
**The Belgian EC's project of a
Template for Patient Information
Leaflet and Consent Form:
Why, When & How ?**

Preceding...

- Next to the ethics principles such as the Declaration of Helsinki and Good Clinical Practice, various Belgian laws focus on the obligation of an **informed consent** and the **level of information** to provide to the person that will accept
 - to participate in a clinical research study,
 - processing of his/her personal data and/or samples of human body material (HBM) for research purposes.

Why - 1

- Excessive increase of the number of pages in the ICD's, provided by the industry.
- Different « templates » between companies & « headquarters » inflexible for local adaptations
- Lack of structure ... clear guidelines for the participant
- Repetitions, irrelevant information
- Copy/paste syndrome
- Etc...

- It is hard to imagine that ICD's are reviewed in its entirety by a member of the study staff and the patient!
- Non ethical 😞

Why - 2

It is often a very complicated document
that even the well schooled have trouble
deciphering unassisted

Informed Consent : The consumer's guide to the risks & benefits
of volunteering for clinical trials
By Kenneth Getz & Deborah Borfitz
Editor: Sara Gambrill
THOMSON - Centerwatch- 2002

Why - 3

- Advantages of a common ICD-template for all commercial/academic sponsors = known guiding points:
 - simplification of editorial work 😊
 - simplification of evaluation work by the Ethics Committee 😊
 - simplification of PI's approach in the process of informing the patient 😊
 - **better information to the patient 😊**

Key words

- The ICD (PIL + ICF) **must**
 - Be as short as possible
 - ... and maximum 15 pages long 😊 😞
 - Be understandable for the majority of participants
 - Be structured ... have a logical guiding principle
- **Common ICD template** for all clinical studies

Recommendation - 1

- 1) Make it clear that the purpose of the PIL is to inform (and not to indemnify).
 - The starting point for a PIL **must not be that** the investigator / sponsor seeks legal indemnity but that the PIL **provides** the study subject with the **information he/she needs** to take a **well-considered decision** about **participation** in the study.

Recommendation - 2

- 2) Guidelines for writing the ICD
 - PIL length: maximum **5 pages A4** (\pm 2500 words).
This is excluding the **informed consent form, additional information** about the organization of the study & any flow charts that might be included, about risks, about rights and protection of the participant.
 - Structure: **layered ICD**.
Dividing the ICD into **principal information** (the five sheets of A4) / **Informed consent form** / **complementary information** (annexes) means that individuals are better served in their differing information requirements.

Recommendation - 3

- Tone of voice : Language level: EU language level 3 (**basic secondary education**).
At this language level the writer will reach about ninety percent of the adult population.
- Contents: does the content of the PIL match that of the protocol?

What do we propose – 1 ?

- Modèle DIC pour étude clinique interventionnelle s'adressant aux adultes
 - Introduction spécifique quand le 1er lecteur du DIC sera le représentant légal
 - Introduction spécifique quand la situation d'urgence est approuvée
- Modèle DIC pour étude clinique observationnelle /non interventionnelle s'adressant aux adultes
- Model ICD voor klinische interventionele studie bij volwassenen
 - toelichting ICD voor wettelijke vertegenwoordiger
 - Toelichting ICD bij deelname in een noodsituatie
- Model ICD voor klinische niet-interventionele / observationele studie bij volwassenen

What do we propose – 2 ?

- Package of writing resources
 - **Exemplary texts**, style guide, checklist and general leaflet
- Issuing points for this information
 - Websites of ethics committees
 - Website of pharma.be
 - Website of FAGG/AFMPS

Practical aspects

ICD – draw-up 1

- Formulated in a way it can be read and understood by persons that are **not health care workers**, that **have not been verbally informed** and in a way that a potential participant may want to read it.
- Definitions of advices for structure and language.

ICD – draw-up 2

- Structured information, clear guiding principle
- Correct sentence structure (focus on literal translation problems from English to French/Dutch, selection of inappropriate terms etc...)
- **Short** sentences, [EU language level 3 - basic secondary education]
- Absence of technical (professional) language
- In the same concept, use of the identical terminology throughout the entire document (example: do not mention study, subsequently research and clinical study)
- Avoid use of too much abbreviations
- Free of **spelling errors**
- **Sufficient font size policy** (Reference: Arial 10) especially if the reader of the ICD is likely susceptible of having vision troubles
- Sufficient **interspace** throughout text

Conventions

- In the template, the text in
 - Red font refers to instructions, draws attention on alternatives or proposes a comment to the document editor.
 - Black font proposes wording we would prefer to see in the final ICD.
 - Blue font indicating what should be added mentioned.
- Certain wording should be adapted
 - In function of the context: phase I study in healthy subjects, cell therapy study, etc.
- In the model, footnotes
 - In red font will be removed in the final ICD (= instructions / reminder)
 - In black font should be kept.

