Information sheet
Safety Reporting in clinical trials

Identification number:	BW101_20_002
Version:	13.0
Valid from:	01.11.2024

Table of contents

1 Notification of Suspected Unexpected Serious Adverse Reactions (SUSARs) occurring with medicinal products in clinical trials of categories B and C (Art. 41 of the Ordinance on Clinical Trials in Human Research (ClinO, SR 810.305)

All Suspected Unexpected Serious Adverse Reactions (SUSARs), occurring in the framework of clinical trials of categories B and C at Swiss trial centres, must be reported to Swissmedic. Please note, that all three criteria (serious + related + unexpected based on the reference safety information) must be fulfilled for an adverse reaction to qualify as a SUSAR.

In addition to a fully completed submission form, the notification must contain the CIOMS form where the following information must be included:

- Trial subject identification code, gender and age/year of birth, details of the suspected trial medication (including the active pharmaceutical ingredient, indication, dosage and route of administration), beginning and end of treatment of the suspected trial medication, listing of concomitant medication(s) and concomitant diseases/medical history.

- The event must be described in sufficient details. This means, that in addition to body site and kind of adverse reaction, it is necessary to include information regarding degree of severity, its evolution over time, information on treatment interruption, treatment discontinuation, rechallenge (reduced or same dose), outcome.

- The assessment of the potential causal relationship between adverse reaction and medicinal product must be provided by investigator and sponsor, as well as the one on unexpectedness. For that purpose, the respective versions of the Investigator's Brochure or Product Information/ Summary of Product Characteristics for IMPs with a marketing authorisation defined as the primary Reference Safety Information (RSI) in the clinical trial application must be used as reference documents. Updates of these documents can be used as RSI if they have been approved by Swissmedic (substantial modifications). In particular, reference should be made to adverse drug reactions (ADR) that have already been documented for the corresponding system of organ class (SOC).

- All SUSARs from Swiss sites need also to be part of the Annual List of Events and Deficiencies or the Development Safety Update Report (Art. 43 para. 1 ClinO) of the respective reporting period.

For notifications relating to **blinded trials**, the treatment of the trial subject suffering from the SUSAR should be unblinded.

Important:

- Comparators and placebos administered in clinical trials are IMPs (independent of their registration status). Therefore, SUSARs associated with a comparator product or a placebo follow the same reporting requirements as the test IMP. Furthermore, events associated with placebo would usually not satisfy the criteria for a SUSAR and therefore for expedited reporting. However, in the rare cases, where SUSARs are associated with placebo (e.g. reaction due to an excipient or impurity), the sponsor should report such cases.
  After initial report of a SUSAR, follow-up reports (FUP) should only be submitted if they influence the causality assessment. Submitted follow-ups for SUSARs without influence on causality will not be processed.

- SUSARs associated with unauthorized Auxillariary Medicinal Products (AxMPs) should be submitted as it is done with IMPs.

- For clinical trials of category A. i.e. with products marketed in Switzerland used according to the marketing authorisation, the sponsor is subject to the notification requirements specified in Article 59 paragraphs 1 and 2 of the Therapeutic Product Act (TPA, SR 812.21). These reports must be sent to Swissmedic Drug Safety Department. Same is true for SUSARs from authorized auxiliary medicinal products (AxMPs).

- SUSAR notification is mandatory also if the investigator (or the sponsor) becomes aware of a suspected case after the clinical trial was completed and the suspected case occurred during or after the clinical trial was completed (Art. 41 para. 4bis ClinO).

Please do not send the following:

- Reports that do not fulfil the criteria stated in the SUSAR definition.
- Follow-up reports of SUSARs that do not influence the causality assessment.
- Individual SUSAR reports occurred in patients enrolled outside of Switzerland. These should be submitted with the Annual List of Events and Deficiencies or the Development Safety Update Report.
- Periodic lists or tables of SUSARs and/or SAEs. Lists/tables must be sent only with Annual List of Events and Deficiencies or the Development Safety Update Report.
- Copies of case report forms (CRFs) instead of CIOMS forms.

How to-report
The SUSAR can be submitted as described on the website under Services und Liste->Submissions->Klinische Versuche Arzneimittel. If you have to submit a follow-up report for a SUSAR, please mention the service order number of the initial SUSAR (included in the acknowledgment of receipt of the initial SUSAR) in the FO submission form in the available field (SA-Number).
Form: Please select SUSAR as form type in the FO submission form and include the CIOMS form (.pdf).

Timelines (Art. 41, par. 4, ClinO)**:**

- Fatal and life-threatening SUSARs: Initial notification within 7 days, follow-up report within 8 days after initial notification (even if no influence on causality assessment).
- Other SUSAR events: Initial notification within 15 days.

……..

2 Notification of safety measures in clinical trials of categories B and C (Art. 37, par. 3, ClinO)

The most important tool for monitoring the safety of trial subjects is the immediate reporting, by the sponsor, of new events that could put the safety of trial participants at risk, taking both national and international data into account.

