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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 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 follow the same reporting requirements as for the test IMP.
- After initial report of a SUSAR, follow-up reports (FUP) should only be submitted if they influence the causality assessment.
- For clinical trials of category A. i.e. with products marketed in Switzerland used according to the marketing authorization, 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 made to Swissmedic Drug Safety Department. This does not apply if marketed products are used according to the marketing authorization in clinical trials of category B or C.

Please do not send the following:

- Reports that do not fulfil the criteria stated in the SUSAR definition.
- Follow-up reports of SUSAR 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.

Address for SUSAR notifications: SUSAR@swissmedic.ch. Please do not submit SUSARs via fax or courier.

The sender will receive an acknowledgement of receipt together with the Swissmedic number (U-Nr.) attributed to the event.

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.
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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.

Address: Swissmedic, Clinical Trials Division. Please send **by regular mail**.

The sender will receive an acknowledgement of receipt.

Form: The notification of safety measures must be accompanied by the form „VO Form – Reporting Related to a Clinical Trial“.

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

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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, throughout the duration of the clinical trial in Switzerland, the ASR reporting period for the last report must cover the LPLV in Switzerland.

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 in the form „VO Form – Reporting Related to a Clinical Trial“ must contain the following information:

- New SUSARs that have occurred at study 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 taken.

Address: Swissmedic, Clinical Trials Division. Please send **by regular mail**.

The sender will receive an acknowledgement of receipt.

Form: Formats similar to DSUR (Development Safety Update Report), PSUR (Periodic Safety Update Report) / PBREER (Periodic Benefit Risk Evaluation Report), or ASR (Annual Safety Report), are accepted.

For IITs, the template of swissethics may be used (www.swissethics.ch).

Please send the complete report in electronic form (e.g. on CD).

The printed version of the executive summary must always be sent with the form „VO Form – Reporting Related to a Clinical Trial“.

Timelines: The ASR is submitted once a year, throughout the duration of the clinical trial in Switzerland. The reference date for 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.

The ASR does not need to be submitted after LPLV in Switzerland since the information on safety will be included in the clinical study report.

4. Information

Contact details:

Swissmedic
Swiss Agency for Therapeutic Products
Clinical Trials Division
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P.O. Box
3000 Bern 9

Information relating to SUSAR notification can be obtained from:

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

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

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

Change history

Version	Valid and binding as of:	Modified without version change	Description, comments (by author)	Author's initials
10	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	21.11.16		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
07	31.05.16		Clarification of Reference Safety Information (RSI) Further clarification of safety reporting modalities	sec
06	05.05.15		Clarification of submission modalities and format of SUSAR	sec
		17.09.14	Demarcation between SAE and SAR, clarification SUSAR number	aju
		31.07.14	New change history inserted in the document	wis