# IVDR compliance audit report

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## Contents



## 1 What this document shows

This document queries all parameters for an example: RUN123 and uses the results to automatically populate a template. This template matches needs for regulatory compliance. The run ID indicates a processing step which can contain the data of one or more subjects which results in an analysis output. The following database extract shows an example of this data for an analysis run for one subject

```
## [1] "SQL database connection is active and ready."
```

```
##   run_id   run_date    status sample_id collection_date       source
## 1 RUN123 2024-07-16 Completed   XYZ_001      2024-07-15 Laboratory A
## 2 RUN123 2024-07-16 Completed   XYZ_001      2024-07-15 Laboratory A
##       analysis_type  result              key metadata_value genome_name
## 1 Variant Detection Success  Pipeline Config        Default        <NA>
## 2 Variant Detection Success Reference Genome         REF001  GRCh38.p13
##   genome_version component_name component_version commit_id
## 1           <NA>           GATK              v4.0   a1b2c3d
## 2           v1.0           GATK              v4.0   a1b2c3d
```

# 2 Introduction to IVDR

The In Vitro Diagnostic Medical Devices Regulation (IVDR) is an essential legislative framework that governs the safety and performance of in vitro diagnostic medical devices (IVDs) within the European Union. Implemented to enhance patient safety and ensure high standards of quality, the IVDR was adopted alongside the Medical Devices Regulation (MDR) to update and replace directives established in the 1990s, reflecting significant technological and scientific advancements in the sector.

Reference examples of U.S. F.D.A cleared or approved companion diagnostic devices (In Vitro and Imaging Tools) can be found at https://www.fda.gov/medical-devices/in-vitro-diagnostics/list-cleared-or-approved-companion-diagnostic-devices-in-vitro-and-imaging-tools.

# 3 Guidance

The European commission guidance for MDCG endorsed documents and other guidance can be found here: (link on health.ec.europa.eu). From here we assess the **Regulation (EU) 2017/746 (IVDR) on in vitro diagnostic medical devices** in English from here: (link on eur-lex.europa.eu). To ensure that we remain updated and complaint, we designed `eur_lex_scraper.R` which retrieves this guideline and converts all 133 articles (20240716) into a table. We then assign criteria to determine the relevance of each article to our product. The following table shows the head of the article titles and subtitles, with the main content hidden.

We use these guidelines to tag and map our variables to ensure that each element in a pipeline/network are accurately covered for regulatory compliance.

| title | content |
|---|---|
| Article 1 | Article 1 Subject matter and scope 1. This Regulation lays down rules concerning the placing on th... |
| Article 2 | Article 2 Definitions For the purposes of this Regulation, the following definitions apply: 'medical... |
| Article 3 | Article 3 Regulatory status of products 1. Upon a duly substantiated request of a Member State, th... |
| Article 4 | Article 4 Genetic information, counselling and informed consent 1. Member States shall ensure that... |
| Article 5 | Article 5 Placing on the market and putting into service 1. A device may be placed on the market o... |
| Article 6 | Article 6 Distance sales 1. A device offered by means of information society services, as defined ... |
| Article 7 | Article 7 Claims In the labelling, instructions for use, making available, putting into service and ... |
| Article 8 | Article 8 Use of harmonised standards 1. Devices that are in conformity with the relevant harmonis... |
| Article 9 | Article 9 Common specifications 1. Where no harmonised standards exist or where relevant harmonise... |
| Article 10 | Article 10 General obligations of manufacturers 1. When placing their devices on the market or put... |

```
##    skipping to end...
```

