

SAE Reporting

Pan European Clinical Trials under current EU regulations

London, 24 Jan 2008

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Aims of SAE reporting system

Assuring the patients' safety

1. Timely overview within the trial: SAE including fatal cases
2. Early detection of serious unexpected adverse reactions
 - Contribution of the trial to overall pharmacovigilance and drug safety by SUSAR reporting

Overview

1. What is an SAE, SAR, SUSAR?
2. Investigators: what to report, how to report and when?
3. Safety Desk: What does the Safety Desk do with SAE reports?

What is an SAE, SAR, SUSAR?

Definitions

1. Adverse event (AE)
2. Adverse reaction (AR)
3. Serious adverse event/reaction (SAE / SAR)
4. Unexpected adverse reaction
5. Suspected unexpected serious adverse reaction (SUSAR)



- Defined in: Directive 2001/20/EC, Detailed Guidance ENTR/CT 3, ICH-E2A

What is an SAE, SAR, SUSAR?

1. Adverse event (AE)

- Any untoward medical occurrence in a patient or clinical trial subject administered a medicinal product and which does not necessarily have a causal relationship with this treatment

What is an SAE, SAR, SUSAR?

2. Adverse reaction (AR)

- All untoward and unintended responses to an investigational medicinal product related to any dose administered
- Judged by either the reporting investigator or the sponsor as having a reasonable causal relationship to a medicinal product → *worst case*
- Reasonable causal relationship: to convey in general that there is evidence or argument to suggest a causal relationship



What is an SAE, SAR, SUSAR?

Adverse reaction, Investigator's judgement

Is SAE related to EURAMOS trial medication?

Is SAE related to EURAMOS trial medication?

Definitely

Probably

Possibly

Unlikely

Unrelated

Yes

No

Reasonable causal relationship

What is an SAE, SAR, SUSAR?

3. Serious adverse event/reaction (SAE/SAR)

- Any untoward medical occurrence or effect that at any dose
 - Results in death
 - Is life-threatening
 - Requires hospitalisation or prolongation of existing inpatients' hospitalisation
 - Results in persistent or significant disability or incapacity
 - Is a congenital anomaly or birth defect



What is an SAE, SAR, SUSAR?

Also serious:

- Important adverse events/reactions
- that are not immediately life-threatening or do not result in death or hospitalisation
- but may jeopardise the subject or may require intervention to prevent one of the other outcomes listed
- According to investigator's medical judgement
 - E.g. treatment in an emergency room or at home for allergic bronchospasm
 - E.g. convulsions that do not result in hospitalisation



What is an SAE, SAR, SUSAR?

Difference between serious and severe!

- Serious: based on patient / event outcome or action criteria
 - Severe: describes intensity (severity)
 - Mild / moderate / severe
 - CTC / CTCAE
-
- Examples: severe headache / mild heart attack
 - CTCAE grades < 4 may also be serious

What is an SAE, SAR, SUSAR?

4. Unexpected adverse reaction

- Nature or seriousness or severity or outcome ... is not consistent with the applicable product information
 - Investigator's brochure or summary of product characteristics (SmPC)
- Not on the basis of what might be anticipated from the pharmacological properties!
 - ICH-E2A

