June 2026

ipsogen® IDH1 RGQ PCR Kit Summary of Safety and Performance

Σ 24

Version 1

IVD

For In Vitro Diagnostic Use
For use with Rotor-Gene Q® instrument
For use with QIAamp® DSP DNA Blood Mini Kit

CE 0197

REF 675223

QIAGEN GmbH, QIAGEN Strasse 1, 40724 Hilden, GERMANY

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Summary of Safety and Performance

This Summary of Safety and Performance (SSP) is intended to provide public access to an up-to-date summary of the main aspects of the safety and performance of the device.

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.

The following information is intended for professional users.

Document revision: 001
Date issued: June 2026
Manufacturer's reference number for the SSP: HB-3824-SPR

1. Device identification and general information	
1.1 Device trade name(s)	*ipsogen*® IDHI RGQ PCR Kit
1.2 Manufacturer's name and address	QIAGEN GmbH, QIAGEN Strasse 1, 40724 Hilden, Germany
1.3 Manufacturer's single registration number (SRN)	DE-MF-000004949
1. 4 Basic UDI-DI	4053228RIDH100000000001BZ
1.5 European Medical Device Nomenclature (EMDN) description / text	W01060299 TESTS FOR ACQUIRED GENETIC OR CHROMOSOMAL ALTERATIONS - OTHER

1.6 Risk Class of the device	Class C
1.7 Year when the first certificate was issued under Regulation (EU) 2017/746 covering the device	2026
1.8 Authorized representative if applicable; name and the SRN	Not Applicable as the manufacturer is within the EU.
1.9 Notified body and the single identification number (SIN)	TÜV Rheinland LGA Products GmbH NB 0197
2. Intended purpose and other indications	
2.1 Intended purpose	The *ipsogen* IDH1 RGQ PCR Kit is a qualitative real-time PCR assay for the detection of single nucleotide variants (SNVs) coding five IDH1 mutations (R132C, R132H, R132G, R132S, and R132L), using genomic DNA

	extracted from fresh or frozen human whole blood or bone marrow aspirate specimens collected in K2-EDTA tubes from patients with acute myeloid leukemia (AML). The test is intended to be used as a companion diagnostic device to aid clinicians in identifying AML patients who may be eligible for treatment with TIBSOVO® (ivosidenib), based on the detection of an IDH1 mutation. TIBSOVO may be administered in combination with azacitidine, in accordance with its approved indications. The test is not intended to guide treatment decisions for azacitidine. Fresh or frozen human whole blood or bone marrow aspirate specimens, collected in K2-EDTA tubes, are processed manually using the QIAamp® DSP DNA Blood Mini Kit. The QIAGEN® Rotor-Gene® Q MDx 5plex HRM instrument is used for automated amplification and detection. The *ipsogen* IDH1 RGQ PCR Kit is not an automated device; however, the analysis is assisted by a dedicated software. The *ipsogen* IDH1 RGQ PCR Kit is to be used by trained personnel in a professional laboratory environment. The *ipsogen* IDH1 RGQ PCR Kit is intended for in vitro diagnostic use.
2.2 Indication(s) and target population(s)	The *ipsogen* IDH1 RGQ PCR Kit is a companion diagnostic device, which is indicated for use as an aid to clinicians in the identification of AML patients in EU who may be eligible for treatment with TIBSOVO (ivosidenib), based on the detection of an IDH1 mutation. TIBSOVO may be administered in combination with azacitidine, in accordance with its approved indications. The test is not intended to guide treatment decisions for azacitidine. It is a qualitative real-time PCR test used to analyze genomic DNA, extracted from fresh or frozen, human whole blood or bone marrow