- All suspected new risks and relevant new aspects of known adverse reactions that require safety-related measures must be reported (e.g. a Dear Investigator Letter)
- The report must contain all the information in the form of a precise, critical summary, indicating the measures taken to minimise the risk.
- In case the urgent safety measure (USM) is based on a report of the minutes of the safety monitoring board (or similar), this document has to be submtted

- The report must be clearly highlighted as an important safety information and sent separately from the annual safety report.
- According to Art. 44 of ClinO regarding radiation protection for category B and C clinical trials with therapeutic products that emit ionising radiation, the investigator shall notify Swissmedic within seven working days, if the permitted radiation dose guidance value is exceeded at any time.

How to report : The safety measure can be notified can be submitted as described on the website under Services und Liste->Submissions->Klinische Versuche Arzneimittel
Form: Please select “REPORTING” as form type and “Safety and Protective Measure Notific.” as form topic in the FO submission form, when notifying the safety measure.

Timelines: Immediately following the occurrence of the circumstances that constitute a safety risk.
……..

3 Annual List of Events and Deficiencies or the Development Safety Update Report (Art. 43 para. 1 ClinO) for clinical trials of categories B and C (Art. 43 para. 3 ClinO)

The Annual List of Events and Deficiencies or the Development Safety Update Report are summaries of the current status of knowledge of the clinical investigation or of the development program with the specific investigation medicinal product (IMP) and describes the general progress of the clinical trial and new safety issues, identified and potential risks of active substances/medicinal products during clinical trials that could have an impact on the protection of clinical trial subjects (Art. 43 para. 1 ClinO).

Separate DSURs/ Annual List of Events and Deficiencies have to be submitted for each IMP. Alternatively, one Annual List of Events and Deficiencies / DSUR focusing on the combination treatment can be submitted instead. Trial-specific safety and progress reports can be submitted as well, where the safety updates about the trial are summarized (used in case the sponsor is not the manufacturer of the IMP).

In accordance with Art. 43, par. 3, ClinO, the Annual List of Events and Deficiencies/DSUR must be submitted for every clinical trial of categories B and C carried out in Switzerland.

The Annual List of Events and Deficiencies/DSUR is submitted once a year, throughout the duration of the clinical trial in Switzerland, and the last Annual List of Events and Deficiencies/DSUR to be submitted must cover the Last Patient Last Visit (LPLV) in Switzerland for that specific trial. There is no need for further ASR/DSUR submissions after LPLV since the information on safety will be captured in the clinical study report.

The following details must be included in the Annual List of Events and Deficiencies /DSUR: report no. (consecutive numbering), product name, clinical trial code, time period covered by the report, date of the report, list of events or adverse reactions (including SUSARs), name and address of the sponsor.

The following information should be filled in the section List of Annual Events and Deficiencies /DSUR of the FO submission form, when sending the annual safety report:

- New SUSARs that have occurred in patients enrolled at clinical trial sites in Switzerland in the time period under review. Please include the service order number under SUSAR identification Number. The service order number is mentioned in the acknowledgment of receipt of the initial SUSAR, the reference number of the trial and the date of the CIOMS report.
- An updated statement from the Sponsor on the benefit/risk ratio of the trial in light of the new safety data collected over the reporting period

How to report : The safety measure can be notified can be submitted as described on the website under Services und Liste->Submissions->Klinische Versuche Arzneimittel
Form: Formats similar to DSUR (Development Safety Update Report), PSUR (Periodic Safety Update Report) / PBRER (Periodic Benefit Risk Evaluation Report), or Annual List of Events and Deficiencies according to Art. 43, par. 1, ClinO are accepted.

DSURs must comply with ICH E2F.
For Investigator initiated trials (IITs), the template “Annual List of Events and Deficiencies” published by swissethics may be used (www.swissethics.ch).

Please send the complete report, including the executive summary.

Timelines:. The reference date for the Annual List of Events and Deficiencies/DSUR submission may differ from the authorisation date of the trial in Switzerland. If the clinical trial has started earlier in Switzerland than in the EU, the overall duration of the trial must be covered in the first annual safety report.

……

4 Information

Contact details:

Swissmedic
Swiss Agency for Therapeutic Products
Clinical Trials Division
Hallerstrasse 7
P.O. Box
3012 Bern

For any information please contact us:

Tel.: +41 58 462 03 87
E-mail: ct.medicinalproducts@swissmedic.ch

Change history

Version	Change	sig
13.0	Updates associated with the revision of ordinances relating to the Human Research Act: new timeline included for the submission of life-threatening SUSARs and notification of SUSARs after completion of a trial; Additional changes: new title in order to better describe the content of this guideline; updates in the submission procedure of SUSAR, USM and ASR/DSUR and updates related to a new version of the submission form released on 01 November 2024	cac
12.0	Reporting of SUSARs associated with AxMPs, safety reporting for radiation protection in case of exceeding dose	sec
11.3	New layout, no content adjustments to the previous version	tsj
11.0	Reporting of SUSARs associated with Placebo added	
10.0	Addition of table of content / Clarification of submission requirements for ASR/DSUR and notification of safety measures / Availability of document in English only	sec
9.0	Precisions concerning the ASR	jaf
8.0	New QM ident: BW101_20_002e_MB Old QM ident: BW101_22_001e_MB The remaining content of the document was not reviewed and stays unchanged.	wkn
7.0	Clarification of Reference Safety Information (RSI) Further clarification of safety reporting modalities	sec
6.0	Clarification of submission modalities and format of SUSAR	sec
	Demarcation between SAE and SAR, clarification SUSAR number	aju
	New change history inserted in the document	wis