Handout

Workshop 3 – Experiences with national differences in information package constitution

Guideline for good clinical practice – E 6 (R1)" (ICH-GCP), section 4.8.10:

Explanations should be given for the following points:

- that the trial involves research (element a)
- the purpose of the trial (element b)
- the trial treatment(s) and the probability of random assignment to each treatment (element c)
- the trial procedures to be followed, including all invasive procedures (element d)
- the subject´s responsibilities" (element e)
- those aspects of the trial that are experimental (element f)
- the reasonably foreseeable risks or inconveniences to the subject and, when applicable, to an embryo, fetus, or nursing infant (element g)
- the reasonably expected benefits. When there is no intended clinical benefit to the subject, the subject should be made aware of this (element h)
- the alternative procedure(s) or course(s) of treatment that may be available to the subject, and their important potential benefits and risks (element i)
- the compensation and/or treatment available to the subject in the event of trial-related injury (element j)
- the anticipated prorated payment, if any, to the subject for participating in the trial (element k)
- the anticipated expenses, if any, to the subject for participating in the trial (element l)
- that the subject´s participation in the trial is voluntary and that the subject may refuse to participate or withdraw from the trial, at any time, without penalty or loss of benefits to which the subject is otherwise entitled (element m)
- that the monitor(s), the auditor(s), the IRB/IEC, and the regulatory authority(ies) will be granted direct access to the subject´s original medical records for verification of clinical trial procedures and/or data, without violating the confidentiality of the subject, to the extent permitted by the applicable laws and regulations and that, by signing a written informed consent form, the subject or the subject´s legally acceptable representative is authorizing such access (element n)
- that records identifying the subject will be kept confidential and, to the extent permitted by the applicable laws and/or regulations, will not be made publicly available. If the results of the trial are published, the subject´s identity will remain confidential (element o)
- that the subject or the subject´s legally acceptable representative will be informed in a timely manner if information becomes available that may be relevant to the subject´s willingness to continue participation in the trial (element p)
- the person(s) to contact for further information regarding the trial and the rights of trial subjects, and whom to contact in the event of trial-related injury (element q)
- the foreseeable circumstances and/or reasons under which the subject´s participation in the trial may be terminated (element r)
- the expected duration of the subject´s participation in the trial (element s)
- the approximate number of subjects involved in the trial (element t)

Other considerations:

- subject or the subject´s representative receives a copy of the written information
- written documentation does not contain any language by which the participant of a trial waives any legal rights or by which the investigator, the investigator´s institution or the sponsor or sponsor´s representatives are released from liability for negligence
- document should be written in laymen language
- subject and investigator should sign the written information in handwriting

Directive 2001/20/EC of 04 April 2001, Article 3

2. A clinical trial may be undertaken only if, in particular:

(…)

(b) the trial subject or, when the person is not able to give informed consent, his legal representative has had the opportunity, in a prior interview with the investigator or a member of the investigating team, to understand the objectives, risks and inconveniences of the trial, and the conditions under which it is to be conducted and has also been informed of his right to withdraw from the trial at any time;

(c) the rights of the subject to physical and mental integrity, to privacy and to the protection of the data concerning him in accordance with Directive 95/46/EC are safeguarded;

(d) the trial subject or, when the person is not able to give informed consent, his legal representative has given his written consent after being informed of the nature, significance, implications and risks of the clinical trial; if the individual 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;

(e) the subject may without any resulting detriment withdraw from the clinical trial at any time by revoking his informed consent;

(f) provision has been made for insurance or indemnity to cover the liability of the investigator and sponsor.

(…)

4. The subject shall be provided with a contact point where he may obtain further information.

Detailed guidance on the application format and documentation to be submitted in an application for an Ethics Committee opinion on the clinical trial on medicinal products for human use
ENTR/CT 2, Rev 1, February 2006

4. 6. Subject information and the informed consent procedure

(…)

The information should be based on the elements set out in the Community guideline CPMP/ICH/135/95. There should also be a description of the arrangements for taking care of the subjects after their participation in the trial has ended, where there is additional care necessary because of the subjects' participation in the trial and where it differs from that normally expected according to the medical condition.

The information sheets given to the subject and/or the parent(s)/legal representative should be kept short, clear, relevant, and understandable to a lay person. They should be in a language the subject knows.