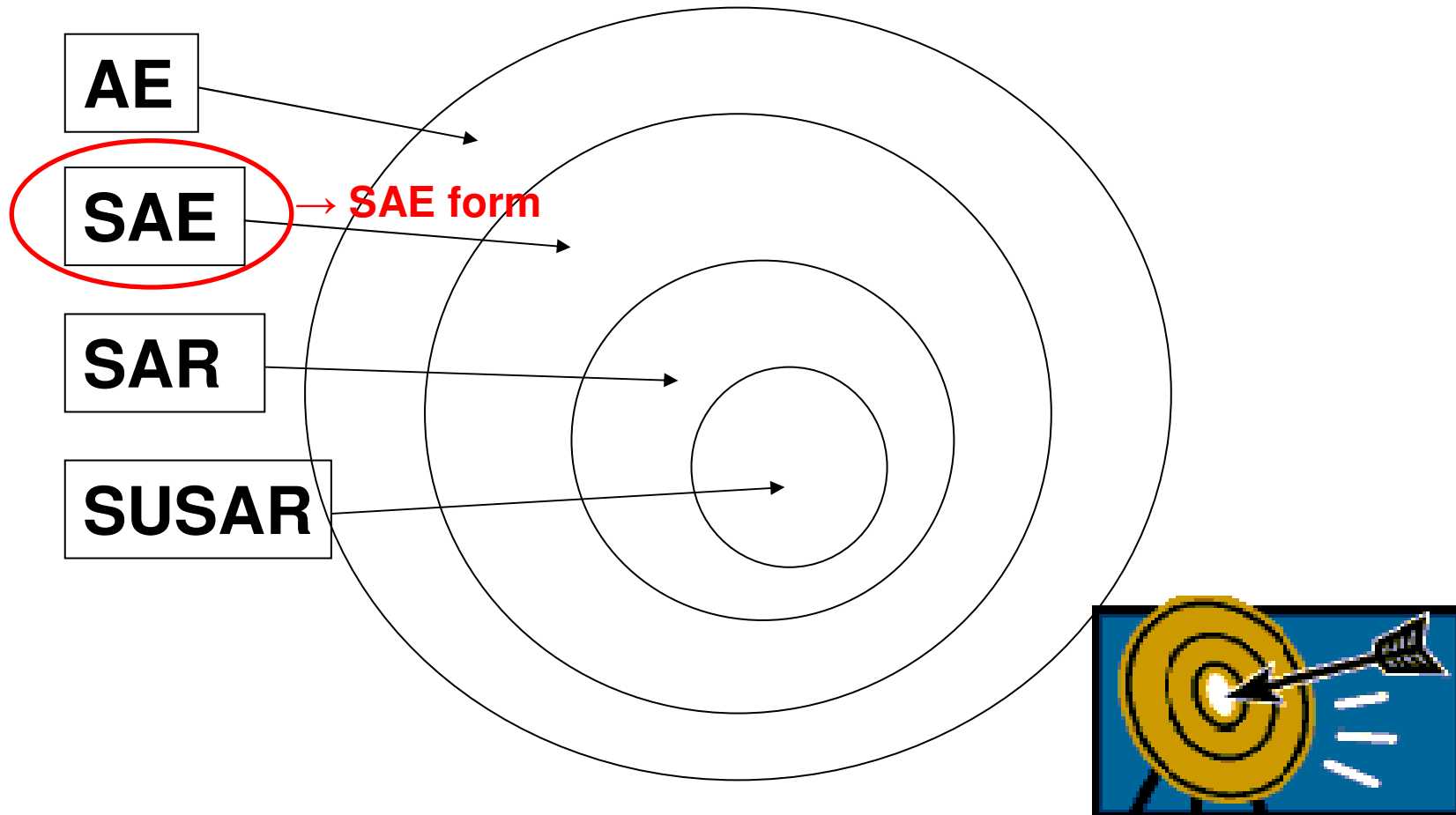
What is an SAE, SAR, SUSAR?

5. Suspected unexpected serious adverse reaction (SUSAR)

- “Triple-yes”
 - Serious
 - Related to investigational medicinal product
 - Unexpected

Suspicion is enough!

What is an SAE, SAR, SUSAR?



Investigators: what, how, and when to report?

Article 16

Notification of adverse events

1. The investigator shall report all serious adverse events immediately to the sponsor except for those that the protocol or investigator's brochure identifies as not requiring immediate reporting. The immediate report shall be followed by detailed, written reports. The immediate and follow-up reports shall identify subjects by unique code numbers assigned to the latter.

Directive 2001/20/EC

Investigators: what, how, and when to report?

DEFINITIONS and EXCEPTIONS for EURAMOS:

- **All deaths** including death due to disease progression during protocol treatment and for 30 days after the last protocol treatment, including treatment with pegylated interferon α -2b, will be reported as an SAE.
- Death due to progression of disease will not constitute a SAE if it occurs at least 30 days after the last protocol treatment.

Investigators: what, how, and when to report?

- **Hospitalization ...**

- a) Hospitalization for chemotherapy is not reported as an SAE. In addition expected side effects of chemotherapy, which are listed in the product information, will not be reported on an SAE form for the purposes of this clinical trial unless in the opinion of the investigator they unexpectedly prolonged the hospitalization or required intensive care therapy.
- b) Hospitalization for procedures required by the protocol e.g. biopsy or surgery are not considered serious adverse events until one of the above criteria are met.

Investigators: what, how, and when to report?

- **Hospitalization...**

- c) Hospitalization due to signs and symptoms associated with disease progression are not considered an SAE unless outcome leads to DEATH during protocol treatment and for 30 days after the last protocol treatment, including treatment with pegylated interferon α -2b.
- d) Elective hospitalization for a pre-existing condition that has not worsened does not constitute a SAE.