	aspirate specimens collected in K2-EDTA tubes, from patients with acute myeloid leukemia.
2.3 Indication whether it is a device for near-patient testing and/or a companion diagnostic	The *ipsogen* IDH1 RGQ PCR Kit is a companion diagnostic device.
2.4 Limitations and/or contra-indications	• The test is not intended to be used as a companion diagnostic device to aid clinicians in identifying patients with locally advanced or metastatic cholangiocarcinoma who may be eligible for treatment with TIBSOVO based on the detection of an IDH1 mutation. • Detection of mutations is dependent on sample integrity and the amount of amplifiable DNA present in the specimen. • The test is designed to detect five mutations within codon 132 of the IDH1 gene. Samples with results reported as "No Mutation Detected" may contain IDH1 mutations not detected by the assay. • The *ipsogen* IDH1 RGQ PCR Kit uses a polymerase chain reaction (PCR) procedure. As with all PCR procedures, samples may be contaminated by external sources of DNA in the test environment and the DNA in the positive control. Use caution to avoid contamination of samples and reaction mix reagents. • The *ipsogen* IDH1 RGQ PCR Kit is only for use with whole blood (WB) and bone marrow aspirate (BMA) samples collected in K2-EDTA tubes. • The *ipsogen* IDH1 RGQ PCR Kit is only for use with the QIAGEN QIAamp DSP DNA Blood Mini Kit.

	• Strict compliance with the *ipsogen* IDH1 RGQ PCR Kit Handbook is required for optimal results. Dilution of the reagents, other than as described in this handbook, is not recommended, and will result in a loss of performance. • The *ipsogen* IDH1 RGQ PCR Kit may only be used when all reaction components from the same kit lot are used together. • The product is intended only for use on the Rotor-Gene Q MDx instrument. • The *ipsogen* IDH1 RGQ PCR Kit is a qualitative test. The test is not for quantitative measurements of percent mutation. • Performance of the *ipsogen* IDH1 RGQ PCR Kit is unknown if microbial contamination is introduced during assay procedures. • Performance of the *ipsogen* IDH1 RGQ PCR Kit could be affected in the presence of cytarabine, decitabine, triglycerides, etoposide, idarubicin hydrochloride, daunorubicin hydrochloride, or azacitidine in the test samples.
3. Device description	
3.1 Description of the device, including the conditions to use the device	**Intended use** The *ipsogen* IDH1 RGQ PCR Kit is a qualitative real-time PCR assay for the detection of single nucleotide variants (SNVs) coding five IDH1 mutations (R132C, R132H, R132G, R132S, and R132L), using genomic DNA extracted from fresh or frozen human whole blood or bone marrow aspirate specimens collected in K2-EDTA tubes from patients with acute myeloid leukemia (AML). This test is intended to be used as a companion diagnostic device to aid clinicians in identifying AML patients who may be eligible for treatment with TIBSOVO (ivosidenib), based on the detection of an IDH1 mutation.

	TIBSOVO may be administered in combination with azacitidine, in accordance with its approved indications. The test is not intended to guide treatment decisions for azacitidine. Fresh or frozen human whole blood or bone marrow aspirate specimens, collected in K2-EDTA tubes, are processed manually using the QIAamp DSP DNA Blood Mini Kit. The QIAGEN Rotor-Gene Q MDx 5plex HRM instrument is used for automated amplification and detection. The *ipsogen* IDH1 RGQ PCR Kit is an in vitro diagnostic medical device. **Intended user** The *ipsogen* IDH1 RGQ PCR Kit is to be used by trained personnel in a professional laboratory environment. **Principle of the procedure** The *ipsogen* IDH1 RGQ PCR Kit is based on the detection by selective amplification of five IDH1 mutations in genomic DNA (gDNA) extracted from WB or BMA specimens. Allele-specific technology allows accurate and highly reproducible detection of target IDH1 mutations, based on the use of specific forward and reverse primer and probe sets; mutation-specific primers bind selectively to the target DNA, which promotes extension and amplification in the PCR reaction.

