ISO/~~CD TS~~ DTS 4424

ISO/TC 215/SC 1~~/WG 1~~

Secretariat: KATS

Date: 2023-09-01

Genomics ~~Informatics~~ informatics — Data ~~Elements~~elements and their ~~Metadata~~metadata for ~~Describing~~describing the ~~Tumor Mutation Burden~~tumor mutation burden (TMB) ~~Information~~information of ~~Clinical Massive Parallel~~clinical massive parallel DNA ~~Sequencing~~sequencing

~~*CD*~~ *Informatique génomique — Éléments de données et leurs métadonnées pour décrire les informations relatives à la charge tumorale mutationnelle (TMB) du séquençage massif parallèle d'ADN*

FDIS stage

~~**Warning for WDs and CDs**~~

~~This document is not an ISO International Standard. It is distributed for review and comment. It is subject to change without notice and may not be referred to as an International Standard.~~

~~Recipients of this draft are invited to submit, with their comments, notification of any relevant patent rights of which they are aware and to provide supporting documentation.~~

Formatted
Style Definition
Style Definition
Style Definition
Style Definition
Style Definition
Style Definition
Style Definition
Style Definition
Style Definition
Style Definition
Style Definition
Style Definition
Style Definition
Style Definition
Style Definition
Style Definition
Style Definition
Style Definition
Style Definition
Style Definition
Style Definition
Style Definition
Style Definition
Style Definition
Style Definition
Style Definition
Style Definition
Style Definition
Style Definition
Style Definition
Style Definition
Style Definition
Style Definition
Style Definition
Style Definition
Style Definition
Style Definition
Style Definition
Style Definition
Style Definition
Style Definition
Style Definition
Style Definition
Style Definition
Style Definition
Formatted
Formatted
Formatted
Formatted

To help you, this guide on writing standards was produced by the ISO/TMB and is available at https://www.iso.org/iso/how-to-write-standards.pdf

A model manuscript of a draft International Standard (known as "The Rice Model") is available at https://www.iso.org/iso/model_document-rice_model.pdf

Formatted: Font: Bold

Formatted: Space Before: 0 pt, After: 0 pt

ISO copyright office
CP 401 • Ch. de Blandonnet 8
CH-1214 Vernier, Geneva
Phone: + 41 22 749 01 11
~~Email~~E-mail: copyright@iso.org
Website: ~~www.iso.org~~www.iso.org

Published in Switzerland

Formatted: Font: 11 pt, Bold
Formatted: Space After: 0 pt, Line spacing: single
Formatted: Font: 11 pt, Bold
Formatted: Font: 11 pt, Bold
Formatted: Left: 1.9 cm, Right: 1.9 cm, Bottom: 1 cm, Gutter: 0 cm, Header distance from edge: 1.27 cm, Footer distance from edge: 0.5 cm
Formatted: Indent: Left: 0 cm, Right: 0 cm, Adjust space between Latin and Asian text, Adjust space between Asian text and numbers
Formatted: French (Switzerland)
Formatted: French (Switzerland)
Formatted: French (Switzerland)
Formatted: Space After: 0 pt, Line spacing: single
Formatted: Font: 11 pt
Formatted: Font: 11 pt

Formatted: Font: 11 pt, Bold
Formatted: Left, Space After: 0 pt, Line spacing: single
Formatted: Font: 11 pt, Bold
Formatted: Font: 11 pt, Bold

Contents

Formatted: Font: 11 pt
Formatted: Space After: 0 pt, Line spacing: single
Formatted: Font: 11 pt
Formatted: Font: 11 pt

Formatted: Font: 11 pt, Bold
Formatted: Font: 11 pt, Bold
Formatted: Space After: 0 pt, Line spacing: single
Formatted: Font: 11 pt, Bold
Formatted: Space After: 0 pt, Line spacing: single
Formatted: Font: 11 pt
Formatted: Font: 11 pt

Formatted: Font: 11 pt, Bold
Formatted: Left, Space After: 0 pt, Line spacing: single
Formatted: Font: 11 pt, Bold
Formatted: Font: 11 pt, Bold
Formatted: Font: 11 pt
Formatted: Space After: 0 pt, Line spacing: single
Formatted: Font: 11 pt
Formatted: Font: 11 pt

Formatted: Font: 11 pt, Bold
Formatted: Font: 11 pt, Bold
Formatted: Space After: 0 pt, Line spacing: single
Formatted: Font: 11 pt, Bold
Formatted: Space After: 0 pt, Line spacing: single
Formatted: Font: 11 pt
Formatted: Font: 11 pt

Foreword

ISO (the International Organization for Standardization) is a worldwide federation of national standards bodies (ISO member bodies). The work of preparing International Standards is normally carried out through ISO technical committees. Each member body interested in a subject for which a technical committee has been established has the right to be represented on that committee. International organizations, governmental and non-governmental, in liaison with ISO, also take part in the work. ISO collaborates closely with the International Electrotechnical Commission (IEC) on all matters of electrotechnical standardization.

