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Biotechnology — Nucleic acid synthesis — Part 2: Requirements for the production and quality control of synthesized gene fragments, genes and genomes

~~DIS stage~~

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Foreword

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This document was prepared by Technical Committee ISO/TC 276, *Biotechnology*.

A list of all parts in the ISO 20688 series can be found on the ISO website.

Any feedback or questions on this document should be directed to the user's national standards body. A complete listing of these bodies can be found at ~~www.iso.org/members.html~~www.iso.org/members.html.

Introduction

Gene fragment, gene and genome synthesis refer to producing synthetic double-stranded DNA in the form of non-clonal fragments (that can be linear) and clonal genes in plasmids (that would be circular) by using appropriate biochemical methods.

Synthesized gene fragments, genes and genomes are important biotechnological products and are widely used in biotechnology, e.g. protein engineering, metabolic engineering, antibody and vaccine development, environmental bioremediation and natural product discovery.

The production and quality control of the synthesized gene fragment, gene and genome products are essential for ensuring the quality and their downstream applications in biotechnology. This document provides requirements for the production and quality control of synthetic gene fragment, gene and genome products, including biosecurity, purity, yield, size, gene cloning accuracy, integrity, sequences, residual impurities and other quality indicators. This document provides a uniform general guideline for the quality control of gene fragments, genes and genomes synthesis. It is intended to help to improve and ensure the quality of products and fair trade based on a unified standard.

This document is intended to be used by synthetic DNA producers during the manufacturing process for quality control to improve the quality of their products, by academic laboratories to evaluate the quality of DNA synthesized in their facilities, and by end users to verify the quality of synthesized gene fragments, genes and genomes provided by manufacturers as required.

In this document, the following verbal forms are used:

— “shall” indicates a requirement;

— “should” indicates a recommendation;

— “may” indicates a permission;

— “can” indicates a possibility or a capability.

Biotechnology — Nucleic acid synthesis — Part 2: Requirements for the production and quality control of synthesized gene fragments, genes and genomes

1 Scope

This document specifies the requirements for the production and quality control of synthesized double-stranded DNA. It describes requirements for quality management, resource management, biosafety and biosecurity, quality control in production, product quality, and delivered product specifications for synthesized gene fragments, genes and genomes.

This document is applicable to synthetic gene fragments, genes and genomes with a length below 10 Mbp (base pairs) in forms of non-clonal fragments (linear) and clonal genes in plasmids (circular).

This document does not provide specific requirements for materials used solely for diagnostic purposes.

When the synthesized nucleic acids are procured and used for diagnostic purposes, the user can take ISO 15189, ISO 13485 and other related clinical standards into account.

2 Normative references

There are no normative references in this document.

3 Terms and definitions

For the purposes of this document, the following terms and definitions apply.

ISO and IEC maintain terminology databases for use in standardization at the following addresses:

— ISO Online browsing platform: available at ~~https://www.iso.org/obp~~https://www.iso.org/obp

— IEC Electropedia: available at ~~https://www.electropedia.org/~~https://www.electropedia.org/

3.1
biosafety
practices and controls that reduce the risk of unintentional exposure or release of biological materials

Note 1 to entry: Biological materials refer to any material comprised of, containing, or that may contain ~~biological agents~~biological agents and/or their harmful products, such as toxins and allergens (see ISO 35001:2019, 3.14).

Note 2 to entry: Biological agents refer to any microbiological entity, cellular or non-cellular, naturally occurring or engineered, capable of replication or of transferring genetic material that may be able to provoke infection, allergy, toxicity or other adverse effects in humans, animals, or plants (see ISO 35001:2019, 3.13).

[SOURCE: ISO 35001:2019, 3.22, modified — Notes to entry were added.]

3.2
biosecurity
practices and controls that reduce the risk of loss, theft, misuse, diversion of, or intentional unauthorized release of biological materials

[SOURCE: ISO 35001:2019, 3.23, modified — Notes to entry were deleted.]

3.3
colony polymerase chain reaction
colony PCR
~~**colony polymerase chain reaction**~~
PCR method used to screen for plasmids containing a desired insert directly from microbial colonies without plasmid extraction and purification steps

3.4
DNA assembly
joining oligonucleotides or smaller gene fragments via regions of complementarity to form a longer double-stranded DNA fragment step by step *in vitro* or *in vivo*

3.5
DNA sequencing
determining the order of nucleotide bases (adenine, guanine, cytosine and thymine) in a molecule of DNA

Note 1 to entry: Sequence is generally described from the 5′ end.

[SOURCE: ISO 17822:2020, 3.19]

3.6
gene cloning
process of introducing a particular gene or DNA sequence using genetic engineering techniques into a host cell and replicating it by asexual reproduction into many identical copies of the gene

3.7
~~**MPS**~~
massively parallel sequencing
MPS
sequencing technique based on the determination of incremental template-based polymerization of many independent DNA molecules simultaneously

Note 1 to entry: Massively parallel sequencing technology can provide millions/billions of short reads per run or long reads based on amplification~~.~~.

[SOURCE: ISO 20397-2:2021, 3.30, modified — Note to entry was edited by adding "or long reads based on amplification.]

3.8
plasmid vector
extrachromosomal DNA molecule in cells physically separated from the chromosome and capable of autonomous replication that can be used as vehicle to carry new genes into cells

[SOURCE: ISO 16577:2022, 3.4.37, modified — “vector” added to the term, and “that can be used as vehicle to carry new genes into cells” added to the definition (from ISO 16577:2022, 3.4.58). Notes to entry deleted~~.~~.]

3.9
quality score
Q score
measure of the sequencing quality of a given nucleotide base

Note 1 to entry: *Q* is defined by the following formula: