Good Clinical Practice

Approaches to Informed Consent in Clinical Trials With Unconscious Patients

Piotr Iwanowski, MD, PhD

1. Association for Good Clinical Practice in Poland
2. Wockhardt – Department of Clinical Research

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What is feasible
What is possible
What is useful
What is feasible
Approaches to emergency informed consent: What is feasible?

**Traditional:**
- In-hospital
- Physician-patient dialogue F2F
- Written document

**Pros:**
- Well known, well recognised
- Comfortable
- Supporting autonomy
- Room for questions
- Access to reference documents

**Cons:**
- Not feasible with incapacitated
- Time consuming
- Selection bias (only transportation survivors/improvers)
- Difficult for proxy consent by relative (arrive late)

modified from Rose and Kasner, 2010
Approaches to emergency informed consent: What is feasible?

**Paramedic:**
On-scene
or at transport

**Pros:**
- Early implementation
- Proxy consent by relative facilitated
- Less selection bias
- Already successfully used

**Cons:**
- Not feasible with incapacitated
- May distract from routine care
- May lack expertise in diagnosis & experimental treatment
- Require training/certificate in bioethics
- May be deemed unacceptable by public and medics

*modified from Rose and Kasner, 2010*
Approaches to emergency informed consent: What is feasible?

**Waiver:**
Exception from consent (No consent!)

- High enrolment
- Early enrolment
- Feasible with incapacitated patient

- May be deemed unacceptable by public & medics

modified from Rose and Kasner, 2010
Approaches to emergency informed consent: What is feasible?

Abbreviated:
On scene and/or in-hospital
Abbreviated scope of information
Short consent form

• Fast
• Increases (!) comprehension
• Preserves autonomy
• Feasible also for paramedics
• Early enrolment
• Fits with deferred full-scope consent

• Incomplete understanding can be claimed
• Increased risk of dropout at deferred full-scope consent
• Double effort when deferred consent sought

modified from Rose and Kasner, 2010
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**Tele-consent:**
Dialogue with physician until hospital arrival (via phone or video)

- Time saving
- Early enrolment
- Medical discussion remains with physician
- Supporting autonomy
- Room for questions

- On-call physicians needed
- Cell network coverage dependent
- Distracting factors (no F2F contact, noise etc.)

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Proxy consent:
Consent given by authorised third party (a relative, a court etc.)

- Full scope consent possible as a rule
- Medical discussion remains with physician
- Room for questions
- Access to reference documents

- Can delay enrolment
- Additional formal/legal burden
- May be deemed to disrespect autonomy

modified from Rose and Kasner, 2010
What is possible
International standards

- Declaration of Helsinki
- ICH Good Clinical Practice
- International Ethical Guidelines for Biomedical Research Involving Human Subjects by CIOMS – WHO
- Convention on Human Rights and Biomedicine by CoE
- Additional protocol on biomedical research to the Convention (CoE)
Regulatory perspective

  „Persons who are incapable of giving legal consent to clinical trials should be given special protection. It is incumbent on the Member States to lay down rules to this effect.”
  „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.”

- Member states:
  – No consent/deferred consent
  – Proxy consent
No/deferred consent: United Kingdom

- Inclusion of incapacitated adults in a clinical trial allowed without consent of legal representative if:
  - treatment is required urgently
  - the nature of the trial requires urgent action
  - it is not reasonably practicable to obtain consent
  - Ethics Committee has approved arrangements

_The Medicines for Human Use (Clinical Trials) Amendment (No. 2) Regulations (Statutory Instrument 2984) implemented December 2006_
Inclusion of emergency patients in a clinical trial allowed without consent if:
- treatment is required urgently
- therapeutic objective is to save patient’s life, recover health or reduce suffering

Mandatory deferred consent once competence to consent gets restored

*Arzneimittelgesetz*
No/deferred consent: Austria

- Inclusion of emergency patients in a clinical trial allowed without consent of legal representative if:
  - the presumed will, or will expressed prior to becoming incapacitated, is respected
  - public was adequately informed by the site that such emergency trial is going to be conducted
  - therapeutic objective is to save patient’s life, recover health or reduce suffering

- Mandatory deferred consent once competence to consent gets restored

*Arzneimittelgesetz*
No/deferred consent: Hungary

- Inclusion of emergency patients in a clinical trial allowed **without consent**:
  - only for the time of emergency treatment
  - therapeutic objective
  - *In practice: relative’s written consent is sought*
- Mandatory deferred consent once competence to consent gets restored

