Table of contents

Swissmedic • Hallerstrasse 7 • 3012 Bern • www.swissmedic.ch • Tel. +41 58 462 02 11 • Fax +41 58 462 02 12

1. Notification of suspected unexpected serious adverse reactions (SUSARs) occurring in clinical trials with medicinal products of the categories B and C (Art. 41 of the Ordinance on Clinical Trials in Human Research (ClinO, SR 810.305)

For all SUSARs occurring in the framework of clinical trials of the categories B and C at Swiss trial centres, notifying the Swiss Agency for Therapeutic Products, Swissmedic, is mandatory. Please note that all three criteria (serious + related + unexpected) must be fulfilled.

The notification must contain the following information:

- Swissmedic reference number of the clinical trial, source of the report, trial subject identification code (with mention of gender and age/date of birth), details of the study medication (including the mention of active pharmaceutical ingredient, indication, dosage and route of administration), beginning and end of treatment, and listing of concomitant medication(s).
- The event must be described in sufficient details. This means that in addition to the type and site of the reaction, it is also necessary to include information regarding the degree of severity, its evolution over time, information on dechallenge, rechallenge and outcome.
- An analysis of the causal relationship between the event and the IMP, as well as assessment of the unexpectedness, must be included. The versions of the Investigator's Brochure, Product Information, or Summary of Product Characteristics (SmPCs 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 only if they have been approved by Swissmedic (substantial amendments). In particular, reference should be made to adverse drug reactions (ADR) that have already been documented for the corresponding system of organ class (SOC).

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

Important:

- Comparators and placebos administered in clinical trials are IMPs. 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, 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 SUSAR follow-ups without influence on causality will not be processed.
- 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. This does not apply if marketed products are used according to the marketing authorisation in clinical trials of category B or C.
- SUSARs associated with authorised as well as unauthorised Auxillary MPs (AxMPs) should be individually submitted as is done for IMPs.

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 from foreign study sites. These should be submitted with the Annual Safety Report (ASR).
- Periodic lists or tables of SUSARs and/or SAEs. Lists/tables must be sent only with the ASR.
- Copies of case report forms (CRFs) instead of CIOMS forms.

Swissmedic • Hallerstrasse 7 • 3012 Bern • www.swissmedic.ch • Tel. +41 58 462 02 11 • Fax +41 58 462 02 12

Address for SUSAR notifications
SUSARs should be submitted as below Paper documents and CD to
Swissmedic
Operational Support Services
Hallerstrasse 7
3012 Bern
Schweiz
Or File Transfer to ct.medicinalproducts@swissmedic.ch
(Via your Account of the File transfer Service tool. If you are not already in possession of a login, please contact ct.medicinalproducts@swissmedic.ch)

Form: CIOMS form (.pdf), always with the accompanying form for SUSARs.
Timelines (Art. 41, par. 4, ClinO)**:**
- SUSARs resulting in death: Initial notification within 7 days, follow-up report within 8 days after initial notification (even if no influence on causality assessment).
- Other SUSAR events requiring notification: 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.
- The report must contain all the information in the form of a precise, critical summary, indicating the measures taken to minimise the risk.
- The report must be clearly indicated as important information and sent separately from the annual safety report.
- According to Art. 44 of ClinO regarding rediation protection of category B and C clinical trials with therapeutic products that emit ionising radiation, if the permitted radiation dose guidance value is exceeded at any time, the investigator shall notify Swissmedic within seven working days after awareness.

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

Address:
Paper documents and CD to
Swissmedic
Operational Support Services
Hallerstrasse 7
3012 Bern
Schweiz

Or File Transfer to ct.medicinalproducts@swissmedic.ch
(Via your Account of the File transfer Service tool. If you are not already in possession of a login, please contact ct.medicinalproducts@swissmedic.ch)

and paper documents to
Swissmedic
Operational Support Services
Hallerstrasse 7
3012 Switzerland

……

3. Annual Safety Report (ASR), Development Safety Update Reports (DSUR) etc. for clinical trials of categories B and C (Art. 43, par. 3, ClinO)

The Annual Safety Report is a summary of the current status of knowledge and describes the identified and potential risks of active substances/medicinal products during clinical trials.
DSURs must comply with ICH E2F.
Separate DSURs have to be submitted for each IMP. Alternatively, one DSUR focusing on the combination treatment needs to be submitted.

