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National Health and Medical Research Council

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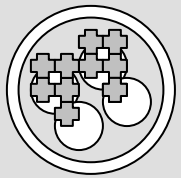
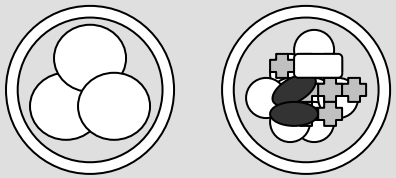
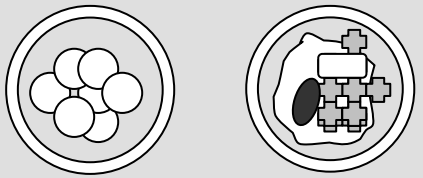
Objective Criteria for determining embryos that are unsuitable for implantation

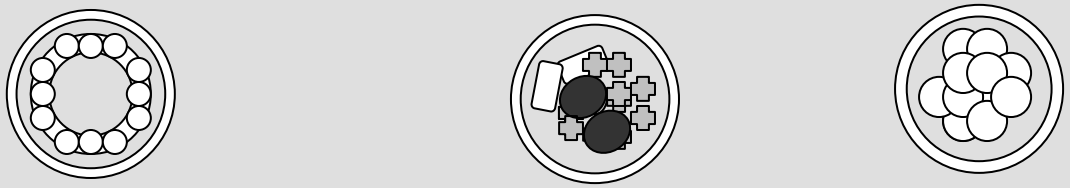
Issued by the Chief Executive Officer, NHMRC on 6 December 2007

Unsuitable for implantation, in relation to a human embryo, means a human embryo that:

(a) has been identified by preimplantation genetic diagnosis as carrying a serious genetic condition; or

(b) is determined by a qualified embryologist* to be unsuitable for implantation according to the objective criteria below;

DAY 1	DAY 2	DAY 3	DAY 4
No 2PN **from the first mitotic division**	 **≥50% frag/deg/vacs**	 **< 4C or with ≥50% frag/deg/vacs**	 **< 8C or with ≥ 50% frag/deg/vacs**

DAY 5 – 7	IN ADDITION
 **Blastocyst with ≥ 80% reduction in size of ICM** **≥ 50% frag/deg/vacs** **No compaction**	**Any embryo with ≥50% multinucleated blastomeres**

= fragmentation **= vacuole** **= degeneration** **= cell**

Definitions

C = cells	**deg** = degeneration, ie non-viable cells	**ICM** = inner cell mass	**vacs** = vacuoles, ie fluid filled space within the cytoplasm of the cell(s)
frag = fragmentation, ie small pieces of the cell that bud off during cell division and accumulate into the extracellular region inside the zona pellucida (the outer 'shell' of the oocyte)	**compaction** = a process occurring on the 4th day of human embryo development where cells merge together so that individual cells can no longer be distinguished from each other	**Blastocyst** = stage of human embryo development occurring on the 5th day consisting of two distinct cell types; a hollow sphere of cells called the trophectoderm (cells which will form the placenta) and an ICM (cells which will form the foetus)	**2PN** = 2 pronuclei indicating successful fertilisation; one pronucleus containing chromosomes from the oocyte, the other pronucleus containing chromosomes from the sperm

- A qualified embryologist is defined as an embryologist who can demonstrate completion of the *Scientists in Reproductive Technology (SIRT)* Training Log Book in sections relating to embryology and embryo assessment or its equivalent and the continuing education requirements outlined in the *Reproductive Technology Accreditation Committee (RTAC) Code of Practice for Assisted Reproductive Technology Units* (ie. have at least 12 hours of accredited continuing education annually in ART or clinical laboratory practice and do at least 20 ART procedures per year).

Note. These objective criteria have been endorsed by the *Scientist in Reproductive Technology (SIRT)* Committee.

Accompanying Contextual Information

Background

In vitro fertilisation (IVF) is a process that is used to assist conception in women who may be unable to conceive naturally. During the IVF process, eggs are harvested from the female donor and incubated with sperm from a male donor under conditions that enable fertilisation to take place. The result of IVF is usually the creation of a number of embryos that can then be transferred to and allowed to implant into the lining of the woman's uterus. The number of embryos created is dependent, amongst other factors, on the quality of the eggs and sperm.

In consultation with the patients, embryologists select embryos that they believe are most likely, once transferred, to implant and result in a pregnancy. The selection of these 'suitable' embryos is based on the observations of a trained embryologist looking at the embryos under a microscope. Usually, a single embryo will be selected for transfer into the woman's uterus. This embryo will be transferred 'fresh' at the time of the patient's IVF treatment. The remaining suitable embryos are then frozen for transfer and implantation at a future date, if required.

During the process of an IVF cycle, not all embryos would be considered to be suitable for transfer and subsequent implantation. Some embryos cease development prior to transfer, while others fragment or die at a very early stage. These embryos, which are classified as 'unsuitable for implantation', are generally discarded because they are considered to be too fragile to be frozen.

An alternative fate for embryos that are excess to the requirement of the patients, and that are considered to be unsuitable for implantation, is to be donated for research purposes under a licence issued by the NHMRC *Embryo Research Licensing Committee*. Objective criteria have been developed for determining which embryos are unsuitable for implantation.

Legislative Requirements for the development of 'Objective Criteria for Embryos Unsuitable for Implantation' Guidelines

The *Prohibition of Human Cloning for Reproduction and the Regulation of Human Embryo Research Amendment Act 2006* (the Amendment Act) was passed by the Parliament in December 2006. The Amendment Act amended the *Research Involving Human Embryos Act 2002* (the RIHE Act) with effect from 12 June 2007. The Amendment Act included a definition of '*unsuitable for implantation*' and required the development of guidelines containing objective criteria for determining when embryos are unsuitable for. The definition of '*unsuitable for implantation'* states

Unsuitable for implantation, in relation to a human embryo, means a human embryo that:

a. is diagnosed by pre-implantation genetic diagnosis as unsuitable for implantation, in accordance with the Ethical Guidelines on the Use of Assisted Reproductive Technology in Clinical Practice and Research (2004), issued by the CEO of the NHMRC; or

b. is determined to be unsuitable for implantation in the body of a woman, in accordance with objective criteria specified in guidelines issued by the CEO of the NHMRC under the National Health and Medical Research Council Act 1992 and prescribed by the regulations for the purposes of this paragraph.

Development of Objective Criteria

The *Objective Criteria for Embryos Unsuitable for Implantation* guidelines (the Objective Criteria) were drafted and released for public consultation in March 2007 in accordance with the requirements of the NHMRC Act. Consultation was undertaken with relevant experts to finalise the Objective Criteria for consideration by the Council of the NHMRC at its 167th Session in October 2007. Council recommended that the Objective Criteria be issued as guidelines by the CEO.

Application of the Objective Criteria

The Objective Criteria must be used for determining embryos that are considered unsuitable for implantation and that may be used for research.

Under the *Research Involving Human Embryos Act 2002* those wishing to conduct research on embryos determined as unsuitable for implantation must obtain a licence to do so from the NHMRC Licensing Committee and comply with the *National Statement on Ethical Conduct in Human Research 2007*.

The NHMRC will continue to work actively with the scientific community to update and further refine these Objective Criteria as additional scientifically authenticated information becomes available.