team
DSUR	Clinical development	Annual development safety review	Clinical sponsor
PADER	US post-market	Periodic adverse experience reporting	NDA/BLA holder
RMP	Lifecycle tool	Risk planning and minimization	MAH / PV / RA

Practical rule
Choose the report by product stage, regulatory region and safety question.

Authoring rules for a clear PBRER

1. Keep structure stable
Do not delete headings. Mark sections as not applicable when needed.

2. Use evidence chains
Connect each conclusion to data, medical judgment and action.

3. Separate facts and interpretation
Use tables for data. Use narrative for meaning and impact.

4. Write for regulators
Use direct language, explain uncertainty and avoid promotional tone.

Common authoring mistakes

Mistake 1
Exposure totals differ between sections.

Mistake 2
Signal status does not match the tracker.

Mistake 3
Risk conclusions do not cite evidence.

Mistake 4
Benefit section repeats old text only.

Mistake 5
Late-breaking information is missing.

Mistake 6
Proposed actions have no owner or timing.

Fix
Use one final consistency pass after medical review and before publishing.

Cross-document consistency checks

Document	Check against PBRER
CCDS / RSI	New or changed safety information matches report claims.
RMP	Important risks and minimization actions stay aligned.
Signal tracker	New, ongoing and closed signal status matches Section 15.
Safety database	Case counts and seriousness filters match tables.
Regulatory commitments	Post-approval actions and studies are current.

Medical and quality review

Medical review
Checks clinical meaning, risk interpretation and benefit-risk logic.

Quality review
Checks data consistency, format, references and traceability.

Final approval
Confirms conclusions, actions, owners and readiness for publishing.

Good practice
Ask reviewers to comment on decisions, not only grammar.

Submission-readiness gates

Gate 1	Gate 2	Gate 3	Gate 4	Gate 5
Scope confirmed	Data reconciled	Medical sign-off	QC complete	Publish and submit

Stop rule
Do not publish until the final conclusions match data, signals, appendices and actions.

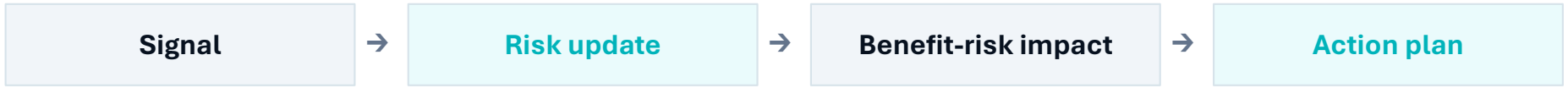
CASE EXAMPLE

Practical example: a signal changes the conclusion

Situation
A new signal appears in literature and spontaneous reports.

Evaluation
Medical review finds plausible causality and relevant exposure.

Action
The team proposes labeling updates and targeted monitoring.



NEXT STEPS

Closing action plan

Today
Build the section map and collect all owners.

This week
Confirm IBD, DLP, interval and regional requirements.

Before submission
Run the final QC checklist and document decisions.

Best habit
Treat the PBRER as a decision document, not a storage document.

FINAL SLIDE

Printable PBRER QC checklist

Print one page

Scope and dates

- ☐ IBD confirmed
- ☐ DLP confirmed
- ☐ Interval correct
- ☐ Regional rules checked

Data quality

- ☐ Exposure reconciled
- ☐ Case tables verified
- ☐ Literature reviewed
- ☐ Late data assessed

Risk and benefit

- ☐ Signals match tracker
- ☐ Risks match RMP
- ☐ Benefits updated
- ☐ Benefit-risk logic clear

Submission package

- ☐ Appendices match body
- ☐ Medical sign-off complete
- ☐ QC comments closed
- ☐ Final actions assigned

Final reviewer notes

Reviewer: _____ Date: _____ Version: _____

Use this checklist before publishing and regional submission.