Investigators: what, how, and when to report?

- **Disability** is defined as a substantial disruption in a person's ability to conduct normal life functions (e.g. blindness, deafness). Disability resulting from tumor surgery does not constitute an SAE.

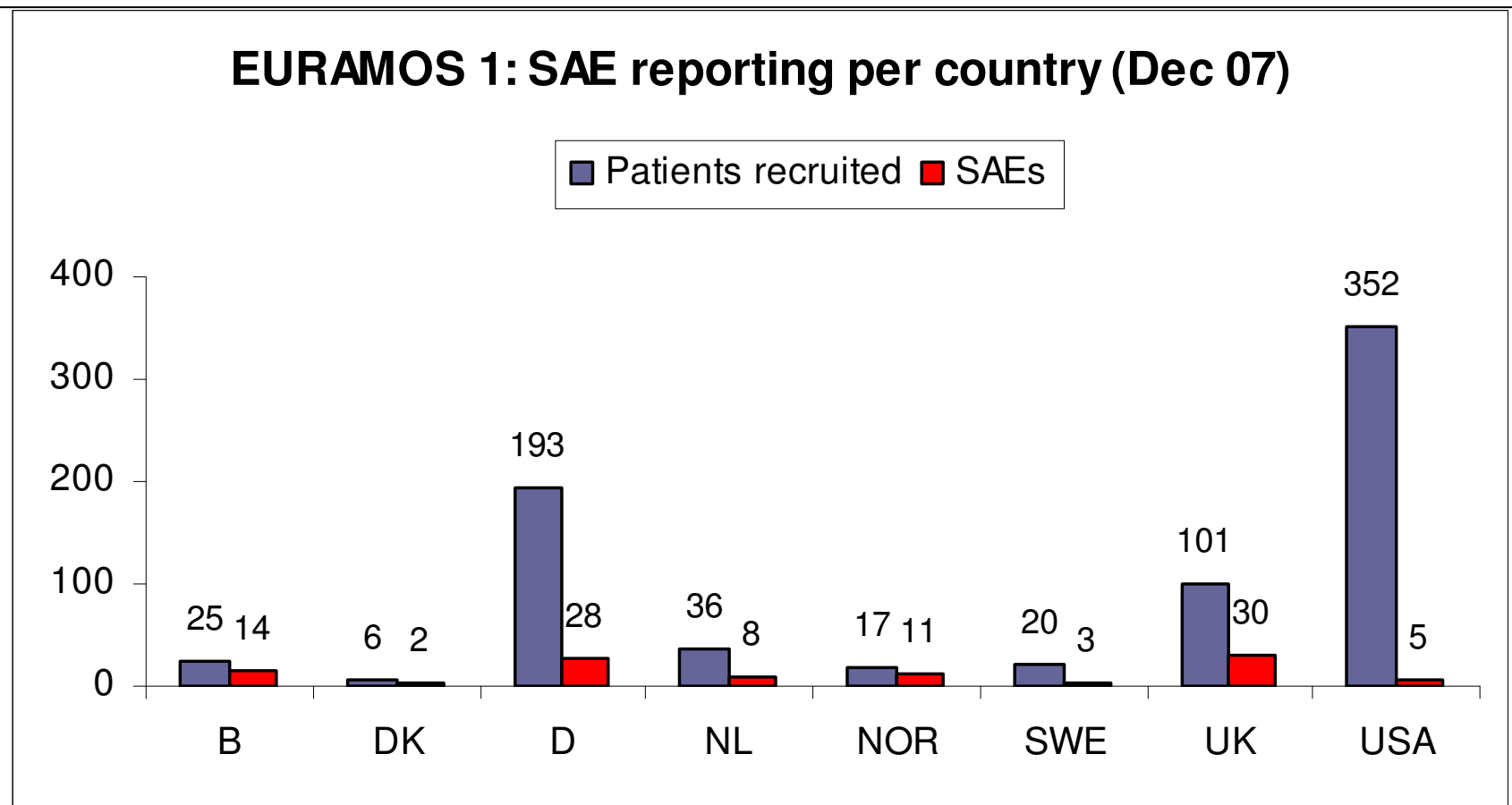
Investigators: what, how, and when to report?

- **Other medically important conditions** are
- Secondary malignancies are also considered to be medically important e.g. skin cancers, myelodysplastic syndrome (MDS) and are reportable on an SAE form during protocol treatment and for 30 days after the last protocol treatment, including treatment with pegylated interferon α -2b.

