EUROPEAN CLINICAL RESEARCH INFRASTRUCTURES NETWORK - TRANSNATIONAL WORKING GROUPS

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Standard Operating Procedures on adverse event reporting

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Work package 6: **Transnational working group on standard operating procedures**

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Table of content

1 Context

The SOP was developed by the WP3 on adverse events reporting, reviewed by the WP6 on standard operating procedures and validated by the WP3.
This SOP will be discussed at the beginning of the next ECRIN project to comply with the objectives of the Quality Unit and the different delegation models to be used for the pilot project.

ECRIN-AE-SOP ØØ1

How to support adverse events reporting in multinational clinical trials on medicinal products

How to support adverse events reporting in multinational clinical trials on medicinal products
Reference: ECRIN AE-SOPØØ1-VØ.1
Version number: draft VØ.1

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1. PURPOSE

The purpose of this SOP is to describe the general procedure and the role of the ECRIN team and their cooperation with the sponsor for the reporting of adverse events in multinational clinical trials.

2. SCOPE

This SOP concerns clinical trials on medicinal products within the scope of Directive 2001/20EC. The requirements for other categories of clinical research will be developed in another SOP.
This procedure will cover all clinical trials selected by the ECRIN scientific board which will be performed within the ECRIN network
The procedure describes the general requirements in term of collection, documentation, investigation, assessment, submission and follow-up of AE which occur in the course of a clinical trial. The procedure also describes the general responsibilities and deadlines regarding the annual safety report and other events.
Specific responsibilities or delegation of responsibilities will be specified in a contract delegation form.

3. DEFINITIONS and ABBREVIATIONS

AE_ Adverse Event: Any untoward medical occurrence in a clinical trial participant administered a medicinal product and which does not necessarily have a causal relationship with this treatment.

AR_ Adverse Reaction : All untoward and unintended responses to an investigational medicinal product related to any dose administered.

Data monitoring committee (DMC): A committee that is usually independent of the investigators, funder and sponsor of a trial. A DMC reviews the accruing trial data on a regular basis to assess whether there are any safety issues that investigators or participants should be aware of. A number of different titles are used for DMCs, for example: Independent Data Monitoring Committee (IDMC), Data and Safety Monitoring Board (DSMB), Independent Safety Monitoring Committee (ISMC) and Data Monitoring and Ethics Committee (DMEC).

SAE_Serious Adverse Event
SAR_ Serious Adverse Reaction
Any untoward medical occurrence or effect that at any dose:
-results in death,
- or is life-threatening
Or requires hospitalisation or prolongation of existing
hospitalisation
or results in persistent or significant disability or incapacity
or consists of a congenital anomaly or birth defect
Medical judgement should be exercised in deciding whether an adverse event/reaction should be classified as serious in other situations. Important adverse events/reactions that are not immediately life-threatening or do not result in death or hospitalisation, but may jeopardise the participant or may require intervention to prevent one of the other outcomes listed in the definition above, should also be considered serious.
*Life-threatening in the definition of a serious adverse event or serious adverse reaction refers to an event in which the participant was at risk of death at the time of the event. It does not refer to an event which hypothetically might have caused death if it were more severe. The definition of seriousness above reflects the definition used in the EU Directive, and from EudraCT guidance. “Other important medical condition” is taken from ICH E2A and can also be used to define an SAE.

SUSAR_ Suspected Unexpected Serious Adverse Reaction
A suspected adverse reaction related to an investigational medicinal product (the tested investigational medicinal products and comparators) which occur in the concerned trial, and that is both unexpected and serious

UAR_ Unexpected Adverse Reaction An adverse reaction, the nature or severity of which is not consistent with the applicable product information (e.g. Investigator's Brochure (IB) for an unapproved investigational product or Summary of Product Characteristics (SmPC) for an authorised product

