Technical Guideline on the Scope and Classification of Gene Therapy Medicinal Products (2026 Edition)[1]

Authorities: **Center for Drug Evaluation of NMPA.**

Document number: No. 40

Promulgation Date: July 1, 2026

I. Foreword

In recent years, the field of Gene Therapy Medicinal Products (GTMPs) has undergone rapid development and technological evolution. This category of medicinal products encompasses a wide range of product types, is characterized by a high degree of innovation, and exhibits significant differences among product categories with respect to risk profiles and control requirements. Accordingly, clearly defining the scope of GTMPs and establishing a scientifically sound classification thereof are of substantial importance for the development of relevant technical requirements, the standardization and guidance of research and development activities, and the promotion of the healthy development of the industry.

For the purposes of this Guideline, "Gene Therapy Medicinal Products" (GTMPs) refer to medicinal products that, in accordance with the applicable pharmaceutical laws, regulations, and administrative requirements, are developed, submitted for regulatory approval, manufactured, distributed, used, and regulated through the medicinal product regulatory pathway, and that achieve their intended purpose within the human body. Where the research, development, or manufacture of GTMPs involves the utilization of human genetic resources or pathogenic microorganisms, such activities shall comply with the relevant national provisions governing human genetic resources and shall conform to all applicable laws, regulations, and ethical requirements relating to biosafety and biosecurity.

This Guideline is intended to clarify the scope and classification of Gene Therapy Medicinal Products in China and does not affect the existing medicinal product registration classification system. It has been developed on the basis of the current state of industry development and regulatory submissions, domestic and international regulatory practices and standards harmonization, the prevailing level of scientific and technological advancement and scientific understanding, and the ongoing revision and development of relevant technical guidelines. As scientific knowledge, technological innovation, and product development in this field continue to evolve, this Guideline will be updated, as appropriate, in light of future developments.

[1]Translated by Health Law Asia – Pharmaceutical, Medical Device, and Cosmetics Law

II. Scope of Gene Therapy Medicinal Products

For the purposes of this Guideline, Gene Therapy Medicinal Products (GTMPs) refer to medicinal products that, by means of nucleic acids (including DNA and RNA), and/or through the delivery of exogenous gene sequences into the human body using viral or non-viral vectors, or through the use of nucleases and/or protein enzymes acting on specific genes, specifically modify the human gene sequence or regulate gene expression, thereby exerting the relevant biological activity through the replacement, supplementation, inhibition, correction, or silencing of specific genes, so as to achieve their intended therapeutic purpose.

Consistent with the established scope of Gene Therapy Medicinal Products as defined by major international medicinal product regulatory authorities and the World Health Organization (WHO), the term Gene Therapy Medicinal Products, as used in this Guideline, does not include:

- Prophylactic vaccines;
- Chemically synthesized oligonucleotide medicinal products.

III. Classification of Gene Therapy Medicinal Products

1. Non-Microbial Vector-Based Gene Therapy Medicinal Products (Non-Microbial Vector-Based GTMPs)

Gene Therapy Medicinal Products whose active substances, such as nucleic acids, nucleases, or nucleic acid–protein complexes, enter cells within the human body by physical or chemical means, or through non-microbial vector-mediated delivery, and exert their effects following intracellular transcription, splicing, translation, or by direct biological activity, are, according to the nature of the active substance, further classified as nucleic acid-based Gene Therapy Medicinal Products, such as plasmid DNA and mRNA, and nucleic acid–protein complex-based Gene Therapy Medicinal Products, such as Transcription Activator-Like Effector Nucleases (TALENs) and Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR)-associated protein (CRISPR-Cas) systems, among others.

2. Microbial Vector-Based Gene Therapy Medicinal Products (Microbial Vector-Based GTMPs)

Gene Therapy Medicinal Products that employ viruses or non-viral microbial vectors genetically engineered by means of genetic engineering technologies to deliver biologically active nucleic acids into the human body, thereby achieving their intended purpose through the correction or compensation of genetic abnormalities or defects, or through the regulation of gene expression, are further classified as viral vector-based Gene Therapy Medicinal Products, such as adeno-associated viral (AAV) vector-based products and lentiviral vector-based products, and non-viral microbial vector-based Gene Therapy Medicinal Products, such as Salmonella-based vector products.

IV. Classification Principles

The classification of Gene Therapy Medicinal Products shall be determined primarily on the basis of the "material basis and active substance(s)", taking into comprehensive consideration such factors as "manufacturing process", "mechanism of action", and other relevant elements.

I) Material Basis and Active Substance(s)

The active substance(s) of GTMPs may consist solely of nucleic acid molecules, solely of nucleases, of combinations of nucleic acids and proteins, or of nucleic acid sequences integrated into or loaded onto vectors, among other forms. They shall be further classified according to whether the delivery vector employed falls within the category of microbial vectors.

Where the active substance(s) consist solely of nucleic acid molecules, or where nucleic acid molecules are recombinantly integrated into a plasmid vector construct, or are loaded onto a non-microbial vector construct, such products shall be classified as nucleic acid-based medicinal products within the category of Non-Microbial Vector-Based GTMPs, for example, recombinant plasmid DNA medicinal products and mRNA medicinal products loaded into lipid nanoparticles (LNPs). Where the active substance(s) consist solely of nucleases, or of combinations of nucleic acids and proteins, and/or where the foregoing active substance(s) are loaded onto non-microbial vector constructs, such products shall be classified as nucleic acid–protein complex-based medicinal products within the category of Non-Microbial Vector-Based GTMPs, for example, TALEN proteins, CRISPR-Cas nucleic acid–protein complexes, and the like, loaded into lipid nanoparticles (LNPs), virus-like particles (VLPs), or extracellular vesicles (EVs).

Where the therapeutic nucleic acid is carried by a microbial vector, the vector itself together with the nucleic acid it carries collectively constitute the active substance(s), and, following delivery of the therapeutic nucleic acid into cells by the vector in vivo, exert their effect through transcription, translation, or the release of nucleic acid material, such products shall be classified as Microbial Vector-Based GTMPs. Among these, medicinal products in which the therapeutic nucleic acid is carried by a viral vector, such as an adenoviral vector, an adeno-associated viral (AAV) vector, a lentiviral vector, or a herpes simplex viral (HSV) vector, shall be classified as viral vector-based medicinal products. Medicinal products in which the therapeutic nucleic acid is carried by a non-viral microbial vector, such as a Salmonella vector or a Listeria vector, shall be classified as non-viral microbial vector-based medicinal products.

Where oncolytic virus or oncolytic bacterial medicinal products carrying exogenous therapeutic genes exert oncolytic activity (Oncolytic abilities), and the viral or live bacterial component functions not only as an active substance but also as a delivery vector mediating the introduction and expression of the exogenous gene sequence, thereby acting synergistically to exert oncolytic activity, such products shall be classified as Microbial Vector-Based Gene Therapy Medicinal Products within the category of GTMPs.

II) Manufacturing Process

Medicinal products whose active substance(s) consist principally of nucleic acids, nucleases, or other similar substances produced by means of biotechnology fall within the scope of GTMPs, for example, plasmid DNA produced by fermentation, mRNA produced by in vitro transcription, TALENs, CRISPR-Cas systems, base editors, Prime Editors (PEs), Adenosine Deaminases Acting on RNA (ADARs), and the like.

Medicinal products employing delivery vectors produced by means of biotechnology (such as viral vectors, bacterial vectors, extracellular vesicles, and the like) to deliver active substance(s), including nucleic acids and nucleic acid–protein complexes, shall be included within the scope of GTMPs.

