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Genomics informatics — Data elements and their metadata for describing the tumor mutation burden (TMB) information of clinical massive parallel DNA sequencing

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National foreword

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Foreword

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

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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. 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]. 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].

The status of TMB 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]. 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]

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 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.

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Genomics informatics — Data elements and their metadata for describing the tumor mutation burden (TMB) information of clinical massive parallel DNA sequencing

1 Scope

This document 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 22220:2011, *Health informatics — Identification of subjects of health care*

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 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

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

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