ICD – format - 1

- **3 parts**
 - **Essential information for understanding of the research project and for taking the decision to participate or not**
 - **The consent**
 - **Complementary information or annexes** collecting all information which **is not immediately part of the decision process, can be read later ...even not being read**

ICD – format - 2

- Point of view of legal experts?
 - OK thus far if:
 - Sequence is announced as of page 1
 - Reference to complementary information or annexes in the consent
 - Page numbering for all 3 parts
- EC's reserved?

ICD – format - 3

- **Site specific adaptation** = sequence
 - Essential Information – Consent – Complementary information
 - or**
 - Essential Information - Complementary information – Consent
- Whatever the sequence is chosen by the EC,
 - The content of the 3 sections remains identical,
 - Only the page numbering is changing.

ICD – format - 4

- Administrative requirement
 - Each **section** of the document should:
 - Have in the header of the document, the complete title of the research project;
 - Be separated from the preceding section by a page break;
 - Have the same version number and version date (footer)
 - **Page numbering** of the entire document (information – consent – annexes) of type "page 1/15" (footer!)

ICD - Content -1

- The edited model is intended for any interventional clinical trial
 - Drug study
 - Medical device study
 - Other
- To be clear : template option = « drug clinical **study** »
 - Adults
 - Legal representative of a minor

ICD - Content - 1a

- **Essential Information for the understanding of the research project and for the decision to participate** or not
 - Optional front page (**page 0**, not counted for 😊)
 - Introduction defining the **concept** of « RESEARCH – CLINICAL STUDY » and **listing** the right of the participant: **1 page**
 - Study objectives, short methodology, benefits and essential risks ... and the obligations for the participant : **4 pages**
- **! Information in 5 pages maximum !**

ICD - Content - 1b

- Optional front page (page 0, not counted for 😊)
 - Study title – sponsor identification, Belgian or European representative of sponsor – local investigators – local contacts – table of contents

- Introduction defining the concept of « RESEARCH – CLINICAL STUDY » and listing the right of the participant: 1 page
 - Specific introduction for studies in which the first reader will likely be the legal representative
 - Specific introduction for studies in which emergency situation is applicable

- The proposed wording for this 1st page is common for all clinical studies.
The EC's and pharma.be would like this wording be respected.

ICD - Content - 1c

- **Study objectives, short methodology, benefits and essential risks ... and the obligations for the participant: 4 pages**
 - Objectives and study protocol description
 - Study course
 - Risks and disadvantages
 - Drug Interactions or others
 - Side effects of study drug
 - Pregnancy
 - Risks related to study related evaluation procedures
 - Notification of new information
 - Benefits
 - Alternative treatment

 - Study discontinuation
 - Treatment after the closure of the study
 - Biological samples collected during the course of the study Echantillons de matériel biologique collecté au cours de l'étude

 - Responsibilities of the participant
 - Contacts

ICD - Content – 1d

- Objectives and study protocol description

- Name and way of action of drug treatments
- Total number of patients / in Belgium needs to be included
- Main inclusion/exclusion criteria

What is my current situation?

Give the disease prognosis for the phase considered in the clinical trial.
Define if in this stage the treatment set-up is curative or palliative.

Mention that the statistical hypotheses, part of the rationale of this clinical trial can be explained in clear wording to the patient by the study doctor, at any request of the patient.

- Study design

Study (randomised/blind/open/crossover, comparing the study drug with " golden standard " / with a placebo)

Descriptive in accessible wording for the participant

Add a glossary peculiar to all studies (suggestion partner pharma.be)

ICD - Content – 1e

- Study roll-out

- Duration of participation

- Study roll-out

- Screening phase , number and rythm of visits after inclusion, early study termination or termination according to plan, follow-up phase.

- Details of the different visits are provided in annex.

- A clear table is often more understandable than long explanations.**

- Procedures or examinations (details in annex)

- **Identify visits & examinations related to standard care/ study procedures**

ICD - Content – 1f

- Risks and disadvantages
 - **Drug interactions** or others
 - **Side effects** of the study drug
 - Likely effects
 - Uncommon (rare) effects, must be identified by the participant in a rapid manner: Allergy
 - Details in **annex**
 - **Pregnancy**
 - Responsibility** female participant & male participant
 - Distinction between** precautionary principle / precautionary measures justified by suspicion / knowledge of any toxic effect
 - Risks of study assessments/procedures in annex

ICD - Content – 1g

- Notification of new information
 - Addendum in ICD
 - New ICD

ICD - Content – 1h

- Benefits

- **Direct** benefits

- no guarantee

- best follow-up ... message « **dangerous** », would mean that the investigator does not ALWAYS considers the best care of patients: **to be avoided**