Investigators: what, how, and when to report?

- **Other medically important conditions**
- Abnormal biological or vital signs commonly occur under chemotherapy and will only be reported as serious when considered **CLINICALLY RELEVANT BY THE INVESTIGATOR** (unexpected) e.g. severe nephrotoxicity (CTCAE Grade 4) or severe cardiac toxicity (CTCAE Grade 4). Expected serious adverse reactions (SAR) such as hematological toxicity or increase in liver enzymes under methotrexate which resolve are examples of SARs which are not considered reportable on an SAE Form by the investigator.

Investigators: what, how, and when to report?



No SAEs received from:

AUS (7 patients recruited), CAN (32), FIN (1), H (11), NZ (6), CH (17)

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Investigators: what, how, and when to report?

- The highest reporting rates (2004 total population) can be found in Sweden, Ireland, Norway, Denmark, the UK, France, and the Netherlands.
 - Assessment of the European Community System of Pharmacovigilance, Fraunhofer ISI, Final Report Nov. 2005
- Same experience in the EURAMOS 1 trial
- May reporting rates be harmonized by applying to the reporting rules in the protocol?

Investigators: what, how, and when to report?

How to report an SAE:

1. Become aware of adverse event
2. Assess as serious
3. Assess as reportable according to protocol
4. Complete SAE-form with as much information as possible (preferably in English)
5. Identify patient by patient ID no., never by name (on attached documents as well!)
6. Sign and date by investigator



Investigators: what, how, and when to report?

How to report an SAE:

7. Fax to Safety Desk immediately
(within 1 working day of knowledge)
8. Await confirmation of receipt / query
(within 1 more working day)
9. Answer query soon
(otherwise: trial site will be suspended 21 d after query!)
10. Further follow-up information may be faxed at any time, sometimes more queries may come
(eg outcome, or questions from Schering Plough)

Investigators: what, how, and when to report?

SAE form Version 2.0

Please use new version

- Otherwise: query for details of medication

Electronically fillable form available

- May prevent query due to readability reasons

➤ Form to be found on www.euramos.org


SAE form, Version 2.0, 20.06.06, electronically fillable PDF version

The European and American Osteosarcoma Study Group (EURAMOS) - Microsoft Internet Explorer

Datei Bearbeiten Ansicht Favoriten Extras ?







Zurück Suchen Favoriten Wechseln zu Links


Adresse http://www.ctu.mrc.ac.uk/euramos/


Monday, 14 January 2008

The European and American Osteosarcoma Study Group

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| <ul style="list-style-type: none"> Home News About EURAMOS About Osteosarcoma <li style="background-color: #f4a460;">EURAMOS I Trial Art Project Clinical Trials Information Our Collaborators FAQs Contacts Useful Links Site Map | <h3>About EURAMOS</h3> <p>EURAMOS is the European and American Osteosarcoma Study Group. The study was founded in 2001.</p> <p>This website contains information about Osteosarcoma and the current EURAMOS I Trial.</p> <p>Trial Design click here.</p> <p>Objectives</p> <p>General Information regarding the EURAMOS 1 trial or any other trial please contact euramos1@ctu.ac.uk</p> <p>Participating Institutions (members)</p> <p>Trial Management Group (members) under current EU regulations: managers, study nurses and junior clinical investigators.</p> <p>24-25 January 2008, the Selsdon Park Hotel, South Croydon, London.</p> <p>Click here to view the course programme.</p> <p>The closing date for registrations is Monday 14 December 2007. If you would like to register for the course please contact Sue Harrison at H2 Events by phone: 0161 477 9877 or email: sueharrison@h2-events.co.uk</p> <p>Bringing Medicine to Life: Images from the Art Project are on permanent display at the Wellcome Trust 'Medicine Now' Gallery, located on the first floor of Wellcome Collection Conference Centre, 183 Euston Road, London</p> <p>Click here to read more about the Art Project.</p>  | <h3>Our Collaborators</h3> <div style="border: 1px solid #ccc; padding: 5px; margin-bottom: 10px;">  </div> <div style="border: 1px solid #ccc; padding: 5px; margin-bottom: 10px;">  </div> <div style="border: 1px solid #ccc; padding: 5px; margin-bottom: 10px;">  </div> <div style="border: 1px solid #ccc; padding: 5px; margin-bottom: 10px;">  </div> <div style="border: 1px solid #ccc; padding: 5px;">  </div> |
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Chugai Pharma UK are happy to support this Website with an unrestricted educational grant.