The procedures used to develop this document and those intended for its further maintenance are described in the ISO/IEC Directives, Part~~-~~ 1. In particular, the different approval criteria needed for the different types of ISO ~~documents~~document should be noted. This document was drafted in accordance with the editorial rules of the ISO/IEC Directives, Part~~-~~ 2 (see www.iso.org/directives).

~~Attention is drawn~~ISO draws attention to the possibility that ~~some of~~ the ~~elements~~implementation of this document may ~~be~~involve the ~~subject~~use of (a) patent(s). ISO takes no position concerning the evidence, validity or applicability of any claimed patent rights~~.~~ in respect thereof. As of the date of publication of this document, ISO had not received notice of (a) patent(s) which may be required to implement this document. However, implementers are cautioned that this may not represent the latest information, which may be obtained from the patent database available at www.iso.org/patents. ISO shall not be held responsible for identifying any or all such patent rights. ~~Details of any patent rights identified during the development of the document will be in the Introduction and/or on the ISO list of patent declarations received (see www.iso.org/patents).~~

Any trade name used in this document is information given for the convenience of users and does not constitute an endorsement.

For an explanation of the voluntary nature of standards, the meaning of ISO specific terms and expressions related to conformity assessment, as well as information about ISO's adherence to the World Trade Organization (WTO) principles in the Technical Barriers to Trade (TBT), see ~~www.iso.org/iso/foreword.html~~www.iso.org/iso/foreword.html.

This document was prepared by Technical Committee ISO/TC 215, *Health informatics*, Subcommittee SC 1, *Genomics ~~informatics~~Informatics*.

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.

Formatted: Left, Space After: 0 pt, Line spacing: single
Formatted: Font: 11 pt, Bold
Formatted: Font: 11 pt, Bold
Formatted: Font: 11 pt, Bold
Formatted: Foreword Text
Field Code Changed
Formatted: Font: Font color: Auto
Formatted: Font: Font color: Auto
Formatted: Font: 11 pt
Formatted: Space After: 0 pt, Line spacing: single
Formatted: Font: 11 pt
Formatted: Font: 11 pt

Formatted: Font: 11 pt, Bold
Formatted: Font: 11 pt, Bold
Formatted: Space After: 0 pt, Line spacing: single
Formatted: Font: 11 pt, Bold

Introduction

Formatted: Body Text

With the rapid advancement of next-generation sequencing (NGS) technologies, clinical sequencing has been applied to realize personalized and precision medicine. ~~ISO/TS 20428[1] Health informatics — Data elements and their metadata for describing structured clinical genomic sequence information in electronic health records has been~~ISO/TS 20428[1] was published to standardize the clinical sequencing reports in electronic health records. After introducing NGS panel sequencings (whole genome, whole exome, targeted gene sequencing), they are widely used in the clinical field.

In the field of cancer treatment, various treatment strategies were tried differently from traditional anti-cancer chemotherapies. Recently, drugs related to the immune system were developed and more efficient for patients with specific tumor molecular characteristics. It is the immune checkpoint blockade drug such as the first approved drug – Ipilimumab, an anti-cytotoxic T-lymphocyte antigen (CTLA4) for non-small cell lung cancer.~~[2]~~[2] Tumors can use these checkpoints to protect themselves from immune system attacks. Currently approved checkpoint therapies block inhibitory checkpoint receptors. Blockade of negative feedback signaling to immune cells thus results in a continued immune response against tumors. It was reported that the status of Programmed Death-Ligand 1 (PD-L1) expression or the status of TMB (Tumor Mutation Burden) could be used as the predictive marker for the efficacy of the immune checkpoint blockade because TMB is considered an indirect measurement of how many tumor cell-specific peptide fragments are presenting and the increase of antigen-presenting leads more immune reaction.~~[3]~~[3]

The status of TMB ~~could~~can be calculated and reported from detected genomic variants by NGS DNA sequencing. According to national regulatory agencies, including US-FDA, several NGS sequencing products are being approved for companion diagnostics.~~[4]~~[4] Some NGS sequencing products provide TMB status and value on their NGS sequencing report. CLIA-certified labs or equivalent-level agencies in countries also serve the TMB value from their own methods. It is forecasted that more clinical NGS sequencing will be approved to report TMB.~~[5]~~[5]

However, there is no international standard for describing TMB status, value, and metadata. The previous ISO/TS 20428 focused on only DNA variations compared with the reference genome. Some research results said that TMB values and how to describe them are different even if using the same sequencing data. The absence of a standard for TMB representation makes it difficult for clinicians and researchers not only to use TMB results for clinical decision support but also for secondary ~~analyzing~~analysing purposes when receiving from more than one sequencing lab. Related metadata should be essential to expand the usage of TMB values.

