Collecting and sharing Patients data

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Mandatory informed patients consents

A) Privacy consent

Consent of processing personal data >>>> condition of lawfulness of the medical treatment/trial/study

B) Informed consent

Form of authorization for health treatment/trial/study after receiving medical information >>>> basis of the lawfulness of the medical treatment/ trial/study, its absence constitutes a crime!

B) INFORMED CONSENT

Evaluation of the patient's capacity

2 main problems:

1) When the individual is deemed competent, the requirement is that he or she expresses a valid consent to participate

2) Informed consent in incapacitated subjects

1) INFORMED CONSENT – COMPETENT Subjects-

Provide a valid consent to participate in the study.

To give valid consent the potential participant should understand and retain relevant information, weigh the information, decide and communicate the decision.

In the context of clinical trials, the information should include:

- the purpose of the trial
- the trial procedures
- the risks and benefits of participation.

Potential participants should understand the concept of “Balance & Imbalance” – of “equipoise” which provides the ethical basis for the conduction of a clinical trial, placebo (if used), and randomization.

Contents and characteristics of the consent form (artt.13 & 14 GDPR)

CONTENTS

- contact details of the Controller and of Data Protection Officer

- finality

- legal basis

- recipients

- possible transfer to third countries

- rights of the interested parties

- storage period

- other…

FEATURES

- concise

- transparent

- intelligible

- easily accessible

- clear and simple language

2) INFORMED CONSENT- Incapacitated subjects

Medical evaluation of the patient's mental capacity
(medical certificate –e.g. neurologist- illustrating clinical reasons why the person may present limitations of the decisional capacity, which may render necessary the appointment of a legal proxy).

INFORMED Consent – Incapacitated Subjects

The 2008 version of the Declaration of Helsinki states that potential research subjects who are incompetent "must not be included in a research study that has no likelihood of benefit for them, unless it is intended to promote the health of the population represented by the potential subject, the research cannot instead be performed with competent persons, and the research entails only minimal risk and minimal burden" (point 27).

"When a potential research subject who is deemed incompetent is able to give assent to decisions about participation in research, the physician must seek that assent in addition to the consent of the legally authorized representative. The potential subject's dissent should be respected" (point 28).

These principles have been adopted by all national legislation in western countries.

As indicated by the Declaration of Helsinki, one possible way to meet the ethical requirements of informed consent in incapacitated subjects is to safeguard the potential participants interests using a **proxy consent** in the recruitment process.

The **practice of obtaining surrogate consent** however can vary according to differences in national legislation.

