ASTRAZENECA STANDARD

Global Standard - BIOETHICS

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ASTRAZENECA STANDARD

KEY PRINCIPLES

- ***AstraZeneca is committed to protecting the rights, safety and wellbeing of clinical study participants.***
- ***AstraZeneca is committed to the responsible care and use of animals in research, development and manufacturing.***
- ***AstraZeneca sources and uses human biological samples and human biological sample-derived data responsibly.***
- ***AstraZeneca applies benefit/risk-based approaches in decision making to ensure the responsible conduct of science and innovation.***
- ***AstraZeneca supports the objectives of the Convention on Biological Diversity and the Nagoya Protocol and is committed to effective biosafety management.***

1 WHY IT MATTERS AND TO WHOM

This AstraZeneca (AZ) Standard sets out the mandatory requirements for upholding bioethical principles across the organisation, which are central to our approach to Research and Development (R&D) and aligned to the R&D Framework. Our commitment to these bioethical principles is embedded in the AZ Code of Ethics (Reference 1 in Section 5).

This AZ Standard sets out the overarching principles that underpin bioethical business decision making. They guide the behaviours and ethical business decisions underpinning our work worldwide. These principles are integrated into AZ's procedural documents covering all activities involved in bringing innovative pharmaceutical, medical device, digital health solutions and combination products (hereafter referred to as 'medical products') to patients.

Any principle not explicitly cross-referenced is governed by this AZ Standard. This Standard applies to all AstraZeneca Group and affiliate companies (collectively referred to as "AZ"), all employees (including permanent, temporary, and contract staff), and any third parties engaged in AZ R&D activities. All applicable parties are required to comply with the requirements set out in this AZ Standard, as well as any supporting global and relevant local procedural documents.

2 WHAT YOU NEED TO KNOW AND WHY

2.1 Responsible Clinical Research and Development

2.1.1 Legal Requirements and International Guidelines

AZ is committed to:

- Upholding the fundamental human rights of participants and other individuals involved in our clinical studies. We ensure that our practices respect the dignity, autonomy and rights of participants including their right to informed consent, privacy and the ability to withdraw from clinical studies at any time without penalty; see Human Rights Standard (Reference 2 in Section 5) for further information.
- Protecting the rights, safety and wellbeing of participants by operating in accordance with applicable legal requirements and our internal mandatory procedures.
- Ensuring we have the required authorisations to conduct our clinical studies and market our commercial products; see Regulatory Affairs Standard (Reference 3 in Section 5) for further information.
- Working to secure and maintain licences in line with legal, Institutional Review Board (IRB)/Independent Ethics Committee (IEC) and Health Authority requirements and current manufacturing methods and safety information; see Regulatory Affairs Standard (Reference 3 in Section 5) for further information.
- Conducting clinical studies in accordance with relevant legal requirements and international standards:

- For clinical trials, this includes adherence to the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) Good Clinical Practice (GCP) guidelines (Reference 4 in Section 5), which are based on the ethical principles originating from the Declaration of Helsinki.
- For clinical studies for medical devices, this includes adherence to ISO 14155 (Reference 5 in Section 5), which is based on the ethical principles originating from the Declaration of Helsinki.

- Confirming the candidate medical product's characteristics through preclinical studies prior to initiating clinical studies, in accordance with the expectations of the medical community, ICH GCP guidelines and applicable legal requirements.
- Peer reviewing preclinical data via the relevant expert committees within AstraZeneca to ensure all safety aspects are thoroughly evaluated and that the anticipated benefits justify the known and potential risks of the medical product.
- Obtaining approval from the relevant Safety Board (for example, Executive Safety Board or First in Safety Review Board) before initiating first-in-human clinical studies.
- Conducting clinical studies only in countries where we intend to seek regulatory approval and market the medical product.
- Submitting our clinical study protocols for independent review by an IRB/IEC and, where required, regulatory authorities in the countries where the clinical study will be conducted.
- Driving global clinical trial transparency by making clinical study protocols, documents and results, including individual level data, accessible when required by law, policies and selected best practices; see Clinical Trial Transparency Standard (Reference 6 in Section 5) for further information.

