

Guideline

Clinical Trials on Medicinal Products: Safety Reports to Austrian Ethics Committees

Preamble

The aim of this guideline is to assure the timely delivery of all reports pertinent to the assessment of the trial subjects' safety to the Austrian Ethics Committees as required by the Austrian Medicines Act (AMG) and other relevant regulations and guidelines. The second goal is to avoid an administrative overload of the Ethics Committees due to redundant and/or irrelevant reports.

Therefore, this guideline comprises an exhaustive list of all reports required including timelines, and – based on the experiences from 2004 to 2006 – an exemplary list of reports that are not required and therefore undesirable.

This guideline refers exclusively to safety reports to Austrian Ethics Committees. Other notification requirements such as the notification of amendments or the notification requirements to the Austrian Federal Agency for Safety in Health Care (BASG) are not affected by this guideline.

1. Abbreviations

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|-----------------|---|
| AMG | <i>Arzneimittelgesetz</i> – Austrian Medicines Act |
| ASR/ASUR | Annual Safety Report/Annual Safety Update Report |
| BASG | <i>Bundesamt für Sicherheit im Gesundheitswesen</i> – Austrian Federal Agency for Safety in Health Care |
| DSUR | Development Safety Update Report |
| IB | Investigator's Brochure |
| ICH-GCP | Note for Guidance on Good Clinical Practice (CPMP/ICH/135/95) – ICH Harmonised Tripartite Guideline |
| SAE | Serious Adverse Event |
| SSAR | Suspected Serious Adverse Reaction |
| SUSAR | Suspected Unexpected Serious Adverse Reaction |

2. Responsibility for reporting

In principle, the sponsor is responsible for the timely submission of the safety reports to the Ethics Committees. The sponsor may – while preserving his responsibility – confer his respective tasks on an institution, an organization, or a person

3. Recipients of the reports

Multicentre clinical trials: the Leading Ethics Committee
Monocentre clinical trials: the responsible Ethics Committee

4. Mode of dispatch

The reports may be forwarded to the Ethics Committee using e-mail, FAX, surface mail, or delivery services.

For each report only one mode of dispatch may be chosen. Refrain from multiple submissions of the same report using different modes of dispatch.

5. Required expedited reports (exhaustive)

5.1. SUSARs

- Type: SUSARs which occurred in a clinical trial that has been reviewed by an Austrian Ethics Committee (identical protocol number) in any national or international centre¹
- Form: *Meldungsformular of the Forum* or covering letter with the same content (EC-number, type of report, etc.), CIOMS-form, MedWatch-form or similar as appendix.
- Term: Fatal or life-threatening SUSARs:
initial report as soon as possible, in any case within 7 days after knowledge by the sponsor, follow-up report within additional 8 days.
Other SUSARs: as soon as possible, in any case within 15 days of first knowledge by the sponsor.

5.2. Follow-up reports to SUSAR-reports according to 5.1

- Type: Follow-up reports that include substantial new information beyond the already reported information (7 + 8 days reports, or 15 days report, respectively), e.g. re-evaluation of causality.
- Form: *Meldungsformular of the Forum* or covering letter with the same content, reference to the primary SUSAR-report, CIOMS-form or similar as appendix.
- Term: Same as in 5.1

5.3. Deviations from the study protocol

- Type: Deviations from, or changes of, the protocol to eliminate immediate hazards to the trial subjects²
- Form: *Meldungsformular of the Forum* or covering letter with the same content, description of the hazards and the actions taken as well as the planned or taken additional measures (stop of recruiting, amendment, etc.)
- Term: immediately after knowledge by the sponsor

5.4. Other safety relevant findings³

- Type: Findings, changes, or new information that
- a) materially alter the current benefit-risk assessment
 - b) affect adversely the safety of the trial subjects
 - c) would be sufficient to consider changes in the investigational medicinal products administration or in the overall conduct of the trial
 - d) affect significantly the conduct of the trial⁶
- Form: *Meldungsformular of the Forum* or covering letter with the same content, description of the findings, and planned or already taken measures (stop of recruiting, amendment, new patient information sheet, etc.)
- Term: immediately⁴

¹ AMG: art. 41e sec. 1 and 2

² AMG art. 37a sec. 4; ICH-GCP: 3.3.8 und 5.16.2

³ ICH-GCP 3.3.8 and 4.10.2

⁴ AMG: art. 37a sec. 4

6. Required periodical report

6.1. Annual safety report

- Form:** Executive Summary of the Development Safety Update Report (DSUR)⁵, supplemented by a line listing according to 6.2 Part 2.
- Term:** The reporting period starts with the date of the first authorisation of the concerned trial in an EC member state. The first report is due one year after this date (plus max. 60 days), the following reports in one-year periods
- Note:** The obligation to submit annual interim reports using the *Berichtsformular* of the *Forum* in order to get a renewal of the vote remains unaffected. The due dates of the annual safety reports (triggered by the first authorisation of the trial in the EC) and of the annual interim report (triggered by the issue date of the vote) will normally be different.

6.2. Alternative annual safety report (ASR/ASUR)

As an alternative to 6.1a report according to AMG art. 41e sec. 3 may be submitted.

- Form:** The report consists of 3 parts:
- Part 1:** Analysis of the subjects' safety including a statement on the necessity to re-assess the benefit-risk ratio, and, if applicable, the result of this re-assessment and the consequences thereof.
- Part 2:** A line listing of all SSARs that occurred in the concerned trial within the reporting period, SUSARs emphasised, including a comment on discrepancies between listed and expedited reported SUSARs, if applicable.
- Part 3:** An aggregate summary tabulation of all SSARs that occurred in the concerned trial.

7. Unrequired reports (exemplary)

7.1. Expedited reports of SUSARs that occurred in trials not reviewed by an Austrian Ethics Committee

This information should be part of an update of the IB which is required at least once a year unless they represent safety relevant findings that have to be reported according to topic 5.4.

7.2. Re-reports of already reported SUSARs entitled "IB Update"

Redundant reports are dispensable.

7.3. Deviations from the study protocol initiated not for the reason of eliminating immediate hazards to trial subjects

7.4. Follow-up reports without substantial new information

7.5. SAE-reports

Only reports according to 5.1 to 5.4 are to be made.

7.6. Periodical safety reports with reporting periods shorter than one year

No "quarterly line listings", no semi-annual safety reports.

7.7. Safety reports to local responsible Ethics Committees

In multicentre clinical trials the safety reports have to be submitted only to the Leading Ethics Committee.

⁵ [ICH guideline E2F - Note for guidance on development safety update reports](#)

8. General information on the form of the reports

In the covering letter it should be refrained from listing all laws and guidelines that formed the basis of the report. Instead, a clear indication of the type of report should be made:

- SUSAR (7-days report, 8-days follow-up report, 15-days report, respectively) – topic 5.1
- Follow-up – topic 5.2
- Deviation from protocol – topic 5.3
- Other safety relevant finding – topic 5.4

Specify whether they significantly affect the safety of the subjects or the conduct of the trial.

In addition, the covering letter must indicate the Ethics Committee reference-code of the clinical trial concerned.

If the report refers to several clinical trials, as possible in the cases of topics 5.4 and 6, all applicable Ethics Committee reference numbers have to be listed.

General statements like "*This report refers to all clinical trials with <investigational medicinal product>*" are not acceptable.

This guideline is coordinated with the Institute for Inspections, Medical Devices & Haemovigilance and the Institute for Pharmacovigilance of the Austrian Medicines and Medical Devices Agency.