

---

# Bioethics

---

AstraZeneca  
Global Policy

---

## 1. Purpose

This policy defines the principles, behaviours and ethical standards governing our research and development worldwide.

## 2. Audience

Everyone involved in R&D activities (globally and in our marketing companies).

All relevant supporting functions (such as purchasing, business development and legal).

All employees must report any possible adverse effects relating to our medicines through the established procedures.

To give effect to this Policy, all SET areas are expected to follow any global standards and procedures or, provided they are consistent with this policy, their own local or functional standards and procedures.

## 3. Scope

While many topics are covered by existing national laws and regulations, this document describes the company's global commitment beyond legal compliance.

---

## 4. Policy Statements

### Key Policy Principles

- 4.1** AstraZeneca Group is committed to working only with contractors, such as suppliers, joint venture or co-promotion partners, and research or licensing partners, who embrace standards of ethical behaviour that are consistent with our own.
- 4.2** We will maintain a portfolio of research and development projects designed to deliver drugs that are effective, safe, differentiated and address patients' needs.
- 4.3** We will conduct clinical studies in accordance with all local regulatory requirements and the recognized international quality and safety standards in all countries in which we operate.
- 4.4** We must ensure that the appropriate informed consent procedures are followed when conducting clinical trials, and that the procedures relating to the protection of personal data are applied when we collect or access any health information.
- 4.5** We will make public information about the registration and results of the Group-sponsored clinical trials for all products in all phases, including marketed medicines, drugs in development and drugs whose further development has been discontinued.
- 4.6** We will maintain our commitment to patient safety throughout all of our activity.
- 4.7** All research involving animals must be carefully considered and justified, and the principles of the 3Rs (replacement, reduction and refinement of animal studies) applied. The welfare of the animals we use is a top priority.
- 4.8** Our use of human embryonic stem cells (hESCs) and other fetal tissue, genetic information, other human biological samples and genetically modified organisms must be in line with the requirements of this policy.
- 4.9** We will comply with international standards of good practice, such as The International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use, Good Clinical Practice and Good Laboratory Practice.
- 4.10** We support the general principles set forth in the Convention on Biological Diversity and the Nagoya Protocol. We govern and record our utilisation of genetic resources in accordance with regional and national access and benefit sharing legislation.

## Selecting Disease Targets

- 4.11** The AstraZeneca Group will maintain a portfolio of research and development projects that are designed to deliver drugs that are effective, safe, differentiated and address patients' needs.
- 4.12** The first decisions we take in selecting disease targets are based on the best scientific and professional assessment of:
- Current and future medical needs.
  - Scientific feasibility, in light of the latest scientific knowledge.
  - Available skills and knowledge.

## Conducting Clinical Research Involving Human Studies

- 4.13** AstraZeneca will conduct clinical studies of a drug in development only in countries where we intend to file and market the product.
- 4.14** AstraZeneca Group will conduct clinical studies with human subjects in accordance with all local regulatory requirements and the recognised international quality and safety standards in all countries and territories in which we operate.
- 4.15** The quality and safety standards applied include Good Manufacturing Practices, Good Laboratory Practices, Good Clinical Practices, and the International Conference for Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH).
- 4.16** AstraZeneca Group is committed to determining the potential for developing paediatric indications for our products. Paediatric subjects will be included in our development programmes when it is clinically and ethically justified in order to assess the efficacy and safety of our products. Paediatric studies sponsored by the Group will meet all laws and regulations required for the study of drugs in the paediatric population.

**4.17** Before any First Time in Human (FTiH) studies, preclinical data must indicate the possibility of the candidate drug delivering a clinical benefit with a favourable benefit/risk ratio. A candidate drug with an acceptable safety profile may also be used to test the concept of a novel mechanism, guiding the development of future medications or investigation in man leading to an increased understanding of a disease and its potential treatment.

**4.18** We may engage in placebo-controlled clinical studies when judged scientifically appropriate and ethical. We will take active and specific steps to safeguard the interests of all participants in AstraZeneca Group clinical studies, including those subjects receiving a placebo control.

**4.19** Our informed consent process gives subjects, parents, legal guardians and other concerned parties information about the benefits and risks of participation in the clinical study, as well as privacy, confidentiality and property rights prior to enrolment. In addition, study participants are free to withdraw at any time without any detriment to their medical care.

**4.20** We must ensure that compensation for research participants is consistent with the principle of voluntary participation in clinical studies. Payments to clinical study organisations and investigators must be based on the work they perform and costs incurred.

