Health Council of the Netherlands

The 14-day rule in the Dutch Embryo Act

executive summary

Scientific research with human embryos

Scientific research with human embryos can yield knowledge that is of great importance to preventing diseases and treating infertility. For that reason, this type of research is permitted in the Netherlands, under certain conditions. The embryos used for this research are spare embryos that remain after IVF procedures and have been donated to science.
The conditions are laid down in the Dutch Embryo Act (Embryowet).
The purpose of this Act is to balance the interests of research with the need to protect human life in its early stages.

Should the 14-day rule be extended?

Under the Dutch Embryo Act, it is not permitted to allow embryos to develop outside the human body for longer than 14 days. This is known as the 14-day rule. In addition, embryo research must always be reviewed in advance to establish whether it serves a need: does it contribute to medical science, and is there no other way in which the research objective can be obtained?

When the Dutch Embryo Act – and with it the 14-day limit – was introduced, it was technically not possible to sustain embryos in vitro for longer than a week. Therefore, the 14-day rule effectively did not restrict medical research at the time. New technological developments have since made it possible to cultivate embryos outside the human body up to 14 days, which has also extended the possibilities for embryo research. As a result, one question raised during the most recent evaluation of the Dutch Embryo Act was whether there are reasons to extend the 14-day rule, for example to 28 days. The Minister of Health, Welfare and Sport asked the Health Council of the Netherlands to answer this question.
The Minister also wishes to know whether there should be a comparable developmental limit for so-called embryo-like structures. To address these questions, the Health Council of the Netherlands established a committee of experts.

Consideration of three elements

To determine an acceptable limit for research, the committee has considered three elements:

1. **the embryo's worthiness of protection**
2. **the importance of research beyond the 14-day limit**
3. **the societal perspective.**

1 The embryo's worthiness of protection

An embryo is considered an early form of human life, that is worthy of a certain degree of protection. Worthy of protection means that embryos deserve respectful treatment, even if – in the case of spare embryos following IVF procedures – they are left to perish. For moral reasons, there are restrictions on the ways in which a human embryo may be used. An embryo may be worthy of protection for its own sake, but also for extrinsic reasons, such as its relational and symbolic value. In this context, 'relational value' means that society derives value from a biological or social relationship with human embryos. Embryos also have a certain symbolic value, because they represent what society considers to be meaningful. This includes the beginning of life and all associated traditions.

The embryo's worthiness of protection is both progressive and relative. This means that the embryo's worthiness increases during successive developmental stages, but also that it can be outweighed by more compelling interests. The committee has presumed that in a pluralistic society, a range of views will exist on the moral worth of human embryos. To do justice to the ideal of a pluralistic society, it is therefore important to identify overlapping consensus among citizens' views. In this advisory report, the committee will discuss criteria that, in principle, can rely on a broad level of support in a secular society. The committee ultimately questioned whether there is a timepoint in the development of the human embryo at which it is hard to imagine that a research interest would outweigh the embryo's moral worth. It is difficult to determine any such moment precisely. One example, in any case, according to the committee, is when awareness and the ability to experience pain (*sentience*) arise – which is not until much later in human embryonic development. Several moments in the development of an embryo have moral significance, such as when monozygotic twinning becomes impossible or when blood circulation or brain functions start. However, according to the committee these moments do not point to a well-defined limit for research. The same applies to the relational and symbolic values of an embryo. While they do account for the embryo's increasing worthiness of protection, such timepoints are not compelling enough for an unambiguous legal limit for embryo research.

The embryo's worthiness of protection

It is impossible to pinpoint a moment in time beyond which research involving the use of embryos becomes ethically unacceptable, except in a late stage of embryonic development.

2 The importance of scientific research

Knowledge on embryonic development is important to help understand the causes of developmental disorders. This knowledge can provide clues as to how such disorders or other diseases can be prevented or treated, and how fertility problems can be treated more effectively. Much of the knowledge gained to date was obtained through studies using animals or human cells. However, as the insights resulting from such studies cannot be applied directly to human beings, research on embryos will remain necessary. All stages of embryonic development are relevant to scientific research. Even so, the committee believes that at the moment, the scientific importance of research with embryos is greatest between day 14 and day 28. At present, there is practically no knowledge about the development of the human embryo after day 14, when crucial processes are taking place. During the third and fourth weeks of embryonic development the body axes are formed and organ development begins. Research in the third and fourth weeks could improve understanding of how congenital cardiac abnormalities and neural tube defects (anencephaly or spina bifida) occur. Such disorders are common among newborns. Knowledge about embryonic development beyond day 28 may be obtained through existing research practices, such as research on foetal tissue from abortions. From 28 days onwards, foetal tissue obtained from abortions is suitable and available for research. While for research into embryonic development foetal tissue tends to be inferior (as it is not always intact), it does reduce the scientific need for research with embryos beyond 28 days.

Knowlegde gap between 14 and 28 days

This relates to, among others, crucial knowlegde on organ formation, developmental disorders, prevention of diseases and fertility treatments. Fetal tissue from abortions is available for research from 28 days after conception.

3 Societal perspective

Embryo research is a sensitive issue. Views on the subject vary widely from person to person. It is important for the legislator to deal with all those views carefully. Insufficient regard for the societal perspective could potentially result in diminished public confidence in embryo research, and might even erode public trust in science altogether. In contrast, support for embryo research among the general public could increase the moral legitimacy of political decisions, including a decision to adapt the 14-day rule. Additionally, acceptance of a new rule would depend on the government's transparency as to its reasons for changing the rule, should it decide to do so. The committee is of the opinion that scientific research after day 14 should serve a clear, evident and justifiable interest.

