The EFGCP Report on
The Procedure for the Ethical Review of Protocols for
Clinical Research Projects in Europe and Beyond

Question 29

How do RECs deal with SUSAR reports and Annual Safety Reports?

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Austria

Ethics Committees review the submitted documents.

Belgium

In a very disparate way and attempts are made to harmonize this.

Bulgaria

SUSARs and ASRs are reviewed by responsible expert and reported at the regular Ethics Committee meetings.

Croatia

The Central EC closely collaborates with the Agency for Medicinal Products and Medical Devices of Croatia (HALMED). According to Croatian law and by-laws, the sponsor or investigator should expedite the reporting to the Agency for Medicinal Products and Medical Devices of Croatia (HALMED) and Central Ethics Committee of all adverse drug reactions (ADRs) that are both serious and unexpected. Such expedited reports should comply with the applicable regulatory requirement(s) and with the ICH Guideline for Clinical Safety Data Management: Definitions and Standards for Expedited Reporting.

The Agency for Medicinal Products and Medical Devices of Croatia (HALMED) must monitor all AE of clinical trials, and send a report to Central Ethics Committee and the Minister of Health as the regulatory authority.

Cyprus

Relevant announcement is included in the Cyprus National Bioethics Committee’s website (www.bioethics.gov.cy).

The Local Principal Investigator (LPI) is responsible for submitting all the relevant details for any SUSAR occurring in a participant in a centre in Cyprus, using the form EEBK 09 Report of Extraordinary Incident to the Ethics Committee (the Form is available at the Cyprus National Bioethics Committee website).

For SUSAR’s occurring in other centres (in case of multi-centred studies) the LPI is responsible for reporting these to the Cyprus National Bioethics Committee using a summarized table. CIOMS forms are not acceptable. The LPI has to make a risk-benefit assessment with regards to the participants in the study.

This risk-benefit assessment should be in a summarized table format, and should include the following:

(i) total number of subjects enrolled in the study in all the centers (in case of multi-center studies),
(ii) the number of SUSAR’s reported and whether these SUSAR’s relate to the Study Protocol or not (as per the investigator’s assessment)

(iii) the number of subjects withdrawn from the study and the reasons for this withdrawal, and,

(iv) the number of subjects still under the protocol and the number of the subjects showing improvement due to the medicine used in the Study.

As for the Reporting timelines, these are set out by the legislation enacted in the Republic of Cyprus (ΚΔΠ 452/2004) and it is the responsibility of the LPI to give information to the CNBC about any SAE/SUSAR’s occurring, in any of the centers participating in the study, in the necessary timelines (for life threatening or fatal SUSARS the timeline for reporting is 7 days and then follow up every 8 days about the outcome whilst for all other cases of SUSARs the reporting timeline is 15 days).

Following the provisions of the Operational Guidelines for the Establishment of Ethics Committees in reviewing Biomedical Research involving Human Subjects (Κ.Δ.Π. 175/2005), in all SUSARs reports, the program/study is re-evaluated by the Ethics Committee, which will communicate its findings and/or decisions to the applicant. The Committee has the right to approve changes in the protocol of the study, to postpone or terminate the study.

**Czech Republic**

With considerable difficulty because of the provision of too much irrelevant information which the REC has no opportunity to solve. More reliance is placed on the Annual Safety Report and 6 Month listing. All RECs want to be provided by SUSAR reports from sites which they approved.

**Denmark**

In clinical trials with medicinal products the sponsor or the chief investigator shall once every year during the entire trial period submit to the committee a list of all serious adverse reactions and all serious events encountered during the period and shall provide information about the safety of the trial subjects.

**Estonia**

All SUSARs are reported at least quarterly, as a line listing accompanied by a brief report by the sponsor. The SUSARs and Annual Reports are submitted for analysis to some of EC members and they are discussed at the EC meetings.