<table>
<tr><td></td><td>Result reporting is fully automated. If both the run controls and the sample results are valid, and assay target amplification is below the pre-determined cutoff threshold, the report will display the IDH1 mutation(s) detected in each sample.</td></tr>
<tr><td>3.2 In case the device is a kit, description of the components (including regulatory status of components, for example, IVDs, medical devices and any Basic UDI-DIs)</td><td>Kit contents

<table><tr><th>Reagent</th><th>Cap color</th><th>Tube ID</th><th>Volume</th></tr><tr><td>IDH1 Reaction Mix 1</td><td>Green</td><td>IDH1 Mix 1</td><td>950 µL</td></tr><tr><td>IDH1 Reaction Mix 2</td><td>Purple</td><td>IDH1 Mix 2</td><td>950 µL</td></tr><tr><td>IDH1 Positive Control</td><td>Red</td><td>PC</td><td>120 µL</td></tr><tr><td>Taq DNA Polymerase</td><td>Mint</td><td>Taq</td><td>85 µL</td></tr><tr><td>Water for NTC</td><td>White</td><td>NTC</td><td>1.9 mL</td></tr><tr><td>Water for sample dilution</td><td>White</td><td>Dil.</td><td>1.9 mL</td></tr></table></td></tr>
<tr><td>3.3 A reference to previous generation(s) or variants if such exists, and a description of the differences</td><td>Not applicable.</td></tr>
<tr><td>3.4 Description of accessories</td><td>There are no accessories provided with the ipsogen IDH1 RGQ PCR Kit.</td></tr>
</table>

intended to be used in combination with the device	
3.5 Description of any other devices and products which are intended to be used in combination with the device	Platform and software The *ipsogen* IDH1 RGQ PCR Kit is specifically designed for use with: • Rotor-Gene Q MDx 5plex HRM Platform* (cat. no. 9002032 (platform) or 9002033 (system)), operating with a personal computer installed with: • Rotor-Gene AssayManager® v2.1 (version 2.1.1 or later) software (cat. no. 9024203) • Gamma Plug-in v1.0 (or later) (cat. no 9025511) • *ipsogen* IDH1 RGQ PCR Kit Assay Profile ("AP_ipsogen_IDH1_Blood_BMA_V1_0_x.iap" where x ≥ 0) **Note**: The *ipsogen* IDH1 RGQ PCR Kit Assay Profile is only compatible with Rotor-Gene AssayManager v2.1 or later. Materials Required but Not Provided The Instruction for Use also provides the full list of materials required but not provided with the kit, as follows: **Additional reagents** • QIAamp DSP DNA Blood Mini Kit (cat. no. 61104)

- DNAZap™ PCR-degrading solutions or equivalent cleaning solutions
- Distel High Level Laboratory Disinfectant and isopropyl alcohol (IPA) wash or equivalent cleaning solution

Consumables

- Strip Tubes and Caps (0.1 mL), for use with 72-well rotor (cat. no. 981103 or cat. no.981106)
- Nuclease-free, low DNA-binding microcentrifuge tubes for preparing master mixes
- Nuclease-free pipette tips with aerosol barriers

Equipment

- Platform and software as described above
- Permanent marker
- Dedicated pipettes* (adjustable) for sample preparation
- Dedicated pipettes* (adjustable) for PCR master mix preparation
- Dedicated pipettes* (adjustable) for dispensing of template DNA
- Benchtop centrifuge* with rotor for 1.5 mL tubes
- Thermomixer*, heated orbital incubator*, heating block* or water bath* capable of incubation at 37°C and 56°C
- Loading Block 72 × 0.1 mL Tubes, aluminum block for manual reaction set up (cat. no. 9018901)
- 72-Well Rotor, for holding Strip Tubes and Caps, 0.1 mL, with reaction volumes of 10–50 µL (cat. no. 9018903); requires Locking Ring 72-Well Rotor
- Locking Ring 72-Well Rotor, for locking Strip Tubes and Caps, 0.1 mL in the 72-Well Rotor (cat. no. 9018904)
- Spectrophotometric quantification instrument*
- Benchtop vortexer

* Prior to use, the user shall ensure that instruments have been checked and calibrated according to the manufacturer's recommendations.

