EUROPEAN CLINICAL RESEARCH INFRASTRUCTURES NETWORK - TRANSNATIONAL WORKING GROUPS

ECRIN-TWG

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Deliverable 25 and 26
Material for European and national educational programs

Final Version

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Work Package 8: **Transnational Working Group on Education**

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1. Abbreviations

AT	Austria
CH	Switzerland
CRC	Clinical Research Centre
CTU	Clinical Trial Unit
CTA	Clinical Trial Authorisation
DE	Germany
DK	Denmark
ES	Spain
FI	Finland
FR	France
GCP	Good Clinical Practice
HU	Hungary
IMP	Investigational Medicinal Product
IR	Ireland
IT	Italy
NHS	National Health System
PI	Principal Investigator
QA	Quality Assurance
QM	Quality Management
REC	Research Ethics committee
SOP	Standard Operating Procedure
SUSAR	Suspected Unexpected Serious Adverse Reaction
SE	Sweden
UK	United Kingdom

2. Definitions

CA: Competent authority
Bodies having the power to regulate. In the ICH GCP guideline the expression Regulatory Authorities includes the authorities that review submitted clinical data and those that conduct inspections. These bodies are sometimes referred to as competent authorities*. (ICH Harmonised Tripartite Guideline: Guideline For Good Clinical Practice E6).*

ECRIN: European Clinical Research Infrastructures Network
Based on the interconnection of national networks of academic clinical research infrastructures, the European Clinical Research Infrastructures Network (ECRIN) is designed to bridge the fragmented organisation of European clinical research and to develop an integrated EU-wide clinical research infrastructure.

Ethics Committees
An independent body in a Member State, consisting of healthcare professionals and non-medical members, whose responsibility it is to protect the rights, safety and wellbeing of human subjects involved in a trial and to provide public assurance of that protection, by, among other things, expressing an opinion on the trial protocol, the suitability of the investigators and the adequacy of facilities, and on the methods and documents to be used to inform trial subjects and obtain their informed consent. *(Directive 2001/20/EC)*

European Correspondent
Is the local support to the sponsor in his/her country and is responsible for the interaction with insurance company and sponsor. He/she is the contact point for the sponsor and is responsible for securing the insurance process based on the information provided by the sponsor.

IMP: Investigational medicinal product
A pharmaceutical form of an active substance or placebo being tested or used as a reference in a clinical trial, including products already with a marketing authorisation but used or assembled (formulated or packaged) in a way different from the authorised form, or when used for an unauthorised indication, or when used to gain further information about the authorised form. *(Directive 2001/20/EC)*

Informed Consent Form
Decision, which must be written, dated and signed, to take part in a clinical trial, taken freely after being duly informed of its nature, significance, implications and risks and appropriately documented, by any person capable of giving consent or, where the person is not capable of giving consent, by his or her legal representative; if the person concerned is unable to write, oral consent in the presence of at least one witness may be given in exceptional cases, as provided for in national legislation. *(Directive 2001/20/EC)*

Multicentre CT: Multicenter Clinical trial
A clinical trial conducted according to a single protocol but at more than one site, and therefore by more than one investigator, in which the trial sites may be located in a single Member State, in a number of Member States and/or in Member States and third countries. *(Directive 2001/20/EC)*

Risk assessment tool:
Risk-assessment tool will be used to adapt monitoring intensity, but should be strongly related to primary risks. Therefore, validity of the risk-assessment tool should be assessed relatively to primary risks, not to monitoring intensity.
A good risk-assessment tool must respect the usual qualities of any good outcome: relevance, validity, and reliability.

SOP Standard Operating Procedure
Detailed, written instructions to achieve uniformity of the performance of a specific function. *(ICH Harmonised Tripartite Guideline: Guideline For Good Clinical Practice E6).*

Sponsor
An individual, company, institution, or organisation, which takes responsibility for the initiation, management, and/or financing of a clinical trial (*Directive 2001/20/EC*).

Vulnerable Population
The definition of vulnerable populations is a matter for national legislation in each member state. Within ECRIN framework, the term vulnerable populations refer to: minors, pregnant/lactating women and incapacitated adults.

3. Background

European Clinical Research Infrastructures Network (ECRIN) is designed to bridge the clinical research in Europe through the interconnection of national networks of clinical research centres (CRC) and clinical trial units (CTU) and to develop services to provide support for multicentre clinical studies in Europe.

Personnel working with clinical trials have different backgrounds and there are special requirements on skills and experience, according to ICH-GCP, for certain professions, and other requirements for others.

