Qlucore Diagnostics BCP-ALL

Summary of Safety and Performance (SSP)

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Summary of Safety and Performance Qlucore Diagnostics BCP-ALL

This Summary of Safety and Performance (SSP) is intended to provide public access to an updated summary of the main aspects of the safety and performance of the Qlucore Diagnostics BCP-ALL.

The SSP is not intended to replace the Instructions For Use as the main document to ensure the safe use of the device, nor is it intended to provide diagnostic or therapeutic suggestions to intended users or patients.

The following information is intended for professional users.

A. Summary of safety and performance for professional users

Document revision: 3.0

Date issued: 2025-02-13

Manufacturer's reference number for the SSP: QLUC-755301155-526

1. Device identification and general information

1.1. Trade Name of Device

- **Qlucore Diagnostics BCP-ALL (IVD medical device)**
  - **Qlucore Diagnostics BCP-ALL model (Component)**
- Qlucore Diagnostics Platform (Accessory to an IVD medical device)

1.2. Name and Address of Manufacturer

Qlucore AB
Qlucore AB(publ)
Scheelevägen 17
223 70 Lund
Sweden

1.3. Single Registration Number (SRN) of Manufacturer

SE-MF-000030781

1.4. Basic UDI

07350148192KC (Qlucore Diagnostics BCP-ALL)

07350148191KA (Qlucore Diagnostics Platform)

1.5. European Medical Device Nomenclature Description / text

W02050192 – NUCLEIC ACID TESTING INSTRUMENTS EXCEPT MICRO-ARRAYS – IVD MEDICAL DEVICE SOFTWARE

1.6. Risk class of Device

Qlucore Diagnostics BCP-ALL is a class C device.

Qlucore Diagnostics Platform is a class A device.

1.7. Indication whether it is a device for near-patient testing and/or a companion diagnostic

The device is not intended for near-patient testing. The device is not a companion diagnostic device.

1.8. Year of First Certificate (CE)

No certificate (to be decided).

1.9. Name and SRN of Authorized Representative

Not applicable.

1.10. Name and Single Identification Number (SIN) of Notified Body (NB)

Notified Body: BSI

Single Identification Number: 2797

2. Intended use of the device

2.1. Intended Purpose

Qlucore Diagnostics BCP-ALL:

The Qlucore Diagnostics BCP-ALL is software intended for qualitative determination of the presence of clinically relevant genetic markers in samples from bone marrow or peripheral blood during the genetic work-up of pediatric B-cell precursor Acute Lymphoblastic Leukemia (BCP-ALL).

The software supports an analysis of RNA-Seq data using gene expression-based classification and gene fusion identification. The classification of the sample is achieved by a machine learning-based classifier, which yields a probability score for the following defined genetic subtypes:

· BCR::ABL1 or BCR::ABL1-like

· DUX4-rearranged

· ETV6::RUNX1 or ETV6::RUNX1-like

· High hyperdiploidy

· KMT2A(MLL)-rearranged

· TCF3::PBX1

Gene fusion identification is performed by fusion callers, and identified gene fusions are exported to a report along with fusion breakpoints. The results obtained from the Qlucore Diagnostics BCP-ALL can be used to aid in the initial classification and management of pediatric patients from one up to 18 years of age, with suspected or diagnosed BCP-ALL. The results of the analyses are not intended for minimal residual disease (MRD) monitoring. Standard laboratory protocols for processing patient blood or bone marrow samples, library preparation from purified mRNA and whole-transcriptome RNA-sequencing should be followed. The operation of the Qlucore Diagnostics BCP-ALL, as well as the interpretation of the analysis results is to be carried out by trained healthcare professionals in a clinical laboratory setting and used in conjunction with other clinical and laboratory findings. Test results are not to be interpreted as a negative result based on the absence of a fusion gene or absence of a specific subtype of BCP-ALL based on the gene expression probability score. The Qlucore Diagnostics BCP-ALL is intended to be used together with the Qlucore Diagnostics Platform software.

Qlucore Diagnostics Platform:

The Qlucore Diagnostics Platform is a software specifically intended to be used together with one or several Qlucore Diagnostics Models, by providing it a hosting environment, execute it, and report analysis results.

The Qlucore Diagnostics Platform is intended to be used by trained healthcare professionals in a clinical laboratory setting.

2.2. Indication and Target Population

Pediatric B-cell precursor acute lymphoblastic leukemia (BCP-ALL).

2.3. Contraindications and/or Limitations

Contraindications:

- patient with ongoing infection
- patient on cytotoxic drugs
- purpose of analysis to follow up after cancer treatment

Limitations: None

3. Device description

3.1. Description of Device

Qlucore Diagnostics BCP-ALL is a software intended for installation at a computer in a clinical lab and is used for analysis, interpretation and display of results based on data from next-generation sequencing of pediatric samples from bone marrow or peripheral blood.