**Finland**

Finnish ECs do not evaluate individual SUSARs.
France

RECs must be informed by the sponsor of every SUSAR in France, and by six-monthly report for other SUSAR. The Annual Safety Reports are examined by the REC.

Germany

Discussion on this is ongoing.

Some RECs do not want to see SUSARs, but only periodic safety reports and listings.

Some RECs want to see only the SUSARs regarding the specific trial in their country, few want to see all SUSARs regarding the IMP.

A consultation group has been established with representatives from BfArM, Paul-Ehrlich-Institut, Robert-Koch-Institut (German federal authorities), VFA, BPI (associations of the German pharmaceutical industry), and of the “Permanent Working Party of German Research Ethics Committees” to come to a common approach. A working group has also been established at the Federal Medical Association (Bundesärztekammer).

Greece

The sponsor submits to the central ethics committee – NEC – and the investigator to the hospital ethics committees all relevant information about a suspected unexpected serious adverse reaction (SUSAR) which is fatal or life-threatening not later than seven days after the sponsor is first aware of the reaction. All other suspected unexpected serious adverse reactions (SUSARs) which are not fatal or life-threatening are reported within 15 days after the sponsor is first aware of the reaction.

The Annual Safety report is submitted by the sponsor to the NEC and by the investigator to the hospital EC within 60 days from the data lock point.

Hungary

The 35/2005 MoH Decree requires that they must be sent both to the NIP and KFEB. The research ethics committee procedure is not specified, they evaluated case by case.

Iceland

The sponsor must see to that the Icelandic Medicines Control Agency (IMCA) and the NBC receive notification of any serious adverse reactions which may arise. If no sponsor is connected to the clinical trial, cf. sub-paragraph i of Art. 2, this shall be the responsibility of the principal investigator or, as the case may be, the investigator. The following time limits shall apply for such notifications:
a) For an adverse reaction resulting in death or an unexpected life-threatening situation caused by the trial medicinal product, notification must be given immediately or within one week (7 days) of the occurrence of the reaction.

b) All suspected serious and/or unexpected adverse reactions must be notified within 15 days.

If a clinical trial lasts for more than one year, an annual report must be sent to the IMCA and the NBC, giving an account of the status of the clinical trial and a summary of all serious adverse events.

No later than one year following the conclusion of the clinical trial, the final report must be sent to the IMCA and the NBC.

**Ireland**

These are usually reviewed by or on behalf of the chairpersons and where necessary are brought to the attention of the Committee.

**Italy**

The Ethics Committees receive SUSARs reports and Annual Safety Reports.

**Latvia**

The procedure is not specified.

**Lithuania**

The detailed guidelines for the SUSAR reporting to the investigators and the EC in Lithuania are regulated by the Decree No. 435 of the Ministry of Health on the Procedure for Issuing Favourable Opinion to Conduct Clinical Trial on Medicinal Product, Approval for Clinical Trial on Medicinal Product, Conducting and Controlling Clinical Trials. The following reports have to be submitted to the Lithuanian Bioethics Committee:

1. Fatal or life-threatening suspected unexpected serious adverse reactions (SUSARs) that occurred in the concerned trial in Lithuania should be reported in CIOMS form no later than within 7 calendar days and follow-up information - within additional 8 days.
2. Other SUSARs (not fatal and not life-threatening) that occurred in the concerned trial in Lithuania should be reported in CIOMS form within 15 days.
3. All SUSARs that occurred in other Member States and, where applicable, from third countries, should be periodically reported at least every 6 months as a line listing and summary table.
4. Other fatal & life threatening SAEs/SARs (only related) that occurred in the concerned trial in Lithuania should be reported no later than within 7 calendar days and follow-up within additional 8 days.
5. Other safety reports that could essentially change the assessment of the risk/benefit ratio should be reported no later than 15 days.

6. Annual safety report of all SUSARs in the concerned trial should be submitted as a line listing and summary table.

The reports are reviewed by the secretariat members and by appropriate experts if needed.