At hospitals and in phase-1 units usually physicians and nurses are responsible for direct actions. By regulations, the investigator must be a physician with experience from previous clinical trials and specialist in the area of concern. The other personnel in the clinical trial team should be skilled and works on delegation from the investigator. Other people involved in clinical trials (project managers, data managers, statisticians and others) must perform their work according to the standards given by the ICH-GCP, although their qualifications are not formally expressed in the ICH-GCP.

In the first ECRIN FP6-funded project (ECRIN-RKP, 2004-2005) a survey was made within the ECRIN member states, to perform a comparative analysis of clinical research education and training.

The comparative analysis presented in the ECRIN-RKP project showed a major diversity in national education programmes for investigators, study nurses and all the personnel involved in clinical research. The definition of clinical research professions and related tasks also differed from one country to another. There was a major diversity between the reporting countries in length of the courses, the topics, the target groups and the course providers.

The education and training of clinical trial personnel is a prerequisite for conducting clinical research according to national and international regulations. The task of European Clinical Research Infrastructures Network (ECRIN) Working Party 8 is to suggest training activities and courses to provide within ECRIN and in the different ECRIN member states.

Based on the outcome of the ECRIN-RKP project, the work of the working party 8 in the second programme (ECRIN-TWG, 2006-2008), is designed to analyse and suggest education and training activities where the outcome of the other working parties (WP1 to WP6) will be implemented as teaching material. In addition, a suggestion on the training of European Correspondents and the coordinating team should be presented.

4. Objective

Clinical research is the basis of a well functioning, evidence-based health care system. In 2004, the European Directive 2001/20/EC aimed to promote harmonisation within European clinical research.

The comparative analysis on clinical research education presented in the ECRIN-RKP project showed a major diversity in national education programmes for investigators, study nurses and all the staff involved in clinical research. The definition of clinical research jobs and related tasks differed from one country to another.

The task of European Clinical Research Infrastructures Network (ECRIN) Working Party 8 is to suggest training activities and courses to provide within ECRIN and in the different ECRIN member states. The European Correspondents of each ECRIN-Country should be possible to fulfil this role. Therefore a Summer School is planned where the European Correspondents will be trained in general as well as specific topics.

The training content consists of theoretical parts about SOP's, Ethical review, Competent Authorities, Adverse event reporting and monitoring. Additionally, the European Correspondents get taught in ECRIN specific content like regulatory frameworks, ECRIN management, Quality Assurance system and the management of multiclinical trials. Another important point is to clarify the role of the European Correspondent. In order to fulfil this role the European Correspondent needs to be able to apply several learning methods and tools. An external speaker will provide this knowledge.

Many lectures will be hold by European Correspondents involved in the development of the respective SOPs. External speakers will complete the global knowledge of the European Correspondents.

The dissemination of knowledge will be carried out in each ECRIN member state by the European Correspondent. The exact procedure for this will be discussed and decided during the summer school in November 2008.

5. Methodology

Material from all the other ECRIN working parties (Working Party 1 to Working Party 6) was collected in form of SOPs. The material was then used to construct topics for educational content. A draft version of the educational content for the planned European Correspondent Summer School in 2008 was presented and discussed during the ECRIN meeting in Brussels on the 19th of May.

Speakers were selected in view of their involvement when preparing the different SOPs. In order to complement the educational content with global knowledge, not included in the SOPs, some external speakers were also selected for different topics.

The final version of the summer school agenda was approved on the Network Committee teleconference on the 17th of July. In order to provide a general overview of the educational program provided by Working Party 8, a list of all SOPs as well as the agenda for the Summer School, which refers to the knowledge of those SOPs, is mentioned in this joint document containing Deliverable 25 and Deliverable 26.

6. Educational purpose of the Summer School

The Summer School of ECRIN is a meeting for all European Correspondents. The aim is to prepare them for their tasks in their national network, in multinational clinical trials and in ECRIN itself.

The training content consists of theoretical parts about Standard Operating Procedures, Ethical review, Competent Authorities, Adverse event reporting and monitoring. Additionally, the European Correspondents get taught in ECRIN specific content like regulatory frameworks, ECRIN management, Quality Assurance system and the management of multiclinical trials. Another important point is to clarify the role of the European Correspondent. In order to fulfill this role the European Correspondent needs to be able to apply several learning methods and tools. The dissemination of knowledge will be carried out in each ECRIN member state by the European Correspondent.

Therefore, there are three directions of content in order to develop the nature of a European Correspondent.