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Investigators: what, how, and when to report?

http://www.ctu.mrc.ac.uk/euramos/secure/Participating_Institutions_Docs/Safety_Reporting/SAE_form_v2_electr_fillable.pdf

EURAMOS 1
EudraCT No. 2004-000242-20

Part 1 of 2

SERIOUS ADVERSE EVENT FORM

PLEASE TYPE OR PRINT LEGIBLY USING BLACK BALL-POINT PEN AND COMPLETE ALL INFORMATION

| PATIENT INFORMATION | | | | | |
|---|---|--------------------|---|------------------------------|---------------------------------------|
| EURAMOS Patient ID no. 12345 | Sex <input type="checkbox"/> M <input checked="" type="checkbox"/> F | Weight 0 5 0 kg | Body surface area 1 . <input type="checkbox"/> <input type="checkbox"/> m ² | Birth date (DAY/MON/YEAR) | For Safety Desk use only Event no. |
| REPORT INFORMATION | | | | | |
| <input type="checkbox"/> Initial report <input type="checkbox"/> Follow-up report | Source of report: <input type="checkbox"/> COSS <input type="checkbox"/> EOIMRC <input type="checkbox"/> SSG <input type="checkbox"/> COG | | | | |
| | Name of investigator: | | | | |
| | Institution: | | | Telephone: | |
| | E-mail: | | | Fax: | |
| TRIAL INFORMATION | | | | | |
| Preoperative chemotherapy <input type="checkbox"/> MAP | Primary site of disease | | | | |
| Randomized? <input type="checkbox"/> No <input type="checkbox"/> Yes | Sites of metastases | | | | |
| Good response patient <input type="checkbox"/> MAP Poor response patient <input type="checkbox"/> MAP <input type="checkbox"/> MAP Ifn <input type="checkbox"/> MAPIE | Start date of first cycle (DAY/MON/YEAR) | | | | |
| Chemotherapy given as in protocol | Day 1 of last chemotherapy cycle prior to SAE | | | | |

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Investigators: what, how, and when to report?

When to report?

- Immediately: 24 h/1 business day after knowledge
- Early report more important than complete report



EURAMOS 1:

All SAEs and SARs, regardless of causal relationship, must be reported to the EURAMOS Intergroup Safety Desk (EISD), Münster, Germany within 1 business day directly by fax +49 (0) 251 83 57112 on the SAE Form. SAEs and SARs will be reported following the first dose of chemotherapy throughout the clinical trial and for 30 days after the last protocol treatment, including treatment with pegylated interferon α -2b.

Safety Desk: What do we do with SAE reports?

1. First Inhouse review → Registration: SAE no.
2. If PegIntron given: Fax to Schering Plough
3. Data entry, coding (MedDRA, ATC)
4. Complete Inhouse review
5. Fax to investigator: Confirm. of receipt / Query

All this to be completed within 1 business day

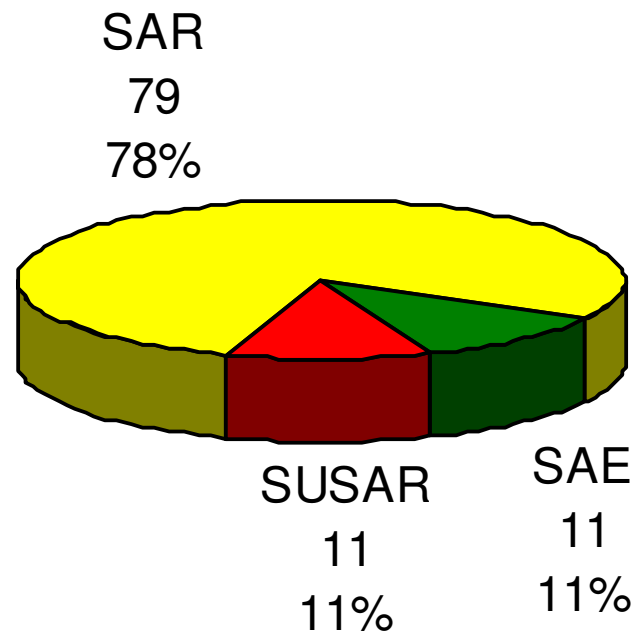


Safety Desk: What do we do with SAE reports?

