Centrala etikprövningsnämnden
CENTRAL ETHICAL REVIEW BOARD
Expert group on misconduct in research

STATEMENT Ref. no. O 16-2016
02/06/2017

Institution that has requested statement

Karolinska Institute
171 77 Stockholm

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Background

The Karolinska Institute, in a letter received on 25 October 2016, has requested a statement from the Expert group for misconduct in research at the Central Ethical Review Board. This letter refers to the fact that misgivings have been expressed by two researchers in respect of the article "Autologous Peripheral Blood Mononuclear Cells as Treatment in Refractory Acute Respiratory Distress Syndrome", published in Respiration 2015. The Acting Vice-Chancellor, Karin Dahlman Wright, has therefore decided to investigate the suspicion of misconduct in research. The authors of the article were [redacted].

On 25 November 2016, the Expert group decided to appoint Professor Emeritus Dag Lundberg, Lund University, to act as a special adviser in this matter. Dag Lundberg has submitted a report on 14 February 2017. The accused researchers have been given the opportunity to respond to Dag Lundberg's report. [redacted] have submitted replies. Dag Lundberg has subsequently submitted his final comments.

Judgement of the Expert group

The accused researchers' replies to Dag Lundberg's report include accusations that Dag Lundberg is biased. The Expert group states that the contact Dag Lundberg has had with the Karolinska Institute has not been of such a nature that there is reason to question his impartiality.

In his report, Dag Lundberg judges that the measures implemented in this matter should be deemed research rather than pure healthcare. To support this judgement, Dag Lundberg cites e.g. journal entries where it can be seen that a decision was reached to treat the patient in study form, that it was not obvious that the patient's condition was so alarming that it justified emergency humane life-saving treatment and that there had therefore been time to contact the regional ethical review board, and that the treatment had dual purposes: to save the patient's life and to be part of development on scientific grounds by generating new molecular biological and immunological knowledge. Against the background of this judgement, Dag Lundberg considers that the responsible researchers have been guilty of misconduct in research, for example by failing to document a risk/benefit analysis and inherent ethical considerations prior to the decision to start the innovative treatment, by failing to contact the regional ethical review board before the measures were implemented despite the fact that the time required for an informal consultation was available, by using a seriously ill patient as a means for advanced preclinical research without ethical permission, by conducting the innovative treatment despite the fact that it was based on fragile theoretical grounds, and by failing to report simultaneous conventional clinical treatment in the article. In summary, Dag Lundberg considers that the innovative treatment that was carried out should be viewed as research and that the matter, despite the occurrence of certain general mitigating circumstances, can be deemed to constitute misconduct in research.

The researchers that have refuted Dan Lundberg's criticism have essentially dismissed it. Several of them have maintained that they only participated to a limited extent in the care and the article, and some have stated that they were not involved in the clinical work. Above all, they state that the patient received adequate care and that the reporting of this in a scientific article is relevant.

In its assessment of the matter, the Expert group has to adopt a stance on whether research has taken place and, if so, when it was launched. It is clear that it was purely a matter of healthcare when the patient came in, and that when the case study was drawn up and finally published, it was exclusively a case of research. Based on the available material, the Expert group cannot determine at what point and in which phase the research commenced. The boundary between care and research is not easy to establish. Dag Lundberg has highlighted a number of important deficiencies and phenomena. However, the Expert group considers that these essentially lie within the framework of healthcare and not research. Any deficiencies that have occurred within the care are not a matter for the Expert group.

In the case, it is notified that the patient has been subjected to 23 bronchoscopies. If this has taken case for the purposes of study, it can be criticised and possibly be considered misconduct in research. However, it cannot be ruled out, bearing in mind the circumstances in the case that this has been done in order to examine how well the experimental treatment was working. In the case, there are also journal entries stating that measures have been implemented for study purposes and that a number of hypothetical assessments have formed the basis for the implemented measures. This can also indicate that the potential benefit essentially exists in new knowledge, not in the relevant care situation. However, it cannot be presumed that this has not been done to study the progress of the care in respect of a patient with life-threatening injuries that had no known treatment method. Bearing these circumstances in mind, the Expert group considers that it is not possible to establish that the measures have been implemented within the framework of research.

The aspect of the case that undoubtedly constitutes research is the actual publication of the case study. The authors of the study have applied for and been granted ethical review permission for the subsequent analyses and for publication. In the judgement of the Expert group, this procedure does not constitute grounds to determine misconduct in research.

This concludes the handling of the matter by the Expert group.

This statement has been agreed by Lena Berke, Chair, Holger Luthman, Elisabeth Rachlew and Elin Wihlborg. In the final administration of the case, the substitutes Christina Moberg and Aleksander Giwercman, administrative director Jörgen Svidén as well as administrative secretary Eva Kaaman Modig have also been present.

For the Expert group for misconduct in research

Lena Berke