In accordance with Art. 43, par. 3, ClinO, an Annual Safety Report must be submitted for every clinical trial of categories B and C carried out in Switzerland.
The ASR is submitted once a year from the date of study approval in Switzerland andthroughout the duration of the clinical trial in Switzerland.The final ASR submission must cover the Last Patient Last Visit (LPLV) in Switzerland.
Furthermore, after the aforementioned ASR (covering LPLV) there is no need for further ASR submissions since the information on safety will be captured in the clinical study report. The report may concern a single trial or several trials with the same IMP. In such a case the individual trials must be clearly identifiable.

The following details must be included in the ASR: Report no. (consecutive numbering), product name, Swissmedic reference number(s) of the clinical trial, time period covered by the report, date of the report, name and address of the sponsor.

The safety report contains a list of events or adverse reactions according to Art. 43 ClinO, as well as a precise, critical summary of the medicinal product's safety profile and new relevant safety aspects and their effect on carrying out the clinical trial.
The chapter concerning the annual safety report“must contain the following information:

- New SUSARs that have occurred at clinical trial sites in Switzerland in the time period under review. The internal number of the sponsor, the date of first report to Swissmedic and the Swissmedic U-number must be provided.
- Whether - in the sponsor’s opinion - the risk/benefit ratio of the trial substance has changed and any measures needed to be taken.

Form: Formats similar to DSUR (Development Safety Update Report), PSUR (Periodic Safety Update Report) / PBRER (Periodic Benefit Risk Evaluation Report), or ASR (Annual Safety Report) are accepted.
For IITs, the template of swissethics may be used (www.swissethics.ch).

Timelines: The reference date for ASR submission may differ from the authorisation date of the trial in Switzerland but the reference date for submission is effective from the date of authorization of the trial by Swissmedic. 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.

Address:
Paper documents and CD to
Swissmedic
Operational Support Services
Hallerstrasse 7

3012 Bern
Schweiz

Or File Transfer to ct.medicinalproducts@swissmedic.ch
(Via your Account of the File transfer Service tool. If you are not already in possession of a login, please contact ct.medicinalproducts@swissmedic.ch)

and paper documents to
Swissmedic
Operational Support Services
Hallerstrasse 7
3012 Switzerland

……

4. Information

Contact details:

Swissmedic
Swiss Agency for Therapeutic Products
Clinical Trials Division
Hallerstrasse 7
3012 Bern

Information relating to SUSAR notification can be obtained from:

Tel.: +41 58 462 03 87
Fax: +41 58 462 04 33
E-mail: ct.medicinalproducts@swissmedic.ch

Information relating to annual safety reports and safety measures can be obtained from:

Tel.: +41 58 462 03 87
Fax: +41 58 462 04 33
E-mail: ct.medicinalproducts@swissmedic.ch

Change history

Version	Valid and binding as of:	Description, comments (by author)	Author's initials
13.0	**13.09.2021**	**Updates in line with upcoming new procedures for submission**	**sec**
12.0	**14.02.2020**	**Reporting of SUSARs associated with AxMPs, safety reporting for radiation protection in case of exceeding dose**	**sec**
11.0	**15.03.2019**	**Reporting of SUSARs associated with Placebo added**	
10.0	**10.10.2017**	**Addition of table of content / Clarification of submission requirements for ASR/DSUR and notification of safety measures / Availability of document in English only**	**sec**
09	**15.12.2016**	**Precisions concerning the ASR**	**jaf**
08	**21.11.2016**	**New QM ident: BW101_20_002e_MB** **Old QM ident: BW101_22_001e_MB**	**wkn**

		The remaining content of the document was not reviewed and stays unchanged.	
07	**31.05.2016**	**Clarification of Reference Safety Information (RSI)** **Further clarification of safety reporting modalities**	**sec**
06	**05.05.2015**	**Clarification of submission modalities and format of SUSAR**	**sec**
	17.09.2014	Demarcation between SAE and SAR, clarification SUSAR number	aju
	31.07.2014	New change history inserted in the document	wis

Swissmedic • Hallerstrasse 7 • 3012 Bern • www.swissmedic.ch • Tel. +41 58 462 02 11 • Fax +41 58 462 02 12