6.1 Content

1. The definition of the European Correspondent. Via discussions and reflections the European Correspondents should determine their own role. The question to be answered: *What is a European Correspondent?*
2. The technical knowledge of the European Correspondent. Via lectures about Standard Operating Procedures the European Correspondent gains the knowledge necessary to teach people involved in multinational clinical trials and knows the conduction of a multinational clinical trial. The question to be answered: *What does a European Correspondent know technically?*
3. The methodic knowledge of a European Correspondent. Via lectures and training sessions the European Correspondents learn how to train people involved a multinational clinical trial. The question to be answered: *What does a European Correspondent know methodically?*

These three steps serve as the basis for the future work of the European Correspondent. This future work, i.e. the dissemination of the knowledge in each national network, will be developed in the last phase of the Summer School. The question to be answered: *How to disseminate this knowledge?*

6.2 Prerequisites

In order to work efficiently within the Summer School the European Correspondents are supposed to bring some basic knowledge:

1. Know the GCP-principles.
2. Know some SOPs
3. Think about the definition of a European Correspondent, country specific elements concerning the conduction of clinical trials

4. Inform about possibilities where and when to spread knowledge and where to apply the knowledge which will be gained during the Summer School

6.3 Goals of the Summer School

1. Documentation about the role of the European Correspondent
2. The European Correspondent can deal with the Content Management System of ECRIN webpage
3. The European Correspondent has an overview over SOPs and their content
4. The European Correspondent is able to train people involved in multinational clinical trials
5. The European Correspondent has a draft version of a national dissemination plan (documentation)

7. Proposed educational content of Summer School

7.1 Speakers

Xavier CARNE (Spain)
Margaret COONEY (Ireland)
Jacques DEMOTES (France)
Nicola FABRIS (Italy)
Gerd FELDER (Germany)
Christian GLUUD (Denmark)
Raquel HERNANDEZ (Spain)
Jean-Marc HUSSON (France)
Valérie JOURNOT (France)
Jean Pierre KRAEHENBUHL (Switzerland)
Christine KUBIAK (France)
Wolfgang KUCHINKE (Germany)
Christian LIBERSA (France)
Ann Marinus (Belgium)
Christian OHMANN (Germany)
Nuria SANZ (Spain)
Matt SYDES (United Kingdom)
Kate WHITFIELD (Denmark)
Michael WOLZT (Austria)
Kurt ZATLOUKAL (Austria)

Facilitators:
Christa JANKO (Austria)
Johannes PLEINER (Austria)
Vienna School of Clinical Research

7.2 Agenda

DAY 1 – Tuesday, 11 November 2008

WELCOME AND INTRODUCTION (09:00 – 09:30)

Jacques DEMOTES /
Michael WOLZT /
Christa JANKO /
Johannes PLEINER

REGULATORY FRAMEWORKS (9:30-10:30)

Jacques DEMOTES/
Christine KUBIAK

Coffee Break (10:30 – 10:45)

QA System and ECRIN management (10:45-11:30)

Jacques DEMOTES

STANDARD OPERATING PROCEDURES (11:30 – 12:00)

- Development, review, approval and management of SOPs

Christine KUBIAK

Lunch Break (12:00 – 13:00)

What do you need to consider before you draft an ECRIN protocol synopsis for a clinical trial on an intervention? (13:00-14:00)

Christian GLUUD

Coffee Break (14:00 – 14:15)

MANAGEMENT OF MULTINATIONAL CLINICAL TRIALS (issues and solutions/sharing experience) (14:15-15:45)

- Euramos Experience

Matt SYDES

- EORTC Experience

Ann MARINUS

Coffee Break (15:45 – 16:00)

ROLE OF THE EUROPEAN COORESPONDENT (16:00-17:30)

Task delegation

LESSONS LEARNED (17:30- 17:45)

- ***Discussion for European Correspondents***

DAY 2 – Wednesday, 12 November 2008

ETHICAL REVIEW (09:00 – 10:30)

- General introduction on Ethics
  Xavier CARNE
  (preliminary speaker)

- SOP Interaction with Ethics Committees before/during/after the conduct of a multi-national clinical trial on medicinal products
  Nuria SANZ/
  Raquel HERNANDEZ
- SOP How to prepare an Information and Informed Consent form for a multi-national clinical trial on medicinal products
  Nuria SANZ
- SOP Vulnerable populations in multinational clinical trials
  Margaret COONEY
- SOP Personal data protection
  Nuria SANZ/
  Raquel HERNANDEZ

Coffee Break (10:30 – 10:45)

COMPETENT AUTHORITIES (10:45 – 12:15)

- SOP Interaction with competent authorities before/during/after the conduct
  of a multi-national clinical trial on medicinal products
  Kate WHITFIELD/
  Christine KUBIAK
- SOP How to archive documents from all types of multinational clinical trials
  Wolfgang KUCHINKE/
  Kate WHITFIELD
- SOP How to manage human biological samples of multinational clinical trials
  Christian LIBERSA
- SOP Management of IMP in multinational clinical trials
  Christine KUBIAK