The measures taken to safeguard the subject's privacy and the protection of personal data should be described as is required according to Directive 95/46/EC10. There should be information on how the identity of the subject, biological material obtained from the subject, and any recorded data will be coded, stored and protected. Information should be given about the person(s) who will have access to the code list, where the list will be kept and for how long, and who will be responsible for keeping it. The information should address the right of the subject to ask for updated information on what data are recorded, to require corrections of errors, and to know who will be responsible for keeping the data and who will have access to them in keeping with Directive 95/46/EC.

The subject should be informed of the possibility to withdraw consent without giving any reason and to require that all previously retained identifiable samples will be destroyed to prevent future analyses, according to national provisions. The information should include a statement that the consequence of the subject's withdrawal of consent will be that no new information will be collected from the subject and added to existing data or a database.

Information should be provided on a contact point where additional information can be obtained about the trial and the right of the trial subjects and whom to contact in the event of trial related injury, according to the system in the Member State.

(…)

The form to be used to verify that information has been given and that the trial subject has consented (the informed consent form) should contain at least three elements:

- consent to participate in the trial;
- consent to make confidential personal information available (direct access) for quality control and quality assurance by relevant personnel from the sponsor, a nominated research organisation on behalf of the sponsor, and inspection by the competent authorities/institutions assigned this task in the Member State or, if applicable, the Ethics Committee;
- consent to archive coded information, and for its transmission outside the Community if applicable.

(…)

Attachment 6

Subject information
This appendix is intended to provide further guidance on items that might be of relevance for the subject information leaflet. It is not intended to provide a complete list of items which should be included, but to give some examples of items that might have to be considered if relevant to the particular trial.

1. Subject information, general aspects.
The information sheet should state clearly the justification for the trial, its relevance and objective and should contain at least all the items listed in the relevant section of the Community guideline on Good Clinical Practice (CPMP/ICH/135/95).

In addition, written information should be provided on:

1. The contact point from which further information may be obtained relating to the trial and in case of injury, according to national requirements.
2. The names and addresses of the investigator, study nurse etc who are responsible for taking care of the included subjects.
3. Any planned procedures for follow up after the end of the trial (for example for trials involving gene transfer medicinal products) and/or plans for additional care that might be needed due to findings during follow up.
4. Any financial or other ties to the sponsor as well as institutional affiliations of the investigator as well as the name and address of sponsor /sources of funding.
5. The Ethics Committee positive opinion.
6. The subject's rights to privacy and the means taken to ensure protection of personal data. This might include information on:
    - procedures for coding
    - the arrangement with code-keys: the name of the person responsible for keeping the key and who will have access
    - in the case of retention of subject samples and information:
        - to whom the data and samples are accessible
        - the location and duration of retention
        - name of the person who will be responsible for keeping the samples and the results
        - procedure for handling any retained identifiable samples
        - plans to anonymise or destroy samples after analysis
7. The subject's right to obtain updated information about what data is recorded as well as the right to require corrections of errors
8. The right of the subject (or parent or legal representative) to withdraw consent to participate in the trial.
9. The fact that in the event of the withdrawal of consent to participate in the trial, no new data will be added to the database and that, according to national provisions, the subject (or parent, guardian or legal representative) may require all previously retained identifiable samples to be destroyed to prevent further analysis.
10. The right of the subject (parent or legal representative) to be informed of any plans for new analyses on retained identifiable material that were not foreseen when the subject consented to participate in the study. The investigator might have to ask for new consent and the subject has the right to refuse further analyses, according to national rules.

(…)

3. Trial specific and general explanatory information to subjects.
It might sometimes be useful to divide the information to be provided in two parts. One part should contain the information necessary for the subject to decide whether or not to participate in the planned trial. It could focus on the information specific for the planned trial and only contain information related to general issues and systems such as protection of privacy, insurance etc. as is relevant to the trial in question.
The second part should contain general information common to trials in the Member State. It might address and explain in more detail the national systems for the protection of the rights, welfare and safety of the subjects. The reasons for quality control and quality assurance and the need for Source Data Verification (SDV) as well as measures to protect the confidentiality of personal information, systems for labelling, analysing and publishing data and availability of insurance/indemnity systems could be explained. This general second part, once approved by the Ethics Committee, could be used where appropriate in similar trials in that Member State.