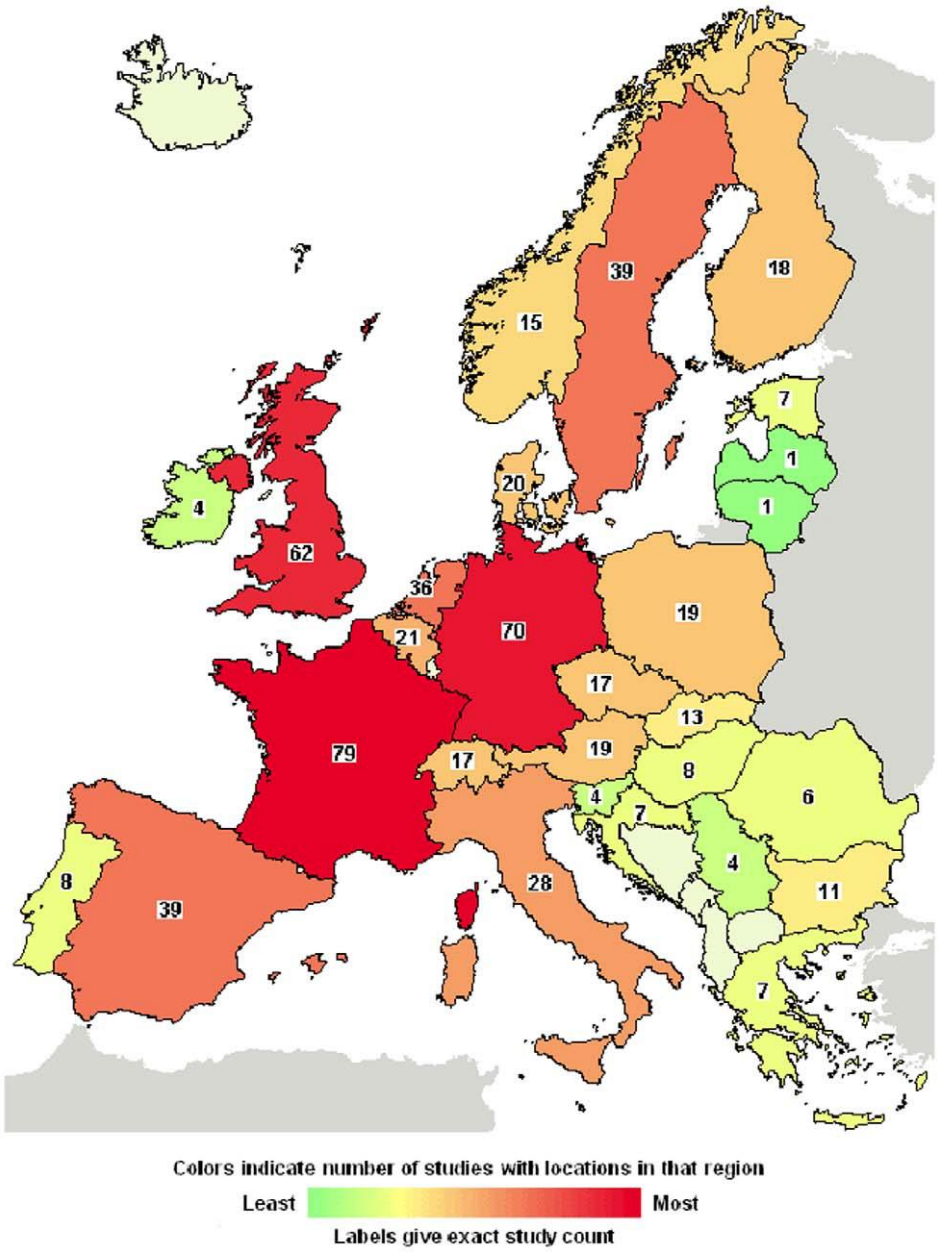
In the European Union (EU) a common legal framework for the inclusion and protection in research of adults who lack capacity is set up by the *Directive 2001/20/EC*, also known as the “Clinical Trials Directive” (hereinafter the Directive).

To ensure legal protection to incapacitated participants in research the Directive requires **the written consent of the participant's legal representative**.

However, according to the Directive “The notion of legal representative **refers back to existing national law** and consequently may include **natural or legal persons, an authority and/or a body provided for by national law”** (introduction, point 5).

In all the analyzed national laws on clinical trials legislation - Belgium, Denmark, Finland, France, Germany, Ireland, Italy, the Netherlands, Spain and the UK- **a relative can take on the role of proxy** (*Gainotti S. et al., PLoS ONE, 2010)*.
Generally, written and signed consent is given by nearest relative (or legal representative) or the person's general practitioner or a person nominated by the relevant health care provider, who can act as legal representative.

However, *only in Germany and Italy* the system of proxy is determined **by the courts** - a procedure which is not necessarily required for the r<u>ecognition of a proxy</u> in other member states.



INFORMED Consent – Incapacitated Subjects

REGULATION (EU) No 536/2014 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

of 16 April 2014 on clinical trials on medicinal products for human use

NB *EMA's Management Board endorsed a delivery timeframe in December 2015. However, the system's* ***go-live date has been postponed*** *due to technical difficulties with the development of the IT systems.*

Chapter V
Article 31
Clinical trials on incapacitated subjects

1. **In the case of incapacitated subjects who have not given, or have not refused to give, informed consent before the onset of their incapacity, a clinical trial may be conducted only where, in addition to the conditions set out in Article 28, all of the following conditions are met:**

a) the informed consent of their legally designated representative has been obtained;

b) the incapacitated subjects have received the information referred to in Article 29(2) in a way that is adequate in view of their capacity to understand it;

c) the explicit wish of an incapacitated subject who is capable of forming an opinion and assessing the information referred to in Article 29(2) to refuse participation in, or to withdraw from, the clinical trial at any time, is respected by the investigator;