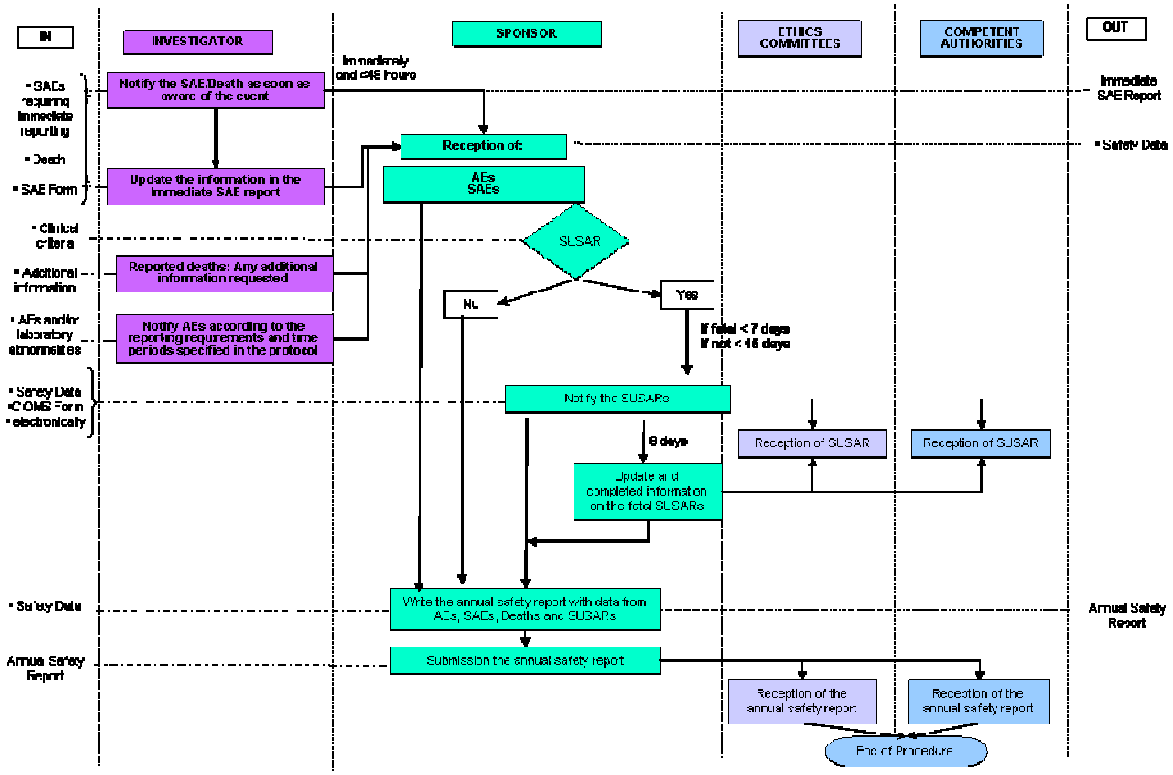
4. RESPONSABILITIES

Common elements	Country specific elements
Investigator: is responsible for collecting and notifying all AE and SAEs according to the protocol requirements to the sponsor. SAEs should be notified immediately. **Sponsor** (or delegated entity or person): is responsible for the continual evaluation of the safety of the IMP , of the notification of data that affects the safety of the participants to the authorities, ethic committees and investigators and of the set-up of rules and written procedures to guaranty the quality of the process (collection of AE, documentation of AE, validation, evaluation, notification, archiving) Must maintain written records of all SAEs. **European correspondent**: - is the contact point and the local support to the sponsor in his/her country - is charge of facilitating the interaction between the sponsor, the investigators, the ethics committee and competent authorities. - Is in charge of ensuring that the process is in place (with the support of its national network and any structure in place) - May be involved in the translation of follow up reports .	

5. DESCRIPTION

5.1. Flow chart

The following flow chart describes a common framework for notifying adverse events, SAEs and SUSARs during a clinical trial on medicinal products.


IN
INVESTIGATOR
SPONSOR
ETHICS COMMITTEES
COMPETENT AUTHORITIES
OUT
Immediately and <48 hours
Notify the SAE/Death as soon as aware of the event
Update the information in the immediate SAE report
Reception of:
AEs
SAEs
SUSAR
No
Yes
If fatal < 7 days
If not < 15 days
Reported deaths: Any additional information requested
Notify AEs according to the reporting requirements and time periods specified in the protocol
Notify the SUSARs
8 days
Reception of SUSAR
Reception of SUSAR
Update and completed information on the fatal SUSARs
Write the annual safety report with data from AEs, SAEs, Deaths and SUSARs
Submission the annual safety report
Reception of the annual safety report
Reception of the annual safety report
End of Procedure
- SAEs requiring immediate reporting
- Death
- SAE Form
- Clinical criteria
- Additional information
- AEs and/or laboratory abnormalities
- Safety Data eCOMS Form electronically
- Safety Data
Annual Safety Report
Immediate SAE Report
- Safety Data
Annual Safety Report

5.2. Reporting from investigator to Sponsor

The investigator should evaluate all individual adverse events with respect to relatedness and expectedness.
He should report all the SAE to the Sponsor immediately, except those defined in the protocol as exempt from expedited reporting.
In addition, the investigator must provide any follow-up information requested.

