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ISO/CD TS <u>DTS</u> 4424

ISO-<u>/</u>TC-_215/SC-_1/WG

Secretariat:-KATS

Date: 2023-09-0

Genomics Informatics informatics — Data Elements elements and their Metadata for Describing the Tumor Mutation Burdentumor mutation burden (TMB)
Informationinformation of Clinical Massive Parallelclinical massive parallel DNA Sequencing

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ISO/DTS 4424

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

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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

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Foreword

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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).

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

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.

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Introduction

With the rapid advancement of next-generation sequencing (NGS) technologies, clinical sequencing has been applied to realize personalized and precision medicine.

180/TS 20428[1] Health informatics — Data elements and their metadata for describing structured clinical genomic sequence information in electronic health records has been[SO/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 anticancer 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 nonsmall cell lung cancer. [21[21]] 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. [23[3]]

The status of TMB couldcan 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. 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.

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 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.

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Genomics informatics—— Data <u>Elements elements</u> and their <u>Metadata metadata</u> for <u>Describing describing</u> the <u>Tumor Mutation</u> <u>Burdentumor mutation burden</u> (TMB) <u>Information information</u> of <u>Clinical Massive Parallel clinical massive parallel</u> DNA <u>Sequencing sequencing</u>

1 Scope

This <u>Technical Specificationdocument</u> 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 2b-6e b-4bb

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. $\label{eq:formula} % \begin{center} \begin{cen$

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

- —_—ISO Online browsing platform: available at https://www.iso.org/obp
- ____IEC Electropedia: available at 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

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ISO/CD TSDTS 4424:(E) Formatted: Font: 11 pt, Bold Formatted: Font: 11 pt, Bold Formatted: Space After: 0 pt, Line spacing: single [SOURCE: ISO/TS 20428:2017, 3.34] Formatted: Font: 11 pt, Bold Formatted: Source 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] Formatted: Source deoxyribonucleic acid DNA molecule that encodes genetic information in the nucleus of cells [SOURCE: ISO 25720:2009, 4.7] Formatted: Source 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. Formatted: Note [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] Formatted: Source 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 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] Formatted: Source 3.137 gene panel technique for sequencing the targeted genes in a genome [SOURCE: ISO/TS 20428:2017, 3.15] Formatted: Source

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