Lunch Break (12:15 – 13:15)

ADVERSE EVENT REPORTING (13:15-14:15)

- Regulatory requirements for Vigilance systems in ECRIN countries
  Nicola FABRIS
- Reporting of adverse events (SUSARS) in multinational clinical trials
  Nicola FABRIS

Coffee Break (14:15 – 14:30)

DATA MANAGEMENT & MONITORING (14:30 – 16:45 incl. at least 1 break)

- Data Management
  Christian OHMANN
- Risk assessment tool
  Valérie JOURNOT
- SOP Monitoring ECRIN studies
  Margaret COONEY

ECRIN WEBPAGE: CONTENT MANAGEMENT SYSTEM (16:45 – 17:15)

- Training Session
  Gerd FELDER

LESSONS LEARNED (17:15 – 17:30)

- **Discussion for European Correspondents**

DAY 3 – Thursday, 13 November 2008

LEARN TO TRAIN (9:00-12:00 incl. 2 breaks)

- How to train (techniques, e-tools, practical exercises, discussion)
  Jean Pierre KRAEHENBUHL
  HSET foundation
- Training of study personnel in ECRIN studies
  Sherry ARMSTRONG-WILKINSON
  (preliminary speaker)

BIOBANKING (12:15-13:15)

Kurt ZATLOUKAL

Lunch Break (13:15 – 14:15)

COMPETENT AUTHORITIES (14:15-14:45)

- Insurance in multinational trials
  Adrian COLLOVRAY
  (preliminary speaker)
- SOP Insurance in multinational trials
  Christine KUBIAK

PRESENTATION OF NATIONAL DISSEMINATION PLANS (14:45 – 16:45)

- **Improvement of web-survey**
- **Presentation**
- **Discussion**

WRAP-UP (16:45 – 17:45)

- **Wrap-up**
- **Feedback on what each European Correspondent learned and how he/she will go on in his/her country**

8 List of SOPs

SOP Reference	SOP Title	WP
ECRIN-GE-SOPØØ 1	Development, Review, Approval and Management of Standard Operating Procedures	WP6
ECRIN-CA-SOPØØ1	Interaction with competent authorities before the conduct of a multinational clinical trial on medicinal products	WP2
ECRIN-CA SOPØØ2	Submission of amendments to competent authorities during the conduct of a multinational clinical trial on medicinal products	WP2
ECRIN-CA-SOPØØ3	Interaction with competent authorities after the conduct of a multinational clinical trial on medicinal products	WP2
ECRIN-CA SOPØØ4	Archiving in ECRIN studies	WP2
ECRIN-EC-SOPØØ1	How to prepare an Information and Informed Consent form for a multinational trial on medicinal products	WP1
ECRIN-EC-SOPØØ2	Interaction with ethics committees before the conduct of a multinational clinical trial on medicinal products	WP1
ECRIN-EC QCDØØ 1	EudraCT: obtention of a trial number and management of the authorisation request form	WP1/WP2
ECRIN-EC-QCDØØ2 AT/ DK/FI FR/DE HU/IT/IE/ES/SE/GB	Practical aspects of interacting with authorities (ethics committees and competent authorities) throughout the conduct of a multinational clinical trial on medicinal products	WP1/WP2
ECRIN-EC-SOPØØ3	Submission of amendments to ethics committees during the conduct of a multinational clinical trial on medicinal products	WP1
ECRIN-EC-SOPØØ4	Interaction with ethics committees after the conduct of a multinational clinical trial on medicinal products	WP1
ECRIN-EC-SOPØØ5	Informed consent in vulnerable populations and incapacitated patients	WP1

ECRIN-CA-SOP ØØ4	Insurance in multinational clinical trials on medicinal products	WP2
ECRIN-GE-SOP ØØ2	Personal data protection	WP1/WP2
Guidance document	Logistics of the Investigational Medicinal Products within ECRIN multinational clinical trials	WP2
Guidance document	Blood and tissue samples: collection, circulation, storage	WP2
ECRIN-AE-SOPØØ1	How to support adverse events reporting in multinational clinical trials on medicinal products	WP3
ECRIN-MO-SOP ØØ1	Monitoring ECRIN studies	WP5

9 Discussion

The Deliverables 25 and 26 present the educational content for European and national educational programs developed from the SOPs within the ECRIN working parties and additional content relevant for the dissemination of knowledge within the national networks.

The dissemination to the different national networks will be carried out by the European Correspondents. This procedure will be presented and discussed during the summer school. It is important to harmonize the dissemination in all the ECRIN member states.