Our position on
Cloning, Genetic Modification, and Stem Cell Technologies

What is the issue?

Cloning, genetic modification, and stem cell technologies continue to develop at pace. The genetic editing of whole organisms (bacteria, fungi, plants, and animals) is now commonplace for research purposes. The use of stem cells to treat diseases and disorders has also increased substantially over recent years.

These developments, coupled with other scientific advances arising from the isolation of human embryonic stem cells, have generated considerable public and regulatory scrutiny pertaining to aspects of cloning, regenerative medicine, stem cell research, and gene editing. This paper outlines GSK's views on the importance of some of these technologies in medical research and, where applicable, our uses of them to bring high-quality and needed healthcare products to treat and prevent diseases for as many people as possible.

Given the complex terminology in these fields, we provide an explanation of technologies in the Annex.

What is GSK's view?

- GSK is committed to working with governments to support appropriate legislation or regulation that addresses societal concerns, while allowing research to continue so the full potential of cloning, genetic modification, and stem cell technologies can be realised.
- GSK's bioethics and codes of practice require compliance with all relevant external legislation, regulation and guidelines for the use of cloning, genetic modification and stem cell technology applications for drug discovery. Our framework applies to our code of practice for all internal and external research on behalf of GSK and outlines criteria for use to consistently develop and deliver effective and safer medicines.

Cloning technologies and genetic modification

- GSK uses cloning technology to replicate molecules and cells for drug discovery and development. The technology has accelerated the testing of life-saving compounds and is critical to future advancements in biomedical research.
- GSK does not use cloning technologies with the intention of reproducing human beings. Such practices are banned by worldwide legislation and there is no medical or research case for doing so. However, other forms of cloning should continue to be applied towards research of currently untreatable or incurable diseases and medical conditions.
- Gene editing technologies are being developed which will offer increased precision and speed for introducing gene modification and correcting defects at the cell and whole organ level. In common with biomedical researchers in universities and other research institutions, we use genetically modified animals (e.g., rats and mice) as research models for many disease areas. Specific genes in these animals may be targeted and then either turned off or increased in number to achieve a better

understanding of biological pathways and discover potential drug targets. GSK sources these animals from external suppliers as well as breeding some in-house.

- GSK does not use gene editing technology to alter genetic information in human germline cells.

Stem cell technology

- Stem cells are an integral element of research in drug discovery. GSK currently uses human pluripotent stem cells as well as human adult stem cells in our research centres and in collaboration with academic centres of excellence. For example, human induced pluripotent stem cells (hiPSCs) derived from human blood or skin are used by GSK to discover novel drug targets and evaluate the safety of medicines.

- GSK believes that use of human embryonic stem cells (hESCs), fetal stem cells, and other fetal material also have a promising place in medical research and drug discovery. GSK and our external collaborators only use hESCs originating from IVF programmes. These are primarily obtained or derived from cell banks, including those overseen by the Medical Research Council in the UK, and the National Institutes of Health in the US. Fetal stem cells and other fetal material used by GSK and our external collaborators are obtained from hospitals and/or clinics with the consent of the woman. This process is separate from a woman's decision whether to terminate her pregnancy and is initiated only after the woman's decision to terminate has been made.

- Any current, or future, use of hESCs or fetal material by GSK, or by outside collaborators follows established ethical requirements and rigorous scrutiny. This includes confirmation that the provider of the material has obtained informed consent from the donor. In addition, any use of hESCs or fetal material by GSK or in collaboration with an external partner requires the approval of the Head of R&D and is strictly not allowed unless it has the potential to provide a significant scientific advance towards treating an unmet need for a serious and debilitating disease that could benefit patients, and where such a scientific advance could not be achieved in any other way.

- GSK does not currently use cybrid embryos in research, however, we recognise their potential value in supporting discovery of novel medicines. Any decision to apply this technology to future GSK research programmes, or those of our external partners, would be made following the same stringent internal guidelines established for embryonic and fetal material use.

Background

Cloning technologies

Cloning is the process of producing an identical copy of something – in the case of biomedical research, a gene, cell, or entire organism. Biomedical researchers have used cloning technology for several decades. The technology has improved our understanding of human biology and led to innovative medical breakthroughs.

There are three main applications of cloning technology in biomedical research: molecular cloning, cellular cloning, and animal cloning – all of which GSK uses in research.

One important example of molecular cloning is to produce a human protein needed to treat a disease. For example, since the discovery of the gene associated with insulin production, molecular cloning has been used to enable bacteria to produce human insulin. The human gene is inserted into bacterial cells that in turn mass-produce human insulin. Prior to this breakthrough, patients with diabetes had to rely on cow or pig insulin, often requiring higher doses and increasing the risk of adverse reactions.

Genetic modification for cell and gene therapies

Current gene editing approaches that provide gene therapies encompasses a range of technologies, either as gene replacement or gene correction. Typically, this involves viral vectors that can introduce new genetic material into a cell; DNA plasmids and RNA molecules can also be used. Whole genes may be inserted into a cell, for example to increase expression of a functional protein. Defective genes can also be corrected using 'molecular scissors' for precise editing that may include TALENS, CRISPR, or base editing. This may be in the patient's own cells, termed autologous therapy, or in cells derived from other adult or stem cell sources, termed allogeneic therapy.