Societal perspective

To ensure societal acceptance of embryo research and public trust in science, it is essential that the scientific benefits of research with embryos can be sufficiently articulated. Moreover, it must be impossible to obtain those significant scientific insights in any other way.

Recommendation: extend the limit for embryo research to 28 days

After considering the three aforementioned elements, the committee recommends that the 14-day limit for embryo research be extended to a 28-day limit. Purely reasoning from arguments of moral status, the committee holds that it is not possible to identify a specific moment when research with embryos becomes unacceptable, other than in a late stage of embryonic development. Before that, there is a period during which the need to protect (early) human life may, in principle, be weighed against research interests. Nevertheless, an important reason for the committee to propose an unambiguous legal limit at day 28 is the societal perspective, which is closely tied to the public interests that embryo research serves. Research up to day 28 in the development of an embryo can yield valuable knowledge that may be used to prevent developmental disorders and treat fertility problems. That knowledge is currently out of reach and cannot be obtained in any other way. Presently, the interest served by research with embryos after day 28 is less evident. From a societal perspective the need for setting a limit beyond day 28 would therefore be less compelling.

Recommendation: also apply the 28-day limit to non-conventional embryos

Embryos formed by the fusion of a human egg cell and a sperm cell are referred to as ‘classic embryos’. Additionally, it is possible to manipulate stem cells to enable them to recapitulate some, or all aspects of embryonic development in vitro. The resulting entities are called ‘embryo-like structures’ (ELS). Some ELS can even represent all aspects of the integrated development of an entire embryo, but others cannot (for example, because they can only form a single organ). According to the committee, ELS that represent entire embryos (integrated ELS) also qualify for protection under the Dutch Embryo Act, because it cannot be ruled out that they have the potential to become a person. The committee refers to this category of embryos as ‘non-conventional embryos’. Even though they are created differently than via the process of fertilisation (hence ‘non-conventional’), according to the committee they still qualify as embryos. The committee is of the opinion that ELS that are not intended to represent the integrated development of the entire

embryos (non-integrated ELS) do not require legal protection under the Dutch Embryo Act.

In determining a research limit for non-conventional embryos, the committee considered the same three elements it considered in the case of classic embryos. According to the committee, non-conventional embryos are equally worthy of protection as classic embryos, because the two categories are morally equivalent. At present, little is known about public opinion on non-conventional embryos. As a result, it is impossible to determine the exact extent to which their relational value and symbolic value differ from those of classic embryos. However, according to the committee non-conventional embryos have at least some relational and symbolic value, and that value can be weighed against the research interest involved. In the committee's view, the scientific importance of research on non-conventional embryos is the same as that of research involving classic embryos. Hence, the committee also recommends a limit for non-conventional embryos that corresponds to the developmental stage of a classic embryo at day 28.

The 28 day-limit should apply to classic embryos and integrated ELS

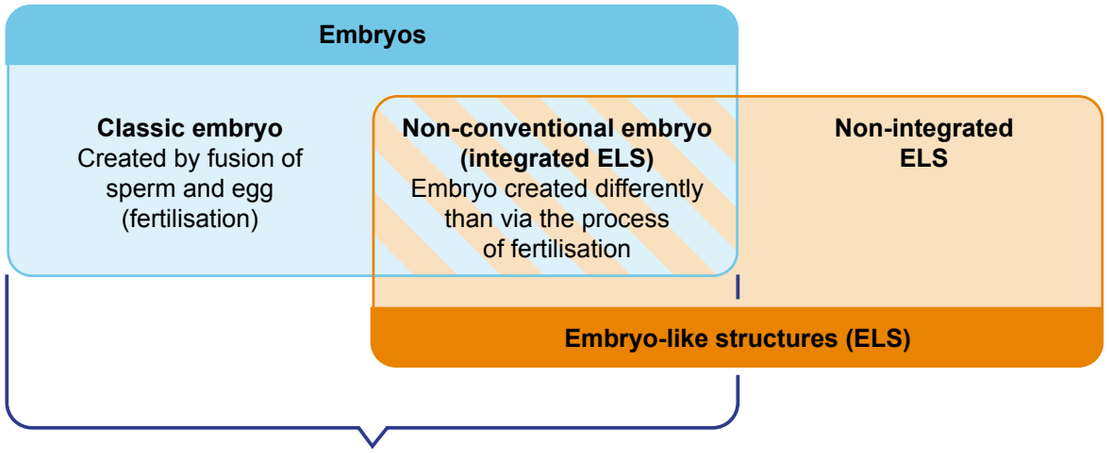

Figure 1 Schematic representation of the relation between embryos and embryo-like structures

Thorough review by the CCMO

While the committee believes that a 28-day limit is acceptable, it is not to say that the embryo is not worthy of protection until that time. It is up to the Central Committee on Research involving Human Subjects (CCMO) to weigh the research interest against the need to protect the embryo, for every proposed study. In current practice the CCMO already thoroughly reviews whether embryos may be used for research, by examining the extent to which the study concerned can be expected to yield important new scientific insights and, if so, whether those insights could not be

obtained in a less invasive manner. The committee believes it is important to maintain this review by the CCMO.

Final remark

The committee does not rule out the possibility that the legal limit for scientific research on embryos may be brought up for discussion again at some point in the future. This might occur when the limit is again found to restrict scientific developments with a huge potential for preventing disease and treating infertility, or when views in society on embryo research change. In such a case, the committee believes that the balance between the embryo's worthiness of protection, the scientific importance and the societal perspective should be reconsidered.

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