| title | content |
|---|---|
| Article 104 | Article 104 Levying of fees 1. This Regulation shall be without prejudice to the possibility for M... |
| Article 105 | Article 105 Funding of activities related to designation and monitoring of notified bodies The costs... |
| Article 106 | Article 106 Penalties The Member States shall lay down the rules on penalties applicable for infring... |
| Article 107 | Article 107 Committee procedure 1. The Commission shall be assisted by the Committee on Medical De... |
| Article 108 | Article 108 Exercise of the delegation 1. The power to adopt delegated acts is conferred on the Co... |
| Article 109 | Article 109 Separate delegated acts for different delegated powers The Commission shall adopt a sepa... |
| Article 110 | Article 110 Transitional provisions 1. From 26 May 2022, any publication of a notification in resp... |
| Article 111 | Article 111 Evaluation By 27 May 2027, the Commission shall assess the application of this Regulatio... |
| Article 112 | Article 112 Repeal Without prejudice to Articles 110 (3) and (4) of this Regulation, and without pre... |
| Article 113 | Article 113 Entry into force and date of application 1. This Regulation shall enter into force on ... |

# 4 Variable definitions

Here are the definitions for the variables included in the audit report, categorised by their respective data sources:

- From the `Runs` Table (Prefix `r.`)
  - r.run_id: Unique identifier for the analysis run.
  - r.run_date: Date on which the analysis run was performed.
  - r.status: Current status of the run (e.g., completed, pending, failed).
  - r.sample_id: Identifier linking to the specific sample used in the run.
- From the `Samples` Table (Prefix `s.`)
  - s.collection_date: Date on which the sample was collected.
  - s.source: Source from where the sample was obtained (e.g., Laboratory A, Patient).
- From the `Analyses` Table (Prefix `a.`)
  - a.analysis_type: Type of analysis conducted (e.g., Variant Detection, RNA-Seq).
  - a.result: Outcome or result of the analysis.
- From the `Metadata` Table (Prefix `m.`)
  - m.key: Key or name of the metadata entry (e.g., Reference Genome, Pipeline Config).
  - m.value as 'metadata_value': Value associated with the metadata key, providing specific details like reference genome IDs or configuration settings.
- From the `ReferenceGenomes` Table (Prefix `rg.`)
  - rg.name as 'genome_name': Name of the reference genome used in the analysis.
  - rg.version as 'genome_version': Version of the reference genome.
- From the `SystemComponents` Table (Prefix `sc.`)
  - sc.component_name: Name of the software or system component used in the run.
  - sc.component_version: Version of the component.
- From the `GitLog` Table (Prefix `gl.`)
  - gl.commit_id: Git commit ID that references the specific version of code or configuration used in the analysis.

# 5 Compliance and audit content

This report provides a complete audit trail for run ID: RUN123. Below are the details of the components used in the analysis, including software versions, reference data, and version control details.

| run_id | run_date | status | sample_id | collection_date | source | analysis_type | result | key | metadata_value | genome_name | genome_version | component_name | component_version | commit_id |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| RUN123 | 2024-07-16 | Completed | XYZ_001 | 2024-07-15 | Laboratory A | Variant Detection | Success | Pipeline Config | Default | NA | NA | GATK | v4.0 | a1b2c3d |
| RUN123 | 2024-07-16 | Completed | XYZ_001 | 2024-07-15 | Laboratory A | Variant Detection | Success | Reference Genome | REF001 | GRCh38.p13 | v1.0 | GATK | v4.0 | a1b2c3d |

## 5.1 Sample details

Details of the sample associated with the run.

| sample_id | collection_date | source |
|---|---|---|
| XYZ_001 | 2024-07-15 | Laboratory A |

## 5.2 System overview

Here we detail the specific components of the system used for the audit run: RUN123.

| component_id | run_id | component_name | component_version |
|---|---|---|---|
| 1 | RUN123 | GATK | v4.0 |

## 5.3 Version control management

Details of the version control for components used in this analysis.

| log_id | run_id | component_id | commit_id |
|---|---|---|---|
| 1 | RUN123 | 1 | a1b2c3d |

### 5.4 Reference genome details

Information about the reference genome information, as linked from the run metadata used for the specified run.

```
## Reference Genome Details for run ID: RUN123 :
```

| reference_id | name | version |
|---|---|---|
| REF001 | GRCh38.p13 | v1.0 |

### 5.5 Compliance Tagging and Audit Trails

Audit trails for compliance checks.