**4.21** We will design clinical programmes to maximise the exploration of potential benefits for our investigational compounds to the clinical study participants and the intended patient populations, while minimising the risks in all clinical studies conducted by AstraZeneca Group or on our behalf.

**4.22** We will communicate our understanding of the potential benefits and risks of our investigational agents and products to the medical community through approved protocols, Investigator's Brochures, periodic regulatory updates and the publication of clinical study results.

# Clinical Trial Transparency

**4.23** AstraZeneca Group is fully committed to global clinical trial transparency and believes there are important public health benefits associated with making clinical study information available to healthcare professionals and the public in a timely, accurate, meaningful and objective way.

**4.24** We ensure this transparency through the timely registration of clinical studies and posting of the clinical study results on websites and/or publication in peer-reviewed journals. We fully comply with laws, regulations and specific requirements for the registration and reporting of results. Our position is:

- We register and communicate results of all AstraZeneca sponsored clinical trials through web-based postings and where possible through publications.
- We post the research protocol (redacted for personal and confidential information) for AstraZeneca Group-sponsored clinical trials on appropriate web-sites when a manuscript has been published in a peer-reviewed journal.
- We are committed to responding to requests for access to de-identified, individual patient-level data from AstraZeneca sponsored clinical trials. Requests are considered on a case-by-case basis in the context of evolving best practice and relevant legal, data privacy and patient confidentiality requirements.
- We submit redacted Clinical Report Packages to the European Medicines Agency in accordance with their policy and they will make this information public.
- We communicate with patients, via our research sites, to thank them for their participation in our trials, and we will be making Trial Results Summaries available in lay language. These will also be posted to the EU portal.

AstraZeneca is committed to good publishing practice and appropriate communication of information on our products and clinical studies to the international medical and scientific community.

## Initiating Clinical Studies

**4.25** Before initiating FTiH studies – a major milestone in developing new medications – the investigational compound’s characteristics must be confirmed through preclinical safety, toxicology and development studies as required by the medical community, ICH and local regulations.

**4.26** We will base decisions about subject populations for FTiH studies (which may include healthy volunteers, subject populations with a specific disease or medical condition, or subjects who are at risk to develop a specific disease or medical condition) on the known risks and potential benefits to the study subjects, while meeting study goals and minimising health risk.

**4.27** Before FTiH clinical studies commence, preclinical data and proposed early clinical studies must be peer-reviewed by an expert committee within the Group in order to ensure that all safety aspects have been evaluated and that the assessment of potential risk/benefit justifies the testing of the new agent in the clinical setting.

**4.28** Following the internal review, our clinical study protocols must be submitted externally to ethical committees and as required regulatory authorities in the countries where the study will take place.

## Obtaining Informed Consent

- 4.29** We must give those who participate in our clinical studies full, truthful and understandable information, usually in writing and orally. In accordance with the World Medical Association's Declaration of Helsinki and ICH Guidelines for Good Clinical Practice, we communicate clearly about:
- The aim of the study.
  - Details of the procedures and investigational product(s), and the benefits and risks involved.
  - Participants' freedom to withdraw at any time without explanation.
- 4.30** Participants and, for minors, their legally accepted representatives are asked to indicate in writing their receipt of this information and their consent to be part of the study. A specific and mandatory Standard Operating Procedure aims to ensure that ethical and legal requirements for the consent process are met.
- 4.31** If important new information about an investigational product becomes available during an ongoing study, we will communicate this to investigators, ethics committees and participants as appropriate in each situation, and in accordance with applicable law and regulations.

## Maintaining Our Dedication To Patient Safety

- 4.32** AstraZeneca Group is committed to detecting any adverse reactions to its investigational products and approved medicines as early as possible and to providing updated information to investigators, prescribers, consumers and research subjects as appropriate.
- 4.33** All reports of adverse events must be scrutinised by medically qualified individuals. Individual cases judged to be potential safety signals will trigger further analyses of existing data and possible subsequent actions.
- 4.34** Safety data from development projects and marketed products must be regularly analysed to ensure adverse reactions and possible safety signals are identified from both clinical and non-clinical sources.
- 4.35** Research subject risk management plans must be prepared for all products in clinical development. These documents will evolve as safety data become available, so that we can minimise risk and optimise benefits.
- 4.36** The safety organisation follows a defined process aimed at ensuring all relevant patient safety information is incorporated in product labelling and investigator's Brochures.
- 4.37** All employees are required to report any adverse events they become aware of involving any AstraZeneca Group investigational product or approved medicine.