REGULATION (EU) 2017/745 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 5 April 2017 on medical devices

NB: ***new regulation will replace the two Directives 93/42/EEC (MDD) and 90/385 EEC (AIMDD) by May 26, 2020***

CHAPTER VI
CLINICAL EVALUATION AND CLINICAL INVESTIGATIONS
Article 64

Clinical investigations on incapacitated subjects

1. In the case of incapacitated subjects who have not given, or have not refused to give, informed consent before the onset of their incapacity, a clinical investigation may be conducted only where, in addition to the conditions set out in Article 62(4), all of the following conditions are met:

a) the informed consent of their legally designated representative has been obtained;

b) the incapacitated subjects have *received the information* referred to in Article 63(2) in a way that is adequate in view of their capacity to understand it;

c) the *explicit wish* of an incapacitated subject who is capable of forming an opinion and assessing the information referred to in Article 63(2) to refuse participation in, or to withdraw from, the clinical investigation at any time, *is respected* by the investigator;

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Article 64

Clinical investigations on incapacitated subjects

d) *no incentives or financial inducements* are given to subjects or their legally designated representatives, except for compensation for expenses and loss of earnings directly related to the participation in the clinical investigation;

e) the *clinical investigation is essential* with respect to incapacitated subjects and data of comparable validity cannot be obtained in clinical investigations on persons able to give informed consent, or by other research methods;

f) the clinical investigation *relates directly to a medical condition* from which the subject suffers;

g) there are scientific grounds for expecting that participation in the clinical investigation will produce a direct *benefit* to the incapacitated subject outweighing the risks and burdens involved.

2. The subject shall *as far as possible take part* in the informed consent procedure.

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Article 65

Clinical investigations on minors

A clinical investigation on minors may be conducted only where, in addition to the conditions set out in Article 62(4), all of the following conditions are met:

(a) the informed consent of their legally designated representative has been obtained;

(b) the minors have *received the information* referred to in Article 63(2) in a way adapted to their age and mental maturity and from investigators or members of the investigating team who are trained or experienced in working with children;

(c) the *explicit wish* of a minor who is capable of forming an opinion and assessing the information referred to in Article 63(2) to refuse participation in, or to withdraw from, the clinical investigation at any time, *is respected* by the investigator;

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Article 65
Clinical investigations on minors

d) *no incentives or financial inducements* are given to the subject or his or her legally designated representative except for compensation for expenses and loss of earnings directly related to the participation in the clinical investigation;

e) the clinical investigation is intended to investigate treatments *for a medical condition that only occurs in minors* or the clinical investigation is essential with respect to minors to validate data obtained in clinical investigations on persons able to give informed consent or by other research methods;

f) the clinical investigation either *relates directly to a medical condition* from which the minor concerned suffers or is of such a nature that it can only be carried out on minors;

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Article 65
Clinical investigations on minors

g) there are scientific grounds for expecting that participation in the clinical investigation will produce a direct *benefit* to the minor subject outweighing the risks and burdens involved;

h) the minor shall *take part* in the informed consent procedure in a way adapted to his or her age and mental maturity;

i) if during a clinical investigation the *minor reaches the age of legal competence* to give informed consent as defined in national law, his or her express informed consent shall be obtained before that subject can continue to participate in the clinical investigation.