WHO	WHAT	WHEN	HOW	To WHOM
Investigator' s responsibilities				
INVESTIGATOR .	**SAE**	As soon as aware of the event (and in line with requirements of the protocol)	Fax, phone or mail **SAE Form** (first notification must be followed by detailed report)	Sponsor (and/or any other structure specified in the protocol) Other person or centre as stated in the protocol **In addition in case of death** ➢ Ethics committee Either directly or through the coordinating investigator
INVESTIGATOR	AE	During the trial and according to the protocol requirements	Case Report Form	Sponsor

Country-specific elements:
In Denmark: all expedited reporting in clinical trials with medicinal products is made by the sponsor and exclusively to the competent authority, the Danish Medicines Agency. Adverse events arsing from these trials are only reported to the ethics committee during the annual and end of trial report, by the sponsor or "the person responsible" for the trial. If, however, the adverse events cause the safety of the trial participants to be questioned, the trial to be re-evaluated, or prematurely terminated, then the investigator must report this to the ethics committee immediately.
UK: Written report must be provided in the UK.If the initial immediate report is by phone SAR reports must include a written report. Also where a death has been reported to the ethics committee, any follow-up information requested by the committee must be provided

5.3. Reporting from Sponsor to Competent Authorities

5.3.1. General rules

The sponsor - **(in conjunction with investigator)** - is responsible for the ongoing safety evaluation of the investigational medicinal product.

The sponsor is responsible for the evaluation of expectedness which is based on knowledge of the adverse reaction and any relevant product information and relatedness

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WHO	WHAT	WHEN	HOW	To WHOM
Sponsor' s responsibilities				
Sponsor (and if needed European correspondent with support of their national network)	**SUSARs**	As soon as possible but not later than -7 days for fatal SUSAR (+ 8 days for follow-up) -15 days for other SUSAR	Through Eudravigilance Clinical Trial Module or paper reports (CIOMs forms)	-Eudravigilance -Competent authorities -Investigators -Ethics committees
	Annual safety report	Once a year during the duration of the clinical trial	**Report**	
	Other safety issues	As soon as possible but no later than 15 days		

In Denmark:
The sponsor interacts with competent authorities. In general, the investigator or "the person responsible for the trial" interacts with the ethics committees. However, the sponsor or "the person responsible for the trial" can submit the annual report to the ethics committee.

In Italy, the sponsor interacts with competent authorities and ethics committees, the investigator only with ethics committees in case of fatal adverse events.

Sweden: The Sponsor should report SUSARs electronically to the Swedish MPA via the EudraVigilance database. In parallel a paper report of the event is sent to the EC. Direct communication with the Investigator may be initiated by MPA and/or EC if complementary information is requested. There is normally no interaction between MPA and EC.