## Privacy Of Information

- 4.38** AstraZeneca Group must protect the privacy of research participants by ensuring all data brought into the Group e.g. clinical, human tissue, health information – are coded, double coded or anonymised to conceal a subject's identity. When studies are performed at our own research units, information about identities must be contained solely within those units. If any research subject information is sent to the Group, it will be handled in a secure and anonymised way.
- 4.39** We will communicate directly with individuals only with their prior consent or in response to requests from prospective volunteers.
- 4.40** We will work with governments and regulators to ensure standards for protecting patient privacy and confidentiality are integral to any new media (Electronic Health Records, online databases, etc.) used to communicate medical data.
- 4.41** It is recognised that we must also be sensitive to the privacy rights of individuals who are defined to be members of small populations, such as rare diseases. In such situations, the 'risk of identification by association with a small population' will be assessed and managed in an appropriate manner.

## Genomic Information And Human Biological Samples

- 4.42** AstraZeneca Group uses genomic information (e.g. from DNA, and/or RNA within human tissues and preclinical models) and human biological samples obtained for research into better understanding of diseases, improved diagnosis or other improvements in healthcare and for the discovery and development of new treatments or drugs. Genomic information and human biological samples are also used for Group-sponsored clinical programmes in the development of pharmaceuticals intended for human use.
- 4.43** The use of genomic information and human biological samples is controlled by application of internal standards that are consistent with relevant legal and regulatory requirements.
- 4.44** Subjects will be given information about the nature and purpose of the investigations and are asked to provide consent to participate. Such consent may be part of the main study consent, for example if the genomic information is used to select patients for therapy, or may be a separate, optional consent if genomic information is to be used for research. If consent is optional, subjects can decide not to take part in the genomics research and still participate in the main clinical study.
- 4.45** AstraZeneca Group may seek access to rare, hard to find historical human biological samples in diagnostic archives where original consent for research is absent. In this situation AstraZeneca Group requests ethical approval for use via an appropriate Research Ethics Committee.

# Genomic Information And Human Biological Samples

**4.46** The genomic data may or may not be returned to the subject depending on the nature of the investigation and on the level of validation of the technology and reagents used to generate it. This will be clearly stated in the consent. If the data is returned to the subject we will specify, in the study protocol, a detailed process for handling such findings. We will communicate in this process to the subjects, and they will acknowledge their acceptance when signing the consent form.

**4.47** As with all clinical research, we take rigorous measures to protect the data privacy of subjects aiming to minimise the risk of their re-identification when processing the data.

**4.48** Human stem cells have the potential to expand understanding of the underlying causes of serious disease. In the laboratory setting, differentiated cell lines derived from stem cells also have the potential to predict drug metabolism and human toxicity more accurately than existing techniques. Increasing knowledge of intracellular pathways should enable us to make different types of mature cells from pluripotent stem cells. This is being used to support discovery of new drugs that may be able to regenerate damaged tissues and organs. For these reasons, AstraZeneca Group is supporting investigation of human stem cell-derived cell lines for use in the laboratory, and we have a rigorous ethical framework that governs our work in this area.

- The majority of AstraZeneca stem cell projects aim to investigate the research potential of human induced pluripotent stem cells (hiPSC) generated by ‘reprogramming’ adult cells to become more stem cell-like. hiPSC can be obtained safely from adult volunteers and do not involve embryos.

We see considerable potential application of cell lines differentiated from hiPSCs in drug discovery including prediction of drug metabolism and human toxicity. We use human embryonic stem cells (hESC) when there is no alternative technology that would provide the scientific information required to increase our knowledge of serious disease.

- Before initiating any hESC research, there must be a clearly defined purpose to increase knowledge about serious disease that cannot be obtained via the use of hiPSC and to apply such knowledge in developing treatments for serious disease.
- The hESC used must come from a fertilised egg that was created through in vitro fertilisation but is no longer needed for reproductive purposes, with fully informed consent to donate the egg for scientific research with no financial inducements.
- We will only use hESC cell lines that have been accepted into a publicly recognised body or bank of registration. All research must be conducted in accordance with applicable local, national and international legislation, regulations and guidelines.
- In rare circumstances, AstraZeneca Group may use human fetal tissue in research to advance our understanding of serious medical disorders. In such rare circumstances, an internal review of the scientific validity of the research proposal will be conducted and permission to use the tissue will be granted only when no other scientifically reasonable alternative is available. In order to further limit and avoid future use of human fetal tissue, we remain on the cutting-edge of scientific advancements and remain committed to implementing industry best practices.