Qlucore Diagnostics BCP-ALL allows the user to import RNA-sequencing data that has been aligned and processed by gene fusion detection algorithms. Following import into Qlucore Diagnostics BCP-ALL, the software enables the use of two key features:

1) identification of gene fusions and
2) classification of the tested sample into known subtypes of BCP-ALL, based on gene expression levels.

The gene fusions are automatically controlled from a quality perspective and presented into different Tiers (Tier 1, 2 or 3) based on their relevance for BCP-ALL.

The gene expression analysis of BCP-ALL subtypes is made using a highly tailored classifier built by Qlucore from a training dataset. These two key features can support each other in subtype classification.

A clinical report, summarizing the results, is automatically generated. The user can then add a conclusion text to the report, if needed, and export the report as a pdf document. The report contains in addition to the results a PCA Plot for illustration.

3.2. Description of kit components

Not applicable.

3.3. Previous generations or variants

Not applicable.

3.4. Description of accessories intended to be used in combination with the device

Qlucore Diagnostics Platform is the accessory to be used with the device, description of platform included in intended purpose and device descriptions above.

3.5. Description of other devices or products intended to be used in combination with the device

Not applicable.

4. Reference to any applicable standards and common specifications applied

Relevant aspects of the standards listed below are to be used to support product conformity of the products Qlucore Diagnostics Platform and Qlucore Diagnostics BCP-ALL:

- EN ISO 13485:2016 - Medical devices – Quality management systems – Requirements for regulatory purposes (ISO 13485:2016),
  EN ISO 13485:2016/A11:2021,
  EN ISO 13485:2016/AC:2018
- EN ISO 14971:2019 – Medical devices – Application of risk management to medical devices (ISO 14971:2019),
  EN ISO 14971:2019/A11:2021
- IEC 62366 :2015+AMD1:2020 CSV - Medical devices - Part 1: Application of usability engineering to medical devices
- IEC 62304:2006+AMD1:2015 CSV - Medical device software - Software life-cycle processes,
- SS-EN ISO 13612:2012 - In vitro-diagnostik - Utvärdering av prestanda för in vitro-diagnostiska medicintekniska produkter,
  SS-EN 13612/AC:2016
- ISO 20916:2019 - In vitro diagnostic medical devices — Clinical performance studies using specimens from human subjects — Good study practice
- SS-EN ISO 20417:2021 - Medicintekniska produkter - Information som ska tillhandahållas av tillverkaren (ISO 20417:2021)
- SS-EN ISO 15223-1:2021 - Medicintekniska produkter - Symboler att användas vid märkning av produkt och information till användare - Del 1: Allmänna krav (ISO 15223-1:2021)
- ISO 20397-1:2022 - Biotechnology – Massively parallel sequencing – part 1: Nucleic acid and library preparation
- ISO 20397-2:2021 - Biotechnology – Massively parallel sequencing – part 2: Quality evaluation of sequencing data
- AAMI+CR34971-2022 - Guidance on the Application of ISO 14971 to Artificial Intelligence and Machine Learning
- IEC 81001-5-1 - Health software and health IT systems safety, effectiveness and security – Security – Activities in the product life cycle
- ISO/IEC TS 4213:2022 - Information technology – Artificial intelligence – Assessment of machine learning classification performance
- ISO/IEC 23894 – Information technology – Artificial intelligence – Guidance on risk management
- ISO/TR 24971:2020 Medical devices – Guidance on the application of ISO 14971
- ISO 18113-1:2022 In vitro diagnostic medical devices – information supplied by the manufacturer (labelling) – part 1: Terms, definitions and general requirements

There are no common specifications available for this type of the device.

5. Risks and warnings

5.1. Residual Risks and Undesirable Effects

- The device is intended to be used for mRNA-based BCP-ALL analysis. The device may give false negative and/or positive results with all quality metrics within approved limits.
- The device is intended to be used for mRNA-based BCP-ALL analysis. The device creates a report based on input files. If the report is created based on incorrect input files or data, the result report cannot be trusted for medical purposes.

- The device is intended to be used for BCP-ALL gene fusion analysis. Significant fusions may be missed because callers do not always detect them and therefore not recognized by the device as tier 1. Instead, those fusions may be listed in the tier 2 or tier 3 tables.
- The device may report errors during a case-run that stop the case execution and prevent erroneous results.
- A residual risk exists that unauthorized users may gain access to the host computer and access and alter input files, output files, or settings, including the log file. This risk may only be further reduced by the responsible healthcare organization (laboratory, hospital, or similar).
- A residual risk exists that unauthorized users may gain access to the host computer and inject unauthorized python code. This risk may only be further reduced by the responsible healthcare organization (laboratory, hospital, or similar), by preventing unauthorized access to the machine.
- The device is intended to be used for BCP-ALL gene fusion analysis. False negative results occur for so called "3-way fusions" in Mitelman as these are ignored by the device and the fusion callers.

