**UW–Madison SCRO Committee**

**Guidance for the** **Oversight for introduction of hPSCs into non-human animals (chimeras)**

**Research Involving Chimeras**

The UW–Madison’s Policy for Human Embryo and Human Pluripotent Stem Cell Research requires the SCRO Committee to review research involving the creation of chimeras when the chimeras are created in either of two ways:

1. By introducing human embryonic stem cells (hESCs), or cells derived from hESCs, into an animal; or
2. By introducing human pluripotent stem cells (hPSCs) obtained from non-embryonic sources, or cells derived from hPSCs, into an animal, when one expected effect of the introduction is that human cells will be integrated into the central nervous system, testes, or ovaries of the animal.

Investigators planning transfer of human pluripotent stem cells and their derivatives into animal hosts need to submit the [chimera worksheet](https://research.wisc.edu/wp-content/uploads/sites/2/2021/12/Chimera-Worksheet-12_21-.docx) to the SCRO Committee for review before starting experiments. Once submitted, the chair or designee will determine if the investigator needs to submit a full SCRO initial review application. Standard teratoma formation assays used to test whether cells are pluripotent fall under expedited review and do not require chimera worksheet submission. All research involving animals must be reviewed by the IACUC and biosafety.

**Assessing Integration**

Particular attention should be paid to at least three factors:

1. the extent to which the implanted cells colonize and integrate into the animal tissue
2. the degree of differentiation of the implanted cells
3. the possible effects of the implanted cells on the function of the animal tissue.

Investigators are encouraged to find further guidance in [Additional Resources.](https://research.wisc.edu/compliance-policy/stem-cell-research-oversight/policies/)

* NAS Guidelines 2016 section 2.1
* 2021 ISSCR Guidelines for Stem Cell Research and Clinical Translation

<https://www.isscr.org/policy/guidelines-for-stem-cell-research-and-clinical-translation/key-topics/chimeras>

* ISSCR guidelines for the transfer of human pluripotent stem cells and their direct derivatives into animal hosts. Hyun et al., Stem Cell Reports 2021

[https://www.cell.com/stem-cell-reports/fulltext/S2213-6711(21)00256-3](https://www.cell.com/stem-cell-reports/fulltext/S2213-6711%2821%2900256-3)

**Limitations**

For researchers requesting to introduce pluripotent stem cells or their derivatives during the embryonic stages of development, researchers must provide rationale for introducing cells at the embryonic stage. In evaluating the application, the Committee will consider the following:

* The possibility the human material could affect the cognitive abilities of the animal research subject in ways that would be morally relevant.
* The possibility that human gametes could form within animal research subjects, the breeding of which could then produce a human conceptus.

The SCRO Committee uses the definition of the embryonic stage to extend through Carnegie Stage 23. In mice, this extends through E16, in rats through E17.5, in chicks through E10, and in pigs through E32.5. ([See for information about other species](https://embryology.med.unsw.edu.au/embryology/index.php/Carnegie_Stages).)

**Prohibitions**

1. The mixing of WA01, WA07, WA09, WA13, WA14 (the original 5 Wisconsin lines) or their modifications with an intact embryo, either human or non-human.
2. The breeding of animals into which hPSCs have been introduced.
3. The introduction of hPSCs, or cells derived from such hPSCs, into non-human primate pre-implantation embryos.
4. The introduction of pluripotent stem cells from any species into human pre-implantation embryos.