# Genetically Modified Organisms

**4.49** Through genetic engineering, the Group produces Genetically Modified Organisms (GMOs) for the discovery, development and manufacture of new medicines. All GMO work (including work carried out by third parties on our behalf) must be conducted under appropriate levels of biosafety containment and in compliance with relevant environmental, health and safety laws and regulations. The GMOs we use include genetically modified animal and human cells and micro-organisms (GMMs) and genetically modified animals. Accordingly, we will:

- Subject all work to prior risk assessment and apply a precautionary approach to uncertainty.
- Conduct all research and development in facilities designed to provide appropriate containment.
- Support transparency and openness about our use of GMOs.
- Treat waste streams containing GMOs to minimise or prevent discharge into the environment.

## Using Animals In Research Studies

**4.50** AstraZeneca Group considers the responsible use of animals to be ethically appropriate in biomedical research and product safety testing, where suitable alternatives are not available. The following principles apply to all animal studies conducted by the Group and third parties who conduct animal studies on our behalf and to the breeding and supplying of animals for use in such studies.

**4.51** A human approach must be adopted in the care and treatment of all animals, and the greatest consideration is given to their health and welfare, consistent with meeting the necessary scientific objectives. The Group is committed to the principles of the 3Rs: Replacement, Reduction and Refinement.

**4.52** All animal studies must be carefully considered and justified to ensure that the study is scientifically necessary; there is no reasonably practicable alternative to the use of animals (Replacement); only the minimum number of an appropriate species of animal will be used to achieve the scientific objectives (Reduction); and that the study is designed and undertaken to minimise pain and distress to the animals involved (Refinement).

**4.53** The Group is committed to sharing of knowledge of good practices and 3Rs achievements both throughout the Group and the wider scientific community.

**4.54** We must ensure that our own facilities and animal welfare programmes, as well as those of third parties who conduct animal studies on our behalf, comply with our policies. All animal studies must be undertaken in compliance with all relevant local and national laws and regulations, and with the principles of the “Guide for the Care and Use of Laboratory Animals” 8<sup>th</sup> Edition, Institute for Laboratory Animal Research. Wherever possible, our preference is to work with third parties accredited by the Association for the Assessment and Accreditation of Laboratory Animal Care International (AAALAC International).

**4.55** The Group does not conduct or resource work using wild-caught non-human primates or great ape species. In the rare case where there is no credible alternative model to develop a treatment for serious disease, exceptions may be considered. The decision to progress requires rigorous secondary ethical and scientific review to challenge the need for the study, followed by Board-level approval.

## Nagoya Protocol

- 4.56** AstraZeneca believes that a coordinated effort is required on the part of communities, governments and businesses to conserve global biodiversity. We support the general principles set forth in both the Convention on Biological Diversity and the Nagoya Protocol, which together govern the conservation of biodiversity and the fair and equitable return for use of its components.
- 4.57** We assess whether (non-human) genetic resources we intend to access are within scope of the Nagoya Protocol. We obtain genetic resources in accordance with regional and national access legislation, where such laws and regulations exist. Consequently, where appropriate, we will ensure that genetic resources are accessed with the prior informed consent of the country of origin, with a contract of mutually agreed terms in place to ensure the fair and equitable sharing of benefits arising from the utilisation of said materials. These benefits may be monetary or non-monetary, as determined on a case-by-case basis. We will then use these materials in accordance with any mutually agreed conditions of use.
- 4.58** When sourcing materials within the scope of the Nagoya Protocol, we take all reasonable steps to ensure that we, and third party suppliers, demonstrate appropriate due diligence and comply with all relevant access legislation.
- 4.59** We seek and keep relevant information relating to the genetic resources we use. We will make available the required due diligence statements to appropriate authorities at designated checkpoints throughout the research and development of any product that emerges.

## 5. Glossary

Not required.

## 6. References

Not required.