In this document, the data elements and their standardized metadata for TMB in electronic health records will be described. The clinical report for TMB will provide proper information on bioinformatics analysis to help clinical decisions.

Formatted: Space After: 0 pt, Line spacing: single
Formatted: Font: 11 pt
Formatted: Font: 11 pt

Genomics informatics — Data Elementselements and their Metadatametadata for Describingdescribing the Tumor Mutation Burdentumor mutation burden (TMB) Informationinformation of Clinical Massive Parallelclinical massive parallel DNA Sequencingsequencing

1 Scope

This Technical Specificationdocument identifies data elements and metadata to represent the information about tumor mutation burden (TMB) when reporting the value for the biomarker using clinical massive parallel DNA sequencing.

This document covers the TMB status and related metadata such as mutation type, sequencing types, and target areas of sequencing from human samples for clinical practice and research.

This document is not intended

— to define experimental protocols or methods for calculating the value of tumor mutation burden,

— for the other biological species, and

— for the Sanger sequencing methods.

2 Normative references

The following documents are referred to in the text in such a way that some or all of their content constitutes requirements of this document. For dated references, only the edition cited applies. For undated references, the latest edition of the referenced document (including any amendments) applies.

ISO 8601 (all parts), *Date and time — Representations for information interchange*

ISO/TS 20428:2017 22220:2011, *Health informatics — Data elements and their metadata for describing structured clinical genomic sequence information in electronic — Identification of subjects of health recordscare*

ISO/TS 27527, *Health informatics — Provider identification*

3 Terms and definitions

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

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

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

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

3.1
biological specimen
biospecimen
specimen
sample of tissue, body fluid, food, or other substance that is collected or acquired to support the assessment, diagnosis, treatment, mitigation or prevention of a disease, disorder or abnormal physical state, or its symptoms

Formatted: Font: 11 pt, Bold
Formatted: Left, Space After: 0 pt, Line spacing: single
Formatted: Font: 11 pt, Bold
Formatted: Font: 11 pt, Bold
Formatted: Main Title 1, Space After: 0 pt
Formatted: Font: Bold
Formatted: Body Text
Formatted: List Continue 1, Indent: Left: 0 cm, First line: 0 cm
Formatted: Body Text
Formatted: RefNorm
Formatted: Body Text
Formatted: List Continue 1, Indent: Left: 0 cm, First line: 0 cm
Formatted: No underline, Font color: Auto

[SOURCE: ISO/TS 20428:2017, 3.34]

3.2
clinical sequencing
next generation sequencing or later sequencing technologies with human samples for clinical practice and clinical trials

[SOURCE: ISO/TS 20428:2017, 3.5]

3.73
deoxyribonucleic acid
DNA
molecule that encodes genetic information in the nucleus of cells

[SOURCE: ISO 25720:2009, 4.7]

3.84
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/TS 17822-1:2014:2020, 3.2019]

3.95
exome
part of the genome formed by exons

[SOURCE: ISO/TS 20428:2017, 3.13]

3.106
FASTA
genomic information representation that includes a name and a nucleotide (3.) sequence for each sequence read (3.)

[SOURCE: ISO/IEC 23092-2:2019, 3.7]

3.11
FASTQ
genomic information representation that includes FASTA (3.10) and quality values

[SOURCE: ISO/IEC 23092-2:2019, 3.8]

3.12
gene
basic unit of hereditary material that encodes and controls the expression of a protein or protein subunit

[SOURCE: ISO 11238:2012, 2.1.162018, 3.29]

3.137
gene panel
technique for sequencing the targeted genes in a genome

[SOURCE: ISO/TS 20428:2017, 3.15]

Formatted: Font: 11 pt, Bold
Formatted: Font: 11 pt, Bold
Formatted: Space After: 0 pt, Line spacing: single
Formatted: Font: 11 pt, Bold
Formatted: Source
Formatted: Source
Formatted: Source
Formatted: Note
Formatted: Source
Formatted: Source
Formatted: Source
Formatted: Source