5.3.2. SUSARs Reporting

Common element	Country specific elements
The sponsor of a clinical trial (Phase I-IV) with at least one investigator site in the Community must report SUSARs according to the following scenarios: a) SUSARs which occur within the concerned trial are subject to expedited reporting.	UK: As per UK legislation (see SI2004/1031, part 5, regulation 33).
b) SUSARs which occur outside the concerned clinical trial	FINLAND: The National Agency for Medicines need not be notified of adverse reactions occurring in clinical trials not conducted in Finland. Unexpected serious adverse reactions occurring abroad are reported only to the European Medicines Agency DENMARK: SUSARs from other trials should only be reported if they may affect ongoing trials in Denmark. When this occurs, an amendment to the protocol must be submitted.
(1) Where the investigational medicinal product has a marketing authorisation in a Member State, and the sponsor is the marketing authorisation holder, the reporting of SUSARs which occur (i) outside the concerned clinical trial and outside any other clinical trial (including SUSARs arising from any organised data collection system other than interventional clinical trials) should be in accordance with the Regulation (EC) No. 726/2004, Directive 2001/83/EC and (ii) if it occurs in a clinical trial according the 'Detailed guidance on the European database of Suspected Unexpected Serious Adverse Reactions (Eudravigilance – Clinical Trial Module)'.	DENMARK*:* SUSARs from other trials, or from third countries should only be reported if they could affect ongoing trials in Denmark. When this occurs, an amendment to the protocol must be submitted. UK: As per UK legislation (see SI 1994/3144 Article 7, item 1 & 2 and SI 2004 /3224). SUSARs occurring in a clinical trial should be reported in accordance with UK legislation (see SI2004/1031, part 5, regulation 33). EudraVigilance reporting will suffice for informing other Member States however for UK trials the MHRA must be informed according to the instructions on their website (http://wwwmhra.gov.uk/Howweregulate/Medicines/Licensingofmedicines/Clinicaltrials/Safetyreporting-SUSARSandASRs/index.htm
(2) For investigational medicinal products that have a marketing authorisation in a Member State and the sponsor is not the marketing authorisation holder. Where the investigational medicinal product has a marketing authorisation in any Member State, and the sponsor is not the marketing authorisation holder, any SUSARs associated with the investigational medicinal products that occur in another trial conducted by the same sponsor in a third country should be reported.	DENMARK*:* SUSARs from third countries should only be reported if they may affect ongoing trials in Denmark. If this is the case, an amendment to the protocol must be submitted UK: As per UK legislation (SI2004/1031 part 5, 33(5)), a sponsor shall ensure that, in relation to each clinical trial in the United Kingdom for which he is the sponsor, the investigators responsible for the conduct of a trial are informed of any suspected unexpected serious adverse reaction which occurs in relation to an investigational medicinal product used in that trial, whether that reaction occurs during the course of that trial or another trial for

	which the sponsor is responsible. UK legislation does not directly specify expedited reporting requirements for SUSARs occurring in another trial in a third country however as per UK legislation SI2004/1031 Part 4, regulation 28 and subsequently ICH-GCP article 5.1.6.2. "the sponsor should promptly notify all concerned investigators and regulatory authorities of findings that could affect adversely the safety of subjects, impact the conduct …… the trial". The sponsor is also required to include this type of information in the annual safety report (SI2004/1031 part 5, 35(1Aii)).
(3) For investigational medicinal products that do not have a marketing authorisation in any Member State of the Community: Where the investigational medicinal product does not have a marketing authorisation in any Member State of the Community, any SUSARs associated with the investigational medicinal products are subject to expedited reporting, as soon as the sponsor becomes aware of them. This includes: - SUSARs which occur in another trial conducted by the same sponsor either in the European Community or in a third country (i.e. in EEA countries), - or which are identified by spontaneous reports or a publication, - or which are transmitted to the sponsor by another regulatory authority. In case of fatal and life-threatening SUSARs, the competent authority and the Ethics Committee in the concerned Member States should be notified as soon as possible but no later than 7 calendar days after the sponsor has first knowledge of the minimum criteria for expedited reporting. In each case relevant follow-up information should be sought and a report completed as soon as possible. It should be communicated to the competent authority and the Ethics Committee in the concerned Member States within an additional eight calendar days. The non fatal and non life-threatening SUSARs and safety issues must be reported to the competent authority and the Ethics Committee in the concerned Member States as soon as possible but no later than 15 calendar days after the sponsor has first knowledge of the minimum criteria for expedited reporting. Further relevant follow-up information should be given as soon as possible. Save in exceptional circumstances electronic reporting should be the expected method for expedited reporting of SUSARs to the competent authority(ies) and EudraVigilance.	AUSTRIA: The relevant follow-up information after a fatal or life-threatening SUSAR has to be reported within an additional 8 days. The non-life threatening SUSARs have only to be reported to the relevant competent authorities (not to the Ethics committee) no later than 15 calendar days. Once a year the sponsor has to provide a list of all SUSARs to the authorities and the Ethics committee. DENMARK: Immediate reporting of SUSARs to ethic committees is not required. Non-commercial sponsors without access to the EudraVigilance database must report on a CIOMS form. UK: As per UK legislation (see SI 2004/1031, Part 5, Regulation 33(1-8)). GERMANY: Notification of other investigators is not part of the obligations from sponsor to authorities in the strict sense In case of fatal and life-threatening SUSARs, the competent authority, the Ethics Committee (and the investigators involved in the trial) in the concerned Member States should be notified as soon as possible but no later than 7 calendar days after the sponsor has first knowledge of the minimum criteria for expedited reporting. The non fatal and non life-threatening SUSARs and safety issues must be reported to the competent authority, the Ethics Committee (and the investigators involved in the trial) in the concerned Member States as soon as possible but no later than 15 calendar days after the sponsor has first knowledge of the minimum criteria for expedited reporting. IRELAND: In IE competent authority will accept paper reporting if academic sponsor and agreed in advance with them FINLAND: Registration with EMEA's EudraVigilance is mandatory for commercial sponsors. Registered sponsors must submit electronic reports via EudraVigilance. If the sponsor is not registered with EudraVigilance, a report must be made in writing to the National Agency for Medicines. The report may not be submitted by fax or email. It can be made in the form of a free-form letter or with the CIOMS-I form.

