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Genomics informatics — Structured clinical gene fusion report in electronic health records

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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*.

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Introduction

With the rapid advancement of next generation sequencing technologies, clinical sequencing has been applied to realize precision medicine. ISO/TS 20428[1] aims at standardizing the clinical sequencing reports in electronic health records but focuses on only DNA variations. However, the importance of transcriptome information has been increased. The transcriptome is the complete set of all messenger RNA molecules, which encode for the amino acid sequence of proteins. RNA sequencing gives us a large amount of information on gene expression and RNA alterations in disease status. From a molecular diagnostic standpoint, RNA-based measurements have the potential for broad application across diverse areas of human health, including disease diagnosis, prognosis, and therapeutic selection.

A fusion gene is a hybrid gene made by the combination of two or more genes that had previously existed independently. It is known to occur due to structural abnormalities of chromosomes such as insertion, deletion, translocation, and inversion. Fluorescence in situ hybridization (FISH) has been used as a gold standard as a method of detecting gene fusion in clinical practice but advances in technology have enabled RNA-based detection of fusion genes that directly affect protein coding. One of the most widely applied RNA-based technologies is qRT-PCR (Quantitative Reverse Transcription-Polymerase Chain Reaction). The relatively inexpensive NGS (Next generation sequencing) method is actively used in clinical practice as it detects many genes at once. There are DNA-based and RNA-based methods for detecting fusion using NGS, but it is recognized that using RNA-based is more accurate in terms of detection sensitivity.

Technological advancements have continually shaped the way that RNA-based (transcriptome) measurements are used in the clinic. There are several commercially available RNA-based clinical tests.[2] In order to complement ISO/TS 20428, the RNA sequencing report is necessary. Among driver RNA sequencing results, the most prevalent gene fusion was chosen as the first step. This document will aid in developing other clinical RNA sequencing or whole transcriptome sequencing reports.

In this document, the data elements and their standardized metadata for gene fusion report using RNA sequencing in electronic health records will be described. A structured clinical report for the fusion gene will provide pertinent information on bioinformatics analysis to help clinical decisions.

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Genomics informatics — Structured clinical gene fusion report in electronic health records

1 Scope

The document defines the data elements and their necessary metadata to implement a structured clinical gene fusion report whose data are generated by next generation sequencing technologies.

This document

— describes the reporting guideline for RNA sequencing approaches focusing on detecting novel and known fusion partners,

— defines the required data fields and their metadata for a structured clinical gene fusion report,

— defines the optional data fields and their metadata,

— covers the fusion gene from human specimen using whole transcriptome sequencing by next generation sequencing technologies for clinical practice and translational research,

— does not cover the fusion gene detection using DNA sequencing methods,

— does not cover the basic research and other scientific areas,

— does not cover the other biological species,

— does not cover the Sanger sequencing methods, and

— does not cover the other structural variations.

This document only defines the data elements and their metadata for the structured clinical sequencing report in electronic health records. Therefore, its layout can be designed based on the institutional decision if all elements are included as in this document.

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 20397-2:2021, *Biotechnology — Massively parallel sequencing — Part 2: Quality evaluation of sequencing data*

ISO/TS 22220:2011, *Health informatics — Identification of subjects of health care*

ISO/TS 22692:2020, *Genomics informatics— Quality control metrics for DNA sequencing*

ISO/TS 27527:2010, *Health informatics — Provider identification*

HGNC:Bruford E.A., Braschi B., Denny P. et al. , *Guidelines for human gene nomenclature*. Nat Genet **52**, 754–758 (2020). https://doi.org/10.1038/s41588-020-0669-3

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