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Clinical research in the ICU: response to Kompanje et al.

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Dear Editor,

In a recent article in *Intensive Care Medicine*, Erwin Kompanje et al. [1] expressed their concern that the proposal by the European Commission of a regulation on clinical trials [2] might impair the conduct of research in emergency situations. Article 32 will permit a waiver of prior consent, an initiative we all applaud. However, its wording raised some concerns, clearly identified by Kompanje as well as in our editorial [3]. Since, the initial draft has been profoundly amended. The final text is expected to be voted by the Parliament in April 2014. The present wording of article 32 is substantially improved and most of the concerns expressed in the paper by Kompanje have been acceptably dealt with.

The first problematic provision spotted by Kompanje et al. was paragraph 32-(e), which says: “The clinical trial poses a minimal risk to, and imposes a minimal burden on, the subject”. This point has been well taken and the final text says now that: “the clinical trial poses a minimal risk to, and imposes a minimal burden on, the subject in comparison with the standard treatment of the subject’s condition”.

Another limitation was that the draft proposed by the Commission in July 2012 said: “the research relates directly to a medical condition which causes the impossibility to obtain prior informed consent and to supply prior information”. Kompanje et al. objected that a medical condition like coma or heavy sedation, often used in ICUs, may have precluded patient’s informed consent long before the occurrence of any emergency episode, which therefore could not be subjected to research. Paragraph 32-(d) now says: “The clinical trial relates directly to the subject’s medical condition because of which it is not possible within the therapeutic window to obtain prior informed consent... and is of such a nature that it may be conducted exclusively in emergency situation”.

During the dialogue, the revision of article 32 went further:

In case of a consent refusal expressed after the trial started, a new paragraph 32-(2a) authorizes the investigator to utilize the data collected before the denial or refusal, provided that the person or his/her representative did not oppose: “If the subject or, where applicable, the legal representative does not give consent, he or she shall be informed of the right to object to the use of data obtained from the trial”.

But, unfortunately, under the pressure of several Member States, the final draft requires now an additional condition for allowing the waiver of consent in emergency research: the trial should provide some “direct benefit” to participants; the new subparagraph 32-(aa) now says: “there are scientific grounds to expect that participation of the subject in the clinical trial will have the potential to produce a direct clinically relevant benefit for the subject...”. It is of note that the concept of direct (individual) benefit of research is nearly totally absent in the regulation,

in which it is accepted instead that a *group benefit* should be provided by the trial in absence of individual benefit. The concept of direct benefit of research has repeatedly been denounced as fallacious, misleading and finally dishonest [4]; it was dropped from the Declaration of Helsinki, when it was revised in 2000 [5]. Despite all that, legislators and regulators of some European countries continue to believe that it adds increased protection to vulnerable populations. Luckily, the individual benefit is only “expected”, which leaves some room for interpretation....

It is certainly good news that emergency research will soon be possible in all European countries.

Conflicts of interest I have no conflicts of interest.

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