(III) Mechanism of Action

GTMPs generally exert their biological activity through active substance(s) consisting of nucleic acids or nucleases and/or protein enzymes acting on specific nucleic acid sequences, by specifically altering (repairing, replacing, inserting, or deleting) human gene sequences or regulating gene expression, whereby their mechanism of action is directly associated with nucleic acid sequences and/or gene expression products in vivo. Common mechanisms of action are exemplified as follows:

GTMPs may exert their effects by altering human gene sequences, including through the insertion, deletion, or mutation of gene sequences. For example, recombinant adeno-associated viral vector-based gene therapy medicinal products intended for the treatment of monogenic genetic disorders achieve their effects through the replacement, repair, insertion, or deletion of the relevant gene(s).

GTMPs may regulate gene expression (including that of exogenous genes), thereby achieving gene supplementation, knockdown (interference), activation, or silencing.

GTMPs may modulate the microenvironment through their gene expression products. For example, recombinant or genetically engineered oncolytic viral or oncolytic bacterial medicinal products are capable of selectively infecting tumour cells and/or replicating within tumour cells, thereby lysing tumour cells, and may simultaneously stimulate or enhance the host anti-tumour immune response through the expression of exogenous genes, thereby exerting a synergistic oncolytic effect.

GTMPs may activate specific immune responses through the in vivo expression of tumour neoantigens. For example, neoantigen mRNA medicinal products.

(IV) Other Considerations

Medicinal products represented by in vivo CAR-T therapies, whose active substance(s) principally comprise nucleic acid sequences delivered by delivery vectors (such as viral vectors, lipid nanoparticles (LNPs), and the like), and which exert their intended biological function through the in vivo generation of chimeric antigen receptor cells, shall be classified as GTMPs.

Where medicinal products employ anucleate cells (e.g., erythrocytes) as cellular vectors, and the active substance(s) principally responsible for their pharmacological activity consist of nucleic acid molecules and/or protein molecules, such as nucleases, loaded therein, and exert their principal effect through mechanisms including the alteration of gene sequences or the regulation of gene expression, such products shall be classified as Non-Microbial Vector-Based GTMPs.

The active substance(s) of neoantigen medicinal products may exist in various forms. Where the active substance consists of a neoantigen nucleic acid (such as DNA or mRNA), or of a neoantigen nucleic acid delivered by a viral vector, such products shall be classified as GTMPs.

For other complex circumstances, or for novel situations arising from technological advances, developers/applicants are encouraged to communicate and consult with the drug regulatory review authority regarding the appropriate classification of their products.

V. References

[1] World Health Organization. Considerations in Developing a Regulatory Framework for Human Cells and Tissues and for Advanced Therapy Medicinal Products. WHO Technical Report Series No. 1048, Annex 3 [EB/OL]. 2023.

[2] European Medicines Agency. Reflection Paper on Classification of Advanced Therapy Medicinal Products (EMA/CAT/600280/2010 Rev.1) [EB/OL]. 2015.

[3] European Medicines Agency. Procedural Advice on the Provision of Scientific Recommendation on Classification of Advanced Therapy Medicinal Products in Accordance with Article 17 of Regulation (EC) No. 1394/2007 [EB/OL]. 2021.

[4] U.S. Food and Drug Administration. Title 21, Code of Federal Regulations, Part 1271 (21 CFR Part 1271) [EB/OL]. 2026.

[5] United States 114th Congress. Public Law 114-255: 21st Century Cures Act, Section 3033 [EB/OL]. 2016.

[6] International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH). ICH Guideline S12: Nonclinical Biodistribution Considerations for Gene Therapy Products [EB/OL]. 2023.

[7] Center for Drug Evaluation, National Medical Products Administration. Technical Guideline for Pharmaceutical Research and Evaluation of In Vivo Gene Therapy Products (Trial Implementation) [EB/OL]. 2022.

[8] Center for Drug Evaluation, National Medical Products Administration. Technical Guideline for Pharmaceutical Research and Evaluation of Oncolytic Virus Products (Trial Implementation) [EB/OL]. 2023.

[9] Center for Drug Evaluation, National Medical Products Administration. Technical Guideline for Pharmaceutical Research and Evaluation in Support of Clinical Trial Applications for In Vivo Gene Therapy Products Based on Recombinant Adeno-Associated Viral Vectors [EB/OL]. 2024.