

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

AMG	<i>Arzneimittelgesetz</i> – Austrian Medicines Act (current law unless otherwise noted)
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
ENTR/CT 3	Detailed guidance on the collection, verification and presentation of adverse reaction reports arising from clinical trials on medicinal products for human use, Revision 2, April 2006
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
Clinical trials according to the AMG 2003 ^{1,2}	all responsible Ethics Committees

¹ AMG as amended by the Federal Law Gazette I No. 12/2003 in conjunction with art. 94a sec. 5 AMG, current law

² Clinical trials which commenced in any centre in Austria before May 1, 2004, and that have not been subjected to the regulations of the Directive 2001/20/EC and to which no EudraCT-number has been allocated.

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 centre³

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: in adequate time after knowledge by the sponsor

5.3. Deviations from the study protocol

Type: Deviations from, or changes of, the protocol to eliminate immediate hazards to the trial subjects⁴

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 findings

Type: Findings, changes, or new information that

- a) materially alter the current benefit-risk assessment⁵
- b) affect adversely the safety of the trial subjects⁶
- c) would be sufficient to consider changes in the investigational medicinal products administration or in the overall conduct of the trial⁵
- 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.)

³ AMG: art. 41e sec. 1 and 2; ENTR/CT 3: 5.1.1.1

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

⁵ ENTR/CT 3: 5.1.1.2

⁶ ICH-GCP: 3.3.8 b) and d), and 4.10.2

Term: immediately⁷

5.5. SAEs

Type: Only SAEs that occurred in trials according to the AMG 2003^{1,2}

Form: Meldungsformular of the Forum or covering letter with the same content, CIOMS-form or similar as appendix.

Term: immediately⁸

Note: The investigator is responsible for the SAE-reporting. Reports by the sponsor or an authorised institution, organisation, or person are acceptable.

6. Required periodical report

6.1. Annual safety report (ASR/ASUR)

Form: The report consists of 3 parts⁹:

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.

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 periods¹⁰.

Note 1: 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.

Note 2: If the sponsor conducts several clinical trials with the same investigational medicinal product, one safety report covering all those trials may be prepared. In this case the reporting period starts with the date of the authorisation for the first of these trials in an EC member state. A global analysis of the safety of the investigational medicinal product should precede the safety reports of the individual trials.

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"

SUSARs are understood as addenda to the Investigator's Brochure. Special notes or redundant reports are dispensable.

⁷ AMG: art. 37a sec. 4

⁸ AMG as amended by the Federal Law Gazette I No. 12/2003: art. 36 no. 9 and art. 41 sec. 1

⁹ AMG: art. 41e sec. 3; ENTR/CT 3: 5.2.1

¹⁰ ENTR/CT 3: 5.2.2

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 from trials with an EudraCT-number assigned

For trials with EudraCT-number 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. Such reports are required only if Ethics Committees receive expedited individual reports solely of SUSARs that occurred in subjects in the concerned member state¹¹. This is not the case in Austria.

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.

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.
- SAE – topic 5.5

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 Inspections Unit and the Science & Information Unit of the AGES-PharmMed.

¹¹ ENTR/CT 3: 5.1.6.5