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Article 68
Clinical investigations in emergency situations

1. By way of derogation from point (f) of Article 62(4), from points (a) and (b) of Article 64(1) and from points (a) and (b) of Article 65, informed consent to participate in a clinical investigation may be obtained, and information on the clinical investigation may be given, after the decision to include the subject in the clinical investigation, provided that that decision is taken at the time of the first intervention on the subject, in accordance with the clinical investigation plan for that clinical investigation and that all of the following conditions are fulfilled:

a) due to the *urgency of the situation*, caused by a sudden life-threatening or other sudden serious medical condition, the subject is unable to provide prior informed consent and to receive prior information on the clinical investigation;

b) there are scientific grounds to expect that participation of the subject in the clinical investigation will have the potential to produce a *direct clinically relevant* benefit for the subject resulting in a measurable health-related improvement alleviating the suffering and/or improving the health of the subject, or in the diagnosis of its condition;

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Article 68
Clinical investigations in emergency situations

c) it is not possible within the therapeutic window to supply all prior information to and obtain prior informed consent from his or her legally designated representative;

(d) the investigator certifies that he or she is *not* aware of any *objections* to participate in the clinical investigation previously expressed by the subject;

(e) the clinical investigation *relates directly to the subject's medical condition* because of which it is not possible within the therapeutic window to obtain prior informed consent from the subject or from his or her legally designated representative and to supply prior information, and the clinical investigation is of *such a nature* that it may be *conducted exclusively in emergency situations*;

f) the clinical investigation poses a minimal risk to, and imposes a minimal burden on, the subject in comparison with the standard treatment of the subject's condition.

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2. Following an intervention pursuant to paragraph 1 of this Article, informed consent in accordance with Article 63 shall be sought to continue the participation of the subject in the clinical investigation, and information on the clinical investigation shall be given, in accordance with the following requirements:

a) *regarding incapacitated subjects and minors*, the informed consent shall be sought by the investigator from his or her legally designated representative without undue delay and the information referred to in Article 63(2) shall be given as soon as possible to the subject and to his or her legally designated representative;

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b) regarding *other subjects*, the informed consent shall be sought by the investigator without undue delay from the subject or his or her legally designated representative, whichever can be done sooner, and the information referred to in Article 63(2) shall be given as soon as possible to the subject or his or her legally designated representative, as applicable.

For the purposes of point (b) where informed consent has been obtained from the legally designated representative, informed *consent to continue the participation* in the clinical investigation shall be *obtained from the subject* as soon as he or she is capable of giving informed consent.

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Article 68
Clinical investigations in emergency situations

3. If the subject or, where applicable, his or her legally designated representative does not give consent, he or she shall be informed of the *right to object to the use of data obtained from the clinical investigation*.

Non profit clinical trials and commercial issues in sharing data (in Italy, D.M. 17.12.2004, 06.11.2007, 14.05.2019 & new ministerial decree was expected for 31 October 2019)

Non profits clinical studies *on medical products* - requirements:

a) promoter is a public institution or institution or equivalent institution or foundation or moral, research and / or health or association / scientific or research association or non-profit research organization or IRCCS or a person dependent on these structures and who plays the role of promoter in the context of his institutional duties;

b) promoter is not the owner of the patent of the experimental drug and that it does not have economic co-interests with the manufacturer of the experimental drug;

c) the ownership of the data relating to the trial, its execution and its results belong to the promoter;

d) that the trial is not aimed at or used for the industrial development of the drug or in any case for profit.

Coordination between public and private promoters in clinical trial/studies

REGULATION (EU) No 536/2014 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 16 April 2014 on clinical trials on medicinal products for human use

CHAPTER XI
SPONSOR AND INVESTIGATOR

Article 71
Sponsor

A clinical trial may have one or several sponsors.

Any sponsor may delegate, in a written contract, any or all of its tasks to an individual, a company, an institution or an organisation. Such delegation shall be without prejudice to the responsibility of the sponsor, in particular regarding the safety of subjects and the reliability and robustness of the data generated in the clinical trial.

The investigator and the sponsor may be the same person.

Article 72
Co-sponsorship

1. Where a clinical trial has more than one sponsor, all sponsors shall have the responsibilities of a sponsor set out in this Regulation, unless the sponsors decide otherwise in a written contract setting out their respective responsibilities. Where the contract does not specify to which sponsor a given responsibility is attributed, that responsibility shall lie with all sponsors.

Can co-sponsorship also encourage studies between profit/commercial promoters and public non-profit promoters?

* The concept of co-sponsorship is foreseen only in the EU regulation on experimentation with medicinal products (but at national level?).

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