Progress in the *in vitro* derivation of human gametes (eggs and sperm) continues to advance. Although a number of technical gaps remain to be overcome, partial reconstitution of human gamete production has been reported for both male and female pathways. Human primordial germ cell like cells (PGCLCs) can be created from induced pluripotent stem cells, "oogonia-like" cells have been derived in culture, and limited parts of the human sperm pathway have been achieved.

Laboratory studies reconstituting gamete development can advance understanding of how this process proceeds in early human development and what genes are responsible at different stages of the pathway. Were *in vitro* human gametes ever approved for clinical use, however, they could provide a novel option for prospective parents and significantly alter the practice of reproductive medicine. Somatic cells taken from parents theoretically could be converted to iPSCs, further differentiated into functional gametes, and these gametes used to create a human embryo through *in vitro* fertilization. This ability could enable couples who are not otherwise able to do so (for example because of conditions such as infertility or same-sex couples) to produce embryos that are genetically related to both parents. The ability to generate large numbers of embryos also could enable many parents who carry known disease-causing mutations to undertake highly efficient preimplantation genetic screening and establish a pregnancy only with an embryo that does not carry that mutation. The ability to genome edit in gamete precursor cells provides yet another possibility that could enable prospective parents to produce embryos without a disease-causing genome, representing a potential alternative pathway for undertaking heritable genome editing.

Any use of *in vitro*-derived human gametes would raise important scientific, ethical, social, and regulatory issues. These are not questions that can be answered by scientific, bioethics, and regulatory communities alone– they will require broader societal engagement. In anticipation of continued research developments, however, now is the time to review the state of the science, understand what is driving progress in this area, what is likely to be achievable and what is likely not to be realistic, and recognize the urgent issues that *in vitro*-derived gametes could raise. A careful assessment now would provide foundational analysis to inform the development of future consultative social, legislative, or regulatory discussions.

STATEMENT OF TASK

A planning committee of the National Academies of Sciences, Engineering, and Medicine will convene a public workshop exploring scientific, ethical, and regulatory implications associated with the research and development of in vitro-derived human gametes. Potential topics will explore:

1. The current state of the science for in vitro derivation of male and female gametes from embryonic or induced pluripotent stem cells, including achievements with other mammalian species, roadblocks that remain to producing human gametes, and near-term prospects for overcoming remaining scientific and technical barriers.
2. The extent to which in vitro-derived human gametes could offer new options or potentially address unmet needs for both laboratory research and for reproductive medicine.
3. The ethical or social issues that would be raised by development or potential use of in vitro-derived human gametes.
4. How research and potential reproductive use of in vitro-derived human gametes would be addressed by current regulation, and whether existing regulatory approaches address the issues discussed during the workshop.

The public workshop will feature invited presentations and discussions. The planning committee will organize the workshop, select and invite speakers and discussants, and moderate the discussions. A workshop proceedings will be prepared by a designated rapporteur based on the information gathered and discussions held during the workshop, in accordance with National Academies policies and procedures.