5.2. Warnings and precautions

- A residual risk exists that unauthorized users may gain access to the host computer and access and alter input files, output files, or settings, including the log file. This risk may only be further reduced by the responsible healthcare organization (laboratory, hospital, or similar).
- A residual risk exists that unauthorized users may gain access to the host computer and inject unauthorized python code. This risk may only be further reduced by the responsible healthcare organization (laboratory, hospital, or similar), by preventing unauthorized access to the machine. A residual risk exists that the local area network may be attacked if viruses and/or malware enter the host computer. This risk may only be further reduced by the responsible healthcare organization (laboratory, hospital, or similar).
- Some Qlucore Diagnostics updates are published to address safety or security related issues. A residual risk exists that the update information is missed or not acted upon.
- Tier 1 gene fusions table may include gene fusions not relevant for BCP-ALL as the definitions in guidelines include wildcards.
- Running the Qlucore Diagnostics application in command-line mode requires knowledge of using the terminal application on your system.
- The model used in command-line mode refers to a model file stored on disk and is completely independent from the models installed in the application using graphical user interaction. Always make sure to specify the correct version of the model when running in command-line mode.

5.3. Other relevant aspects of safety

There are no other relevant aspects of safety applicable.

6. Summary of performance evaluation and post-market clinical follow-up (PMCF)

6.1. Summary of scientific validity of the device

Scientific validity of the Qlucore Diagnostics BCP-ALL has been evaluated through the review of external data and the device clinical performance study.

The general association between genetics and subtypes is well-known, whereas the specific methods used by Qlucore Diagnostics BCP-ALL are novel. The scientific validity of the Qlucore Diagnostics BCP-ALL is well

established in scientific literature and clinical guidelines and further supported by the data collected on the device.

6.2. Summary of performance data from the equivalent device, if applicable

Not applicable.

6.3. Summary of performance data from conducted studies of the device prior to CE-marking

The Qlucore Diagnostics BCP-ALL performance has been shown in a clinical performance study, using retrospective data from 257 patients. A subset of 106 samples had a state-of-the-art reference test result enabling them to be used for calculating diagnostic accuracy, providing the device diagnostic sensitivity of 91.5% (86.2 - 96.8) and a diagnostic specificity of 98.3% (97.2 - 99.4). A subset of 46 samples having a state-of-the-art reference test for gene fusion analysis showed 100% equivalent results. The complete data set of 257 samples were included in calculating diagnostic accuracy and supported the high Qlucore Diagnostics BCP-ALL performance in statistical calculations of positive and negative agreement.

The clinical performance is further supported by a supportive classifier test using 70 clinical samples, showing high performance, as well as the usability testing showing the users ability to correctly load and retrieve information from Qlucore Diagnostics BCP-ALL.

6.4. Summary of performance data from other sources, if applicable

Not applicable.

6.5. An overall summary of the performance and safety

Qlucore has collected clinical evidence on the Qlucore Diagnostics BCP-ALL. The clinical evidence collected on Qlucore Diagnostics BCP-ALL supports the device performance and safety as stated in the intended use. The clinical evidence is considered of sufficient quality and quantity.

6.6. Ongoing or planned post-market performance follow-up

There has not yet been any post-market clinical follow-up performed.

The following post market performance follow up activities are planned:

1. Screening of scientific literature with focus on clinical performance.

2. Screening of Acute lymphoblastic leukemia (ALL) classification guidelines (e.g., WHO, ICC) or current protocols for pediatric ALL

3. Screening of scientific literature for confirmation of scientific validity.

4. Risk management sections that may affect PSUR and PER.

5. Performance evaluation report sections that may need to be updated in PMPF.

6. Post-market clinical performance study.

7. The metrological traceability of assigned values

7.1. Explanation of the unit of measurement, if applicable

Not applicable.

7.2. Identification of applied reference materials and/or reference measurement procedures of higher order used by the manufacturer for the calibration of the device

Not applicable.

8. Suggested profile and training for users

Qlucore Diagnostics is intended to be used by trained healthcare professionals in a clinical laboratory setting. Specially roles such as:

- geneticist, laboratory scientist or bioinformatician for the bioinformatic pipeline,
- geneticist or laboratory scientist for running a case
- bioinformatician, geneticist or laboratory scientist for command-line usage and
- pathologist/Medical Doctor specialist within genetics and or oncology for interpreting the report.

No specific user training, prior to using the device is required.

9. Revision history

SSP revision number	**Date issued**	**Change description**	**Revision validated by the Notified Body**
Revision 2.0	2024-08-19	Address corrected, EMDN code corrected	☒Yes Validation language: English ☐No (only applicable for class C (IVDR, Article 48 (7)) for which the SSP is not yet validated by the NB)
Revision 3.0	2025-02-13	Editorial changes to layout	☐Yes ☐Validation language: English