In 2016 GSK received marketing authorization from the European Commission for a stem cell gene therapy to treat patients with Severe Combined Immune Deficiency (ADA-SCID), a rare and life-threatening disorder that affects approximately 350 children worldwide. It was the first corrective gene therapy for children to be awarded regulatory approval anywhere in the world.

Stem cell technologies

Human pluripotent stem cells are unspecialised cells that can renew themselves indefinitely and develop into specialised, more mature cells. For example, pluripotent stem cells give rise to blood, skin, liver, muscle, and a variety of other tissues and organs. Recent advances in stem cell research herald a new approach for producing human cell models for many different organs for use in drug discovery. Human stem cells and stem cell-derived tissues are also used for transplantation and for the treatment of many debilitating diseases and injuries, including macular degeneration, Parkinson's disease, Alzheimer's disease, diabetes, spinal cord injuries, and rare genetic diseases.

Two features of pluripotent stem cells – their potential for differentiating into various specialised cells and their capacity for self-renewal – makes them the logical focus of research into tissue regeneration and production of disease relevant cell types for drug discovery. GSK uses two distinct scientific approaches to develop new medicines using human stem cells:

1. Regenerative therapeutics – identifying medicines which activate stem cells in patients and regenerate cells lost in the disease process, e.g., pancreas cells in diabetes or brain cells in Parkinson's disease.
2. Cellular tools – using stem cells to generate a range of cell types (many of which cannot be safely or physically collected from patients) to identify novel drug targets or determine drug activity and toxicity, e.g., liver hepatocytes, brain neurons, or cultures of contracting heart cells.

Annex

Cloning definitions

Molecular cloning: Molecular cloning involves placing a new piece of DNA into a cell in such a way that every time the cell divides, the DNA is reproduced. This process generates many copies of identical genetic material that can be studied and used in the research process. It also enables production in industrial quantities of the specific protein encoded by a gene.

Cellular cloning: Cellular cloning is used to produce and maintain cell lines of identical cells. A combination of cellular cloning and molecular cloning enables the sequencing of the human genome, which is providing researchers with the ability to investigate the underlying causes of diseases to develop better prevention, treatments, and cures.

Animal cloning: Animal cloning involves a wholly different technique called somatic cell nuclear transfer (SCNT). Somatic cells are non-germline/reproductive cells. This technique removes the nucleus of an unfertilised egg cell (ovum), replaces it with material from the nucleus of a "somatic cell" (a skin cell, for example), from the same species, and then stimulates this reconstructed egg cell (ovum) to begin dividing.

Cybrid embryos: UK legislation passed in 2008 allows research into life-saving diseases using cytoplasmic hybrids, or cybrids. These are made by using eggs from animals, such as rabbits or cows, which have had their nuclei replaced with genetic code from human cells.

Stem cell definitions

Embryonic stem cells: Formed within the first few cell divisions after fertilisation, embryonic stem cells are considered ‘pluripotent’, i.e., they can form almost all the cell types in a body. This unique feature of embryonic stem cells has given scientists optimism that human stem cell research will result in new ways of treating disease.

The most common source of human embryos, from which stem cells are obtained, are surplus embryos from in vitro fertilisation (IVF) programmes, where a woman’s egg is fertilised outside of her body to generate the embryo. Most human embryonic stem cell lines in common usage were generated between 1998 and 2008.

Another potential source is human SCNT as described above (see Animal Cloning).

Fetal stem cells: Fetal stem cells are derived from fetal tissue, where the transition from embryo to fetus in humans is generally defined as being at 9 weeks. Scientists in many research institutions use fetal stem cells because of the scientific limitations of animal cells and adult human stem cells. For example, scientists have found a way of implanting human fetal stem cells into the brains and spinal cords of rats as a step toward creating new therapies for neurodegenerative diseases like Parkinson's disease and Alzheimer's disease.

Adult stem cells: Adult stem cells are “multipotent”. After cells differentiate to become tissues and organs in a human body, some tissues retain a group of these versatile cells to replace mature cells that are damaged or aged. One example is blood stem cells serving to replenish mature blood cells, which are short lived.

Adult stem cells can be collected from both adults and children; they include blood stem cells, which are found in the bone marrow continuously replenishing the body's red blood cells, white blood cells, and platelets.

Induced pluripotent stem cells (iPSCs): Human iPSCs are derived from donor somatic cells and can theoretically divide indefinitely and differentiate into any cell type of the body. They can therefore be used in personalised medicine approaches and are an alternative to the use of embryonic and/or fetal material. They can then be transplanted back into the person from whom they were taken, via a process called autologous cell therapy and thereby avoid rejection. For drug discovery purposes, iPSC technology allows the creation of banks of human cells with defined genotypes of interest to multiple diseases. As such, they provide a highly sophisticated platform to support medicine development.