- care « free of charge » ... message « **commercial** » assumes an encouraging character: **to be avoided**

- Benefits for the **community**

ICD - Content – 1i

- Alternative treatment
 - Indication of existing alternative treatment that could be considered by the patient instead of participation in the study.
 - In the situation where standard treatment options, aimed to improve survival, are exhausted, inform that **palliative care** without any additional disease-specific treatment is a therapeutic option

ICD - Content – 1j

- Study withdrawal
 - By the participant
 - Free, without justification
 - Attention : study withdrawal ><consent withdrawal
 - by the PI
 - Health / lack of compliance
 - By a regulatory authority / EC
 - By the sponsor
 - Recommendation DSMB
 - Termination R&D

ICD - Content – 1k

- Treatment after end of study
 - What is foreseen to offer to the participants **an access to interventions that are identified as beneficial** in view of the study? (see points 14 and 33 in the declaration of Helsinki) **or JUSTIFY that the study drug will not be made available** due to the existence of treatment alternatives with comparable efficacy.

Proposal / return to best available treatment by PI

Roll-out of an extension study

Compassionate use / MNP

ICD - Content – 1I

- Collected biological samples
 - For the study objectives
 - For additional research

- What happens?
 - Destroyed after validation of the analyses/biobank
 - Limited use
 - outlined frame-work: disease and its treatment
 - other: approval EC required
 - Duration of storage

- Participants right to ask for destruction of their samples

ICD - Content – 1m

- Obligations / Advices to participants
 - Collaborate & communicate
 - Not to participate in another research study
 - Patient ID-card / emergency card
 - General practitioner
 - autonomy / security
 - respect for **specific preference of site**

ICD - Content – 1n

- Contacts
 - Questions related to the study
 - PI and study staff
 - Emergency
 - Patient ID card/emergency card
 - Medical file (section clinical research)
 - Questions related to the participants rights
 - Ombudsman
 - Ethics Committee

ICD - Content – 2a

- Informed consent Form
 - Consent form of participant
 - Wording of the role of the legal representative
 - Wording of the role of the witness / the translator
 - ID, date & signatures
 - Wording of the ethics commitment of the PI and his/her staff
 - ID, date and signature – clinical research assistant
 - ID, date and signature of investigator

The consent form is a **contract**
between the participant & the investigator

ICD - Content – 2b

- **Particular case**
 - Studies in minors: Must both parents sign??
 - Divergent points of view
 - Imperative
 - Not necessary
 - Recommendations :
 - **Choice left to site**
 - Take into account familial situation
 - If the signature of a single parent is accepted, please foresee a wording of commitment of the signing parent:
 - I the undersigned, mother/father of my child, confirm to act taking into account the presumed will of the other parent of my child that I represent.*
 - I shall inform him/her as soon as possible.*

ICD - Content - 3

- **Complementary information** ... which is not immediately part of the decision process but contains:
 - Useful information on the roll-out of the study such as the number, rhythm and content of each foreseen consultation
 - Complementary information related to risks
 - Risks related to different molecules
 - Risks related to evaluation procedures, essential for the research
 - Detailed information on the patient rights that are briefly mentioned in part 1

ICD - Content – 3a

- **Annex 1** : additional information about the organisation of the study
 - Detailed planning of the different procedures the patient has to undergo according to foreseen visits/summarising table of flowchart type
 - Make a correct distinction between
 - Routine** visits / consultations and procedures (SC for standard of care) of which the results are possibly used in the study,
 - Visits and procedures **related to the study** (RS).
 - To avoid**: **dispute** participant / PI & participant / invoice department

ICD - Content – 3b

- **Annex 2** : Complementary information about the risks related

- to the experimental treatment

- Research on animals

- Use in humans

- Side effects classified by system and frequency of occurrence and by severity.

- Pregnancy and spermdonation

- Female participant & male participant

- Distinguish precautionary principle / suspicion / knowledge of potential toxic effects on the progression of pregnancy, fetus

- To the standard treatment (add on therapy)

- To the study procedures

ICD - Content – 3b

FDA guidelines say that study volunteers should understand the risks they are taking, but they don't require a drug's complete track record be shared

ICD - Content – 3c

- **Annex 3** : Supplemental information on the rights and protection of the participant
 - Ethics Committee
 - Voluntary Participation
 - Costs related to your participation
 - Guarantee of confidentiality
 - What about your sample(s)
 - Insurance
 - Contact
- The rights of the participant being identical for all studies, the EC's recommend that the proposed wording in the model is included as such,
 - Alternative wording possible for adaptation to phase I studies, to Cell therapy studies.