	UK: UK legislation specifies expedited reporting requirements for any SUSARs occurring in a trial conducted in the UK but it does not *directly* specify expedited reporting requirements for SUSARs occurring in trials conducted outside the UK, or spontaneous reports such as the examples given. However as per UK legislation see SI2004/1031 Part 4, regulation 28 and subsequently ICH-GCP article 5.1.6.2, the sponsor should promptly notify all concerned investigators and regulatory authorities of findings that could affect adversely the safety of subjects, impact the conduct ..... the trial". In addition, a sponsor shall ensure that, in relation to each clinical trial in the United Kingdom for which he is the sponsor, the investigators responsible for the conduct of a trial are informed of any suspected unexpected serious adverse reaction which occurs in relation to an investigational medicinal product used in that trial, whether that reaction occurs during the course of that trial or another trial for which the sponsor is responsible (SI2004/1031 part 5, 33(5)). Finally as per SI2004/1031 part 5, regulation 34, If a clinical trial is being conducted at a trial site in a third country in addition to sites in the United Kingdom, the sponsor of that trial shall ensure that all SUSARs occuring at that site are entered into the European database established in accordance with Article 11 of the Directive. UK: Use of EudraVigilance website is acceptable for notification of SUSARs to other Member States. For SUSARs to be reported to the UK authority follow instructions on MHRA Website (http://www.mhra.gov.uk/Howweregulate/Medicines/Licensingofmedicines/Clinicaltrials/Safetyreporting-SUSARSandASRs/index.htm). Mandatory electronic reporting to the UK authorities is being phased in for commercial sponsors. Testing must be completed prior to being authorised to submit in this manner.

Common element	Country specific elements
The sponsor is responsible for the prompt notification to all concerned investigator(s), the ethics committee and competent authority of each concerned Member State of findings that could adversely affect the health of participants, impact on the conduct of the trial or alter the competent authority's authorisation to continue the trial. The sponsor is responsible for arranging systems and written standard operating procedures to ensure that the necessary quality standards are observed in every step of the case documentation, data collection, validation, evaluation, archiving and reporting. In accordance with national legislation Member States may provide that the concerned Ethics Committee only receive expedited individual reports of SUSARs that	DENMARK: For clinical trials on medicinal products,it is only necessary to give prompt notification to the competent authority (the Danish Medicines Agency) not to the ethics committee. FRANCE : The Regulations require the sponsor to keep detailed records of all adverse events relating to a clinical trial which investigators in that trial have notified to them, unless they have been documented in the protocol as not required. The sponsor may be required to submit these records to the competent authority (AFSSaPS) on request. GERMANY: Directive 2001/20/EC: In Germany: GCP-Verordnung § 13 [sponsor's responsibilities]