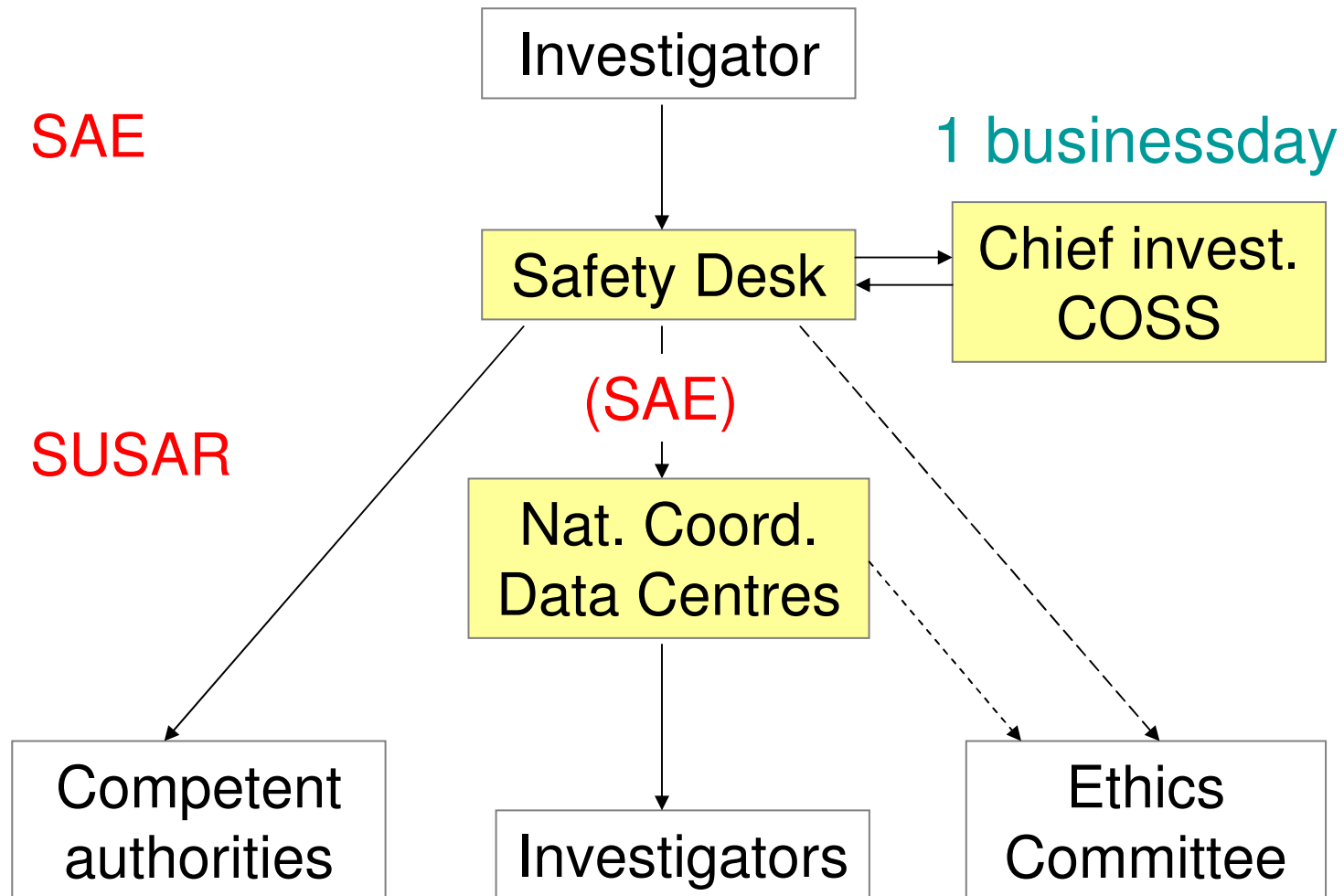
6. Fax to Chief Investigator (Assessment until d 3)
7. Reporting form incl. narrative
8. Fax to National Coordinators/Data Centers (d3)
9. If SUSAR: Fax also to all Competent Authorities and to Ethics Committee of country where SAE occurred
(No more SUSAR reports from other trial received)
10. For follow-up information: repeat previous steps, as applicable

Safety Desk: What do we do with SAE reports?

EURAMOS 1: Assessment of SAEs (n=101, Dec 07)



Safety Desk: What do we do with SAE reports?



Safety Desk: What do we do with SAE reports?

Annual Safety Report

- All SAR (including SUSARs) will be summarized in the Annual Safety Report

➤ 3rd EURAMOS 1 ASR submitted in October 2007

Thank you!

Aims of SAE reporting system

- Early detection of unknown reactions
- Timely overview of patients' safety in the trial
- Ensuring the safe use of medicines



... can be archived