| audit_id | run_id | event | event_time | details |
|---|---|---|---|---|
| 1 | RUN123 | Compliance Check | 2024-07-17 12:00:00 | Passed initial compliance checks |

## 6 Database relationship network

The database relationship network plot visually represents the interconnectedness of various elements within the database, in this case DNAsnake_v1.0. The ability to make this plot demonstrates how different pieces of data are related and how they flow through the analysis pipeline. Here's a detailed explanation of what this plot means in terms of SQL and how it is used to audit any element at any stage of our analysis:

1. **Nodes**:
   - Each node in the graph represents a specific piece of data within the database, labeled with both the variable name and its value. For example, 'r.sample_id: XYZ_001' represents the sample ID used in the run.
   - Nodes are derived from different tables in the database such as 'Runs', 'Samples', 'Analyses', 'Metadata', 'ReferenceGenomes', 'SystemComponents', and 'GitLog'.
2. **Edges**:
   - Edges represent the relationships between these pieces of data. For example, an edge from 'r.run_id: RUN123' to 'r.sample_id: XYZ_001' shows that the run identified by 'RUN123' is associated with the sample 'XYZ_001'.
   - These relationships are based on the foreign key constraints defined in the database schema.

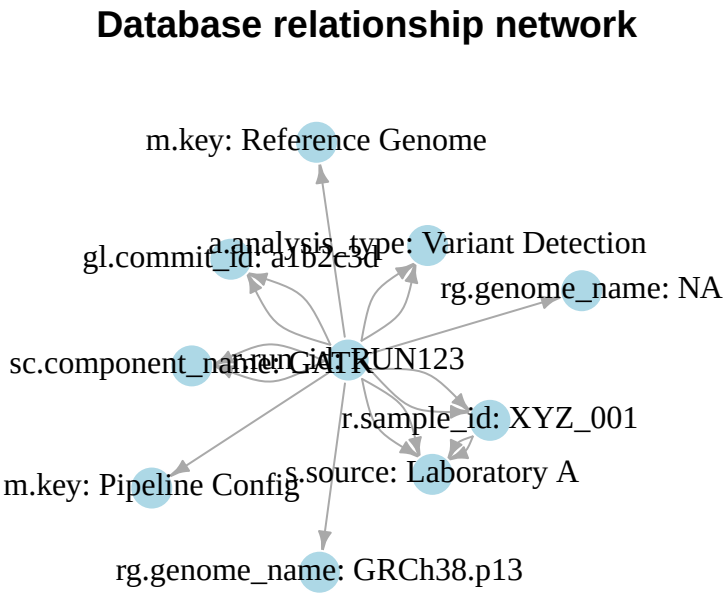
### 6.1 SQL and the data flow

In SQL terms, the relationships depicted in the plot are the result of JOIN operations between tables. Here's how different tables are joined to form a comprehensive view of the data:

- **Runs Table (`r.`)**: Contains information about each analysis run, such as 'run_id', 'run_date', 'status', and 'sample_id'.
- **Samples Table (`s.`)**: Provides details about the sample, including 'collection_date' and 'source'.
- **Analyses Table (`a.`)**: Stores the type of analysis conducted and the result.
- **Metadata Table (`m.`)**: Holds additional metadata related to the run, such as the reference genome used.
- **ReferenceGenomes Table (`rg.`)**: Contains details about the reference genomes.

- **SystemComponents Table (`sc.`)**: Lists the software components used in the analysis and their versions.
- **GitLog Table (`gl.`)**: Tracks the specific Git commits associated with the software components used.
- **AuditTrail Table (`at.`)**: Records events and details related to compliance checks.

By maintaining such a detailed and interconnected database, we ensure that all data used in analyses is transparent, verifiable, and compliant with the IVDR guidelines. This approach significantly enhances the reliability and credibility of the analysis results, supporting the overall goal of ensuring high standards of quality and patient safety.




This report shows the graph-based approach to our data tracking system which allows use to initiate an audit process from any arbitrary data point (e.g. sample ID, software ID, run) and demonstrates compliance with IVDR standards for all of the related information.