## 5. Revision History

Version	Description of Change
All	Correction of minor typographic errors. Where AstraZeneca is referenced amended to The Company for consistency throughout the document. Where the “partners” is referenced amended to “Third parties who conduct work on our behalf” for consistency throughout the document.
Conducting Clinical Research Involving Human Studies	Additional paragraph to provide a link to the Global Paediatric Standard that was issued on 26th October 2012.
Genetic Information and Human Biological Samples	Minor word amendment for clarity
Genetically Modified Organisms	Removed the word “Micro” to clarify that the scope of genetic modification is not confined to micro-organisms and includes hESCs and whole animals.
Using Animals in Research Studies	Minor word changes for clarity. In general removed examples to avoid them being dated. Removed “avoid pain” as in the UK legislation makes assumption if you use an animal there is some form of pain – so this comment is technically incorrect.
Using Animals in Research Studies	Legislation has now been adopted and new wording reflects The Company’s revised position on use of non-human primates.
Data Privacy	Wording amended to clarify previously ambiguous statement.
Clinical Trials	Removal of one word (rigorous)
Using Animals in Research Studies	General amendments to this section to reflect agreement on global standards for animal use and welfare.
Human Stem Cells	<p>Changed section headings from ‘Human Embryonic Stem Cells’ to ‘Human Stem Cells’.</p> <p>Change accommodates the increasing Company use of human induced pluripotent stem cells (hiPSC). Since these cells can be safely derived from adult donors, their acquisition is less ethically contentious than stem cells derived from human embryos (hESC). Text changes describe the now majority and still increasing use of hiPSC, but the need to also continue with hESC, while the ongoing work both inside and outside the Company continues to fully evaluate and validate the utility of both technologies.</p>
Genetically Modified Organisms	<p>In-keeping with previous changes to the ‘Use of Animals section of this Policy, now emphasises the responsibility of 3rd parties acting on our behalf to align with the principles of our Policy.</p> <p>Added the term ‘genetically modified animals’, in addition to ‘genetically modified cells’ and ‘micro-organisms’. Use of these genetically modified animals (including ‘knock-ins’, knock-outs’, transgenic, and harmful mutants) have been common place in Pharma R &amp; D for several years, but are now specifically itemised in the GMO section.</p> <p>Changed a sentence pertaining to treatment of waste streams to clarify meaning, and minor wording change to remove unintended restrictive meaning.</p>

<b>Version</b>	<b>Description of Change</b>
<b>All</b>	Where AstraZeneca or the 'Company' is referenced, amended to 'AstraZeneca Group' or 'the Group'.
<b>Key Policy Principles</b>	Wording amended to include 'other fetal tissue' and 'other' human biological samples, to reflect the use of human fetal tissue in rare circumstances.
<b>Clinical Trial Transparency</b>	New wording reflects The Group's revised position on clinical trial transparency.
<b>Genetic Information and Human Biological Samples</b>	Additional paragraph reserves the right to access rare, hard to find human biological samples where original consent is absent, given appropriate ethical approval.
<b>Human Stem Cells and Fetal Tissues</b>	<p>Changed section heading from 'Human Stem Cells' to 'Human Stem Cells and Fetal Tissue'.</p> <p>Additional paragraph reflects the potential use of human fetal tissue in rare circumstances, where there is no other scientifically reasonable alternative. Text also emphasises the commitment to limit and avoid future use if possible.</p>
<b>Key Policy Principles</b>	New statement describing AstraZeneca's commitment to the Nagoya Protocol
<b>Clinical Trials</b>	New statement on conditions relating to geographical placement of our clinical studies (Statement 13 in V7.0)
<b>Clinical Trials</b>	Reworded Statement 21 in V7.0 to better describe the general purpose/intent of conducting clinical trials.
<b>Clinical Trials Transparency</b>	Two new AstraZeneca commitments to transparency: submission of Clinical Report Packages; connection with patients who have participated in our trials and publication of lay language summaries.
<b>Genomic Information and Human Biological Samples</b>	Expanded use of 'genetics' to genomics' throughout (whole genome), which is more relevant today. Made clearer throughout that we have two main sets of genomic information: a) for genomics research, which is exploratory & de-identified; b) for clinical studies where patients are selected by genomic data – in this case genomic data is mandatory for trial inclusion, carried out in clinical laboratory and identified at the point of treatment e.g. see Statement 42.
<b>Genomic Information and Human Biological Samples</b>	Statement 43: A more accurate description of our adherence to standards when using data from human subjects.
<b>Genomic Information and Human Biological Samples</b>	Statement 44: A more transparent description of our process when obtaining consent to use samples and data.
<b>Genomic Information and Human Biological Samples</b>	Statement 46: A clearer description on the conditions of returning information (or not) to the study subject.
<b>Genomic Information and Human Biological Samples</b>	Statement 47: A more realistic description of what we can achieve towards maintaining data privacy.
<b>Genomic Information and Human Biological Samples</b>	Human stem cells and fetal tissue content is now contained in this section. Material rearranged to aid flow and understanding.
<b>Nagoya Protocol</b>	New section (Statements 56-59) describing AstraZeneca's commitment to adhere to the legislative requirements of the Nagoya Protocol and concomitant Access & Benefit Sharing.