2.1.2 Pharmacovigilance and Patient Safety

AZ is committed to:

- Maintaining controls to ensure the safety, efficacy and quality of our medical products throughout their lifecycle; see Pharmacovigilance and Patient Safety Standard (Reference 7 in Section 5) for further information.

2.1.3 Informed Consent

AZ is committed to:

- Following appropriate informed consent procedures to ensure research and clinical study participation is voluntary and that participants are fully informed.
- Providing participants (or legally acceptable representatives) with comprehensive information about all aspects of the research and/or clinical study, including the nature and purpose, to enable potential participants to assess the benefits, risks and burden of participating and make an informed decision on whether or not to participate.
- Obtaining written (handwritten or electronic) evidence of receipt of this information and consent to participate from participants (or legally acceptable representatives) in accordance with ethical and legal requirements.
- Respecting the rights of all participants, including minors, to withdraw from the research or clinical study at any time without penalty or loss of benefits to which they are otherwise entitled.

- In emergency situations, where prior consent cannot be obtained, securing consent from participants (or legally acceptable representatives) as soon as possible, in accordance with ethical and legal requirements and processes approved by an IRB/IEC.

2.1.4 Patient Centricity

AZ is committed to:

- Promoting the accessibility and patient-centricity of clinical trials through support and compensation initiatives that reduce barriers to, and negative impacts from, participation in clinical studies while avoiding any form of coercion or undue influence.
- Ensuring clinical study populations, wherever possible, reflect the real-world population; see Diversity in Clinical Trials Standard (Reference 8 in Section 5) for further information.
- Developing medical products for paediatric indications to fulfil unmet medical needs; see Paediatric Development Standard (Reference 9 in Section 5) for further information.
- Providing early access to medical products for eligible patients with serious or life-threatening diseases or conditions, in line with AZ's access to medicines principles; see Pre-Marketing Authorisation Access to Medicines Standard (Reference 10 in Section 5) for further information.

2.2 Responsible Care and Use of Animals

AZ is committed to:

- Ensuring the scientific and ethical justification of animal work and the development, application and dissemination of the 3R's:
    - *Replacement: Use of predictive and robust models and tools to replace the use of animals in research, development and manufacturing.*
    - *Reduction: Appropriately designed and analysed animal experiments that are robust and reproducible and add to the knowledge base.*
    - *Refinement: Advancing laboratory animal welfare by using the latest in vivo technologies to minimise pain, suffering and distress and improve understanding of the impact of welfare on scientific outcomes.*
- Requiring, as a minimum, animal care and welfare standards that are consistent with the principles of the latest edition of the Guide for the Care and Use of Laboratory Animals, Institute for Laboratory Animal Research, and compliant with the legislative or administrative controls that apply in the region where the work is being conducted.
    - Facilities accredited by the Association for the Assessment and Accreditation of Laboratory Animal Care International (AAALAC International) have demonstrated that this standard is being met and should be used in preference to facilities with equivalent resources and capabilities that are not so accredited.
- Not conducting or resourcing animal work using wild-caught primates or great ape species.
    - In the rare cases where there is no suitable 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 AZ Board-level approval.

See the Responsible Care and Use of Animals Standard (Reference 11 in Section 5) for further information.

2.3 Responsible Use of Human Biological Samples and Genomic Information

AZ is committed to:

- Respecting a participant's rights to self-determination for all aspects of the lifecycle of human biological samples (HBS) and HBS-derived data.
- Following and using appropriate processes and platforms to ensure HBS due diligence has been conducted for all sourcing and collaborations involving HBS.
- Obtaining informed consent for the collection and use of HBS and genomic information. This may be part of the clinical study consent process, for example, if the genomic information is used to select participants for therapy, or may be part of a separate, optional consent process if genomic information is to be used for research or cell and gene therapy. In circumstances of optional consent, participants can decide not to take part in genomics research or optional and future use of samples or data beyond legal requirements but still participate in the main clinical study, where relevant.
- Ensuring that exceptions to sourcing and use policies (for example, hard-to-find historical HBS in diagnostic archives, where original consent for research is absent), are only granted in rare circumstances and only after full review by the HBS Governance Council as well as any appropriate IRB/IEC approval.
- Specifying in the clinical study protocol and informed consent form if there is an intention to return genomic data to the participant, dependent on the nature of the clinical study and on the level of validation of the technology and reagents used to generate it.
- Using human embryonic stem cells and human foetal tissue only when there is no alternative technology that would provide the scientific information required to increase our knowledge of serious diseases.
- Working only with Category 1 animals containing human material, as defined by the Academy of Medical Sciences, that do not present ethical issues beyond those of the routine use of animals in research and can be conducted under the normal regulatory structures that govern animal research.
- Ensuring all necessary biosafety and biosecurity procedures and risk assessments are completed prior to commencing work due to the potential biohazards HBS present.