occurred in participants who have been recruited in the concerned trial in that Member State. In this case, it is strongly recommended that: a) all SUSARs from other Member States and, where applicable, from third countries, are periodically reported at least every 6 months as a line listing accompanied by a brief report by the sponsor highlighting the main points of concern. Those periodic reports should only include SUSARs reported within the period covered by the report. A copy of the report should be sent to the concerned competent authority; b) any changes increasing the risk to subjects and any new issues that may affect adversely the safety of the subjects or the conduct of the trial should also be provided as soon as possible, but no later than fifteen days.	In Germany: • Expedited individual SUSAR reporting comprises all cases which occur within all CTs world-wide with the same IMP. • Additional periodic line-listings are not required ITALY: Legislative Decree 211/03 SPAIN: Each Ethic Committee only receive expedited individual reports of SUSAR that occurred in participants who have been recruited in the concerned centre participating in the trial in Spain. UK: In the UK, the sponsor is ultimately responsible for interacting with competent authorities however this interaction may be delegated e.g. to the Chief Investigator, provided this is in writing. The Chief Investigator is responsible for submitting the application for ethics committee approval (see SI 2004 / 1031, regulation 14). As per UK legislation see SI2004/1031 Part 4, regulation 28 and ICH-GCP article 5.1.6.2. As per UK legislation see SI2004/1031, Schedule 1, Part 2, regulation 13. The UK clinical trials regulations only specify expedited reporting requirements for individual reports of SUSARs that occur in subjects recruited in the concerned trial in the UK (see SI2004/1031 Part 5, regulation 33) however as per UK legislation (SI2004/1031 Part 4, regulation 28 and ICH-GCP article 5.1.6.2) the sponsor is required to promptly notify investigators and regulatory authorities of any findings that may affect safety. UK Ethics Committees require 6-monthly safety reports on the safety of subjects in all clinical trials of the investigational medicinal product (IMP) for which the sponsor is responsible worldwide, with a global line listing of SUSARs occurring in these trials in the reporting period however these are only necessary where the sponsor is a commercial sponsor and is conducting the trial or other trials of the IMP outside the UK. Non-commercial sponsors, and commercial sponsors conducting trials in the UK only, will not need to submit any 6-monthly reports, but are still required to submit annual safety reports both to the main REC and the MHRA. (see (http://www.nres.npsa.nhs.uk/applicants/after-ethical-review/safetyreports/safety-reports-for-ctimps/))

5.3.3. Assessment of Adverse Events in Blinded Trials

Common elements	Country specific elements
For blinded trials involving a placebo and an active drug, seriousness, causality and expectedness should be evaluated as though the participant was on active drug. As a general rule treatment codes should be broken by the sponsor before reporting a SUSAR to CA and EC. Only those events occurring among participants on the active drug (or in the case of placebo excipient) should be considered to be SUSARs requiring reporting to the regulatory authority and ethics committee (in the case of placebo excipient the reporting is recommended). For blinded trials involving two active drugs, the evaluation is more complex. However, the person responsible for the evaluation for causality and expectedness might be able to state that if the participant were on drug A the event would be causal and/or unexpected, but if on drug B it would be expected. If the event were unexpected for either of the active drugs, the case should be unblinded by the individual charged with unblinding, who would then classify the event accordingly. The investigators will be informed about all potential SUSAR cases (verum and placebo). Thus they will be blind regarding the treatment arms of their participants.	.