*Health law*

*Regulation 35/2005*
Proxy consent: Belgium

- Informed Consent needs to be obtained from the legal representative.
- This Informed Consent has to express the presumed will of the incapacitated adult.
- The subject’s will, expressed prior to becoming incapacitated, has to be respected.
- In absence of power of attorney, informed consent needs to be obtained from (in this order): cohabitating spouse, legal cohabitating partner or factual cohabitating partner, major child, parent, major brother or sister.
- Mandatory deferred consent once competence to consent gets restored

*Law of 7 May 2004 on Experiments on the human person*
Proxy consent: Spain

- Informed Consent needs to be obtained from a relative or actual partner.
- The subject’s refusal expressed prior to becoming incapacitated has to be respected.
- Mandatory deferred consent once competence to consent gets restored

Real Decreto 223/2004
Proxy consent: France

• Informed Consent needs to be obtained from a family member or assigned person of patient’s confidence (a parent, a relative, a physician).
• Mandatory deferred consent once competence to consent gets restored.

*Code de la santé publique*
Proxy consent: Poland

- Informed Consent needs to be obtained from the 
guardianship court (pharma law)
- Medical law allows trials with no consent at all in emergency; 
yet option not used in practice

Prawo farmaceutyczne
(...), informed consent may be obtained after the start of the clinical trial to continue the clinical trial and information on the clinical trial may be given after the start of the clinical trial provided 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, it is impossible to obtain prior informed consent from the subject and it is impossible to supply prior information to the subject;

(b) no legal representative is available;

(c) the subject has not previously expressed objections known to the investigator;
(d) the research relates directly to a medical condition which causes the impossibility to obtain prior informed consent and to supply prior information;
(e) the clinical trial poses a minimal risk to, and imposes a minimal burden on, the subject.
(...) Regarding *incapacitated subjects and minors*, the informed consent (...) shall be obtained as soon as possible from the legal representative (...);

(...) Regarding *other subjects*, the informed consent (...) shall be obtained as soon as possible from the legal representative or the subject, whichever is sooner (...).

(...) Where informed consent has been obtained from the legal representative, informed consent to continue the trial shall be obtained from the subject as soon as it is capable of giving informed consent.
What is useful
Investigators’ attitudes towards consenting to GCP\textsubscript{pl} in emergency: own research - Poland

- Anonymous 14-item questionnaire for investigators experienced in emergency trials in Poland,
- Approx. 1000 copies distributed to 43 cardiology and 22 stroke Polish centres
- 214 questionnaires returned
- 73.8% had experience with acute coronary syndrome trials; 25.2% with acute stroke trials

What was the scope of information and how it was delivered to trial participants?

- Full-size information (like non-emergency trials), verbal + written: 53.3%
- Abbreviated info, verbal and written: 38.8%
- Full-size verbal info + abbreviated written info: 15.0%
- Abbreviated verbal info + full-size written info: 10.7%
- Only abbreviated verbal info: 4.2%
- Only proxy consent (guardianship court): 0.0%

N = 214
Did you additionally seek consent of participant’s relative(s)?

- yes, always: 18.3%
- yes, sometimes: 43.7%
- rarely or exceptionally: 25.3%
- never: 12.7%

N = 214
Is an emergency patient able to understand the nature of the trial and consciously decide to participate?

- always / most often: 32.3%
- some patients are able: 46.7%
- no or few patients are able: 17.3%
- uncertain: 3.7%

N = 214
The amount of information supposed to be given to patient was in general:

- too broad: 80.4%
- adequate in regard to patient’s condition: 17.7%
- too brief: 0.0%
- uncertain: 1.9%

N = 214
Which of the following models of informed consent in emergency settings would be the best?

- Full-size information (like non-emergency trials), verbal & written: 14.0%
- Abbreviated info, verbal and written + abbreviated consent form, with obligatory full-size written consent to continue the trial once the participant’s status has sufficiently improved: 78.0%
- Abbreviated oral info + only verbal consent, with obligatory full-size written consent to continue the trial once the participant’s status has sufficiently improved: 7.5%
- Other: 0.5%

N = 214
Consent for clinical trials in emergency - proposal for Poland

Patients with **full or partially limited competence** to consent (conscious, acute state):

- Immediate Own
- Deferred Own

Patients with **no competence** to consent (unconscious):

- Immediate Proxy
- Deferred Own
- Deferred Proxy

- Documented effort/application for a deferred proxy consent
- Positive opinion by a second physician
What is feasible

What is possible

What is useful