**Luxemburg**

The SUSARs and ASRs are sent to each member for review, and mark their agreement with the continuation of the studies, either directly (email or phone notification), or through implicit consent.

**Malta**

A member of the HEC is appointed as rapporteur and s/he delivers an overview of the documentation that s/he has reviewed to the rest of the committee during a meeting. If there are any concerns the sponsor is contacted. The information is retained in a local database.

**Netherlands**

SUSARs and SAEs are now submitted electronically to the MRECs and Competent Authority using the webportal ReviewOnline (ToetsingOnline). From 1 January 2010 onwards, the use electronic submissions on SAEs and SUSARs using the web portal is compulsory. The web portal provides the METC and the investigator with a comprehensive overview of SUSARs and SAEs on a study basis and facilitates an efficient administrative process of the assessment.

**Norway**

They are received and reviewed by the committee, but this is usually delegated to the chairman.

There are attempts to exempt SUSAR reports from the REC – and to leave their review only to the Norwegian Medicines Agency.

**Poland**

Individual SUSAR reports are received and evaluated by the expert who evaluated the original protocol and than presented during sessions of Bioethics Committees. In questionable or doubtful cases Bioethics Committee asks for further clarifications. Any expert’s opinion and SUSAR reports are included within the project archives.

Annual Safety Reports are evaluated by the member of the Bioethics Committee, or expert, who evaluated the original protocol.
Portugal

The guideline: “Detailed guidance on the collection, verification and presentation of adverse reaction reports arising from clinical trials on medicinal products for human use” should be followed.

National SUSARs should be reported by e-mail to the following address: ceic@infarmed.pt. Annual safety reports and quarterly line-listings should be sent by mail to the CEICs address using paper or a CD-ROM.

The EC procedures are currently being developed.

Romania

NECCT receive the SUSAR reports and the Annual Safety Report.

Russia

The Reports are reviewed by the REC Secretariat and appropriate experts, if needed.

They file what is sent to them.

Serbia

If serious and unexpected adverse reactions SUSAR or serious adverse events (SAE) occur during the CT, a sponsor shall immediately notify the Agency and LEC of a legal entity in which the CT is conducted by Law.

Slovakia

They usually “take note of them” at their next regular meeting. They also put them on file. When asked by sponsors, they provide written confirmation of having done so.

Slovenia

Prompt reporting of suspected unexpected serious adverse events/reactions (SUSARs) to the NMEC is required when it may be considered by the sponsor/CRO or the responsible investigator that the risk to the participants could exceed the anticipated or acceptable level, or that the originally estimated risk / benefit ratio is changed unfavourably. This also includes cases of unexpectedly frequent occurrence of the anticipated SAEs. Regarding other SAEs, quarterly, semi-annual or annual safety reports accompanied with a comment by the sponsor/CRO or the clinically responsible principal investigator are sufficient. The reports to the NMEC can be sent by e-mail to tone.zakelj@kclj.si as PDF files attached to the main message giving all the necessary study identifying data.
Spain

SUSARS are routinely received and Annual Safety Reports are required. However, SUSARS reception overburdens CEICs activities.

Sweden

They are filed.

Switzerland

The REC takes notice mainly on the local events.

Turkey


United Kingdom

Individual expedited reports of SUSARs occurring in medicinal trials in the UK are acknowledged and filed. The committee is not expected to carry out any sort of review.

Sponsors of medicinal trials are also required to submit an annual safety report with a global line listing and a safety assessment. This must be in the ICH E2F format for Development Safety Update Reports. The Executive Summary of the DSUR is reviewed by the Chair and by a member with appropriate expertise (for example, a clinical pharmacologist, pharmacist or specialist in the disease field). Receipt of the report is notified in writing to the committee and may be placed on a meeting agenda for discussion if there appear to be any concern about safety or a need to update the participant information sheet.

April 2012

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