See the HBS Standard (Reference 12 in Section 5) for further information.

2.4 Responsible Conduct of Science and Innovation

2.4.1 Quality Management

AZ is committed to:

- Proactively identifying risks and continuously improving our quality management system to ensure safety, quality and efficacy of all our medical products; see Quality Management System Standard (Reference 13 in Section 5) for further information.
- Applying science- and risk-based approaches to decision making in order to mitigate risks to acceptable levels.

2.4.2 Data Privacy

AZ is committed to:

- Collecting personal data only by fair, lawful and transparent means, and being open with individuals about how we use their personal data, with whom we share it, and where it may be sent.
- Protecting any personal data collected, used, retained and disclosed to support our business activities by following the relevant usage, technical and organisational policies, standards and processes.
- Using personal data only where we have a legitimate business need or a legal obligation. We will only process personal data in the way described in the applicable privacy notice and in accordance with any consent we have obtained from the individual.

See the Data Privacy Standard (Reference 14 in Section 5) for further information.

2.4.3 Artificial Intelligence

AZ is committed to:

- Creating and deploying artificial intelligence systems that are private and secure, explainable and transparent, fair, accountable, human-centric and socially beneficial; see Artificial Intelligence (AI) and Analytics Management Standard (Reference 15 in Section 5) for further information.

2.4.4 Cell and Gene Therapy

AZ is committed to:

- Designing cell and gene therapy clinical studies, including long-term follow-up studies, to account for the specific characteristics of these medical products, as well as potential risks to participants, the investigator's team, supply chain, manufacturing and others (for example, offspring and close contacts).
- Excluding human germline targeting of cell and gene therapies at this time.

2.4.5 Externally Sponsored Research

AZ is committed to:

- Managing its support of Externally Sponsored Scientific Research (ESR) in line with the applicable ESR strategy for the AZ medical product or therapeutic area of interest set forth by the relevant Product Team; see Externally Sponsored Scientific Research (ESR) Standard (Reference 16 in Section 5) for further information.

2.4.6 Publications

AZ is committed to:

- Publishing results from our research studies in peer-reviewed journals in a timely way to demonstrate transparency, and publishing irrespective of whether results are positive, negative or inconclusive.
- Following International Committee of Medical Journal Editors (ICMJE) Recommendations and Good Publication Practice (GPP) guidelines by sharing objective and meaningful scientific information about our studies.

See the Publications Standard (Reference 17 in Section 5) for further information.

2.5 Responsible Use of Biological Resources

2.5.1 Biological Diversity

AZ is committed to:

- Supporting the objectives of the Convention on Biological Diversity and the Nagoya Protocol, which together govern the conservation of biodiversity and the fair and equitable use of its components.
    - When sourcing genetic resources within the scope of the Nagoya Protocol, for example, plant, animal or viral genetic material, we take all reasonable steps to ensure that we demonstrate appropriate due diligence and comply with all relevant access legislation.

See Natural Resources and Biodiversity Standard (Reference 18 in Section 5) and Non-Human Genetic Resources Standard (Reference 19 in Section 5) for further information.

2.5.2 Biosafety

AZ is committed to:

- Ensuring effective biosafety management through conducting work in a safe, ethical, and environmentally safe way.
    - This applies to intentional work with biological materials including, but not limited to, biological agents, genetically modified organisms, toxins of biological origin when they exist together with the organism producing them, and materials that may contain or be contaminated with the above.

See OneSHE Biosafety Standard (Reference 20 in Section 5) for further information. See Section 2.3 of this Bioethics Standard for information on biosafety and biosecurity procedures in relation to HBS.