5.3.4. Annual safety report, other events

Common elements	Country specific elements
In addition to the expedited reporting, sponsors shall submit, once a year throughout the clinical trial or on request a safety report to the competent authority and the Ethics Committee of the concerned Member States, taking into account all new available safety information received during the reporting period. The aim of the annual safety report is to describe concisely all new safety information relevant for one or several clinical trial(s) and to assess the safety conditions of participants included in the concerned trial(s). The annual safety report should be the same for the competent authorities concerned and the Ethics Committee concerned.	DENMARK*:* The sponsor or "the person responsible for the trial" makes the annual reports to the ethics committees, the sponsor reports to the competent authority, the Danish Medicines Agency. The competent authorities require reporting of SARs and the ethics want SAEs. However, in practice the same report is accepted. The annual report should be delivered one year after the first approval, whether from the CA or EC. UK: As per the UK legislation (see SI 2004/1031, Part 5, Regulation 35). Sponsors may adopt their own format both for expedited reports and periodic safety reports however both Ethics committeess and competent authoriy in the UK advise provision of the information set out in the European Commission guidance '(ENTR/CT3v2 A standard covering form must accompany all reports sent to the Ethics Committee (http://www.nres.npsa.nhs.uk/applicants/after-ethical-review/safetyreports/safety-reports-for-ctimps/) In addition, the MHRA has specific requirements with regard to the format of any submissions it receives see: http://www.mhra.gov.uk/Howweregulate/Medicines/Licensingofmedicines/Clinicaltrials/MakingclinicaltrialsubmissionstotheMHRA/index.htm.
The annual safety report of a clinical trial should have three parts: Part 1: Analysis of the participants' safety in the concerned clinical trial. Part 2: A line listing of all suspected serious adverse reactions (including all SUSARs) that occurred in the concerned trial, including also serious adverse reactions from third countries. Part 3: An aggregate summary tabulation of suspected serious adverse reactions that occurred in the concerned trial. Other safety issues also qualify for expedited reporting where they might materially alter the current benefit-risk assessment of an investigational medicinal product or that would be sufficient to consider changes in the investigational medicinal products administration or in the overall conduct of the trial, for instance: a) an increase in the rate of occurrence or a qualitative change of an expected serious adverse reaction, which is judged to be clinically important, b) post-study SUSARs that occur after the participant has completed a clinical trial and are reported by the investigator to the sponsor, c) new events related to the conduct of the trial or the	. DENMARK**:** the annual safety report to the ethics committee should also list SAEs. SUSARs from other trials, or from third countries should only be reported if they could affect ongoing trials in Denmark. When this occurs, an amendment to the protocol must also be submitted FINLAND: NAM requires a signed analysis of the participant's safety in the trial (=Part 1) every year from the local person in charge of the research ("Tutkimuksesta vastaava henkilö"). FRANCE: The report should include a summary of any published literature relevant to the safety of participants in the trial, or aggregated reports of any other relevant unpublished data known to the sponsor. It may also usefully include a summary of any concerns or recommendations from the DMC on safety of participants in the trial. The reporting time frame for annual reports starts from the date of the first authorisation of the clinical

development of the investigational medicinal products and likely to affect the safety of theparticipants, such as: - a serious adverse event which could be associated with the trial procedures and which could modify the conduct of the trial, - a significant hazard to the participant population such as lack of efficacy of an investigational medicinal products used for the treatment of a life-threatening disease, - a major safety finding from a newly completed animal study (such as carcinogenicity) - any anticipated end or temporally halt of a trial for safety reasons and conducted with the same investigational medicinal products in another country by the same sponsor, d) recommendations of the Data Monitoring Committee, if any, where relevant for the safety of the participants.	trial (CTA) by a competent authority in any member state (or from the first authorisation of the trial in a European Economic Area (EEA) state). The anniversary of this date is designated as the cut-off date for data to be included in the annual report. The report should be submitted within 60 days of this cut-off date. In the case of short-term trials (less than 6 months), the Safety Report may be submitted within 90 days of the end of the trial together with the notification of the end of the trial

6. REFERENCES

ECRIN references	Country Specific references
International Conference on Harmonisation -ICH E6 Good Clinical Practices (1996)	Denmark: http://www.dkma.dk/1024/visUKLSArtikel.asp?artikelID=6758 http://www.dkma.dk/1024/visUKLSArtikel.asp?artikelID=6181
EU directive 2001/20/EC	
Detailed guidance on the collection, verification and presentation of adverse reaction reports arising from clinical trials on medicinal products for human use (April 2006)	

7. REFERENCED GUIDE /SOP

- ECRIN EC-SOP ØØ2 "Interaction with Ethics Committees before the conduct of a multinational clinical trial on medicinal products"
- ECRIN EC-SOP ØØ 3 "Interaction with Ethics Committees during the conduct of a multinational clinical trial on medicinal products"
- ECRIN EC-SOP ØØ 4 "Interaction with Ethics Committees after the conduct of a multinational clinical trial on medicinal products
- ECRIN CA-SOP ØØ 1 "Interaction with competent authorities before the conduct of a multinational clinical trial on medicinal products"
- ECRIN CA-SOP ØØ 2 "Interaction with competent authorities during the conduct of a multinational clinical trial on medicinal products"
- ECRIN CA-SOP ØØ 3 "Interaction with competent authorities after the conduct of a multinational clinical trial on medicinal products"

8. APPENDICES

Not applicable