4. Reference to any harmonized standards and CS applied

4.1 Harmonized standards and Common Specifications (CS) applied	Harmonized Standards • EN ISO 13485:2016+AC:2018+A11:2021 – Medical devices – Quality management systems - Requirements for regulatory purposes (ISO 13485:2016) • EN ISO 14971:2019+A11:2021 – Medical devices – Application of risk management to medical devices • EN ISO 15223-1:2021 – Medical devices – Symbols to be used with medical device labels, labeling and information to be supplied – Part 1: General requirements • EN ISO 20916:2024 – In vitro diagnostic medical devices – Clinical performance studies using specimens from human subjects – Good study practice (ISO 20916:2019) Common Specifications (CS) N/A as CS are only applicable to some Class D medical devices.
5. Risks and warnings	
5.1 Residual risks and undesirable effects	Risks have been mitigated as far as possible and deemed as acceptable. Refer to the Instructions for Use (Handbook) and the *Rotor-Gene Q MDx 5plex HRM Platform User Manual* for additional warnings, precautions, and procedures to control residual risks. Residual risk remains if the user does not follow the instructions for safe use of the RGQ instrument. The residual risk is disclosed to the users through the *Rotor-Gene Q MDx 5plex HRM Platform User Manual*, which contains warnings against incorrect use. Mitigations have been implemented into the RGQ instrument to reduce and, where possible, eliminate electrocution risk. However, it is not possible to fully eliminate all sources of electrocution, particularly in scenarios where the instrument is operated in a manner other

	than detailed in the manual. This is an inherent risk that cannot be eliminated nor reduced further.
5.2 Warnings and precautions	Warnings and Precautions Please be aware that you may be required to consult your local regulations for reporting serious incidents that have occurred in relation to the device to the manufacturer and/or its authorized representative and the regulatory authority in which the user and/or the patient is established. **Warnings** For in vitro diagnostic use. For use with the Rotor-Gene Q MDx 5plex HRM Platform. For use with the QIAamp DSP DNA Blood Mini Kit, using the manual isolation and purification of genomic DNA by microcentrifuge procedure. **Safety information** When working with chemicals, always wear a suitable lab coat, disposable gloves, and protective goggles. For more information, please consult the appropriate safety data sheets (SDSs). These are available online in convenient and compact PDF at www.qiagen.com/safety, where you can find, view and print the SDS for each QIAGEN kit and kit component. ● Specimens and samples are potentially infectious. Discard sample and assay waste according to your local safety procedures. ● For safety information regarding the Rotor-Gene Q MDx 5plex HRM instrument, see the user manual supplied with the instrument. ● For safety information for the QIAamp DSP DNA Blood Mini Kit (cat. no. 61104), see the *QIAamp DSP DNA Blood Mini Kit Handbook*.

Emergency information

CHEMTREC
Outside USA & Canada +1 703-527-3887

Precautions

The user must always adhere to the following precautions when using the *ipsogen* IDH1 RGQ PCR Kit:

- The test is for use with whole blood or bone marrow aspirate specimens collected in K2-EDTA tubes.
- All chemicals and biological materials are potentially hazardous. Specimens and samples are potentially infectious and must be treated as biohazardous materials.
- Discard sample and assay waste according to your local safety procedures.
- Reagents for the *ipsogen* IDH1 RGQ PCR Kit are diluted optimally. Do not dilute reagents further as this may result in a loss of performance. Do not use reaction volumes (reaction mix plus sample) of less than 25 µL.
- All reagents in the *ipsogen* IDH1 RGQ PCR Kit are formulated specifically for use with the tests provided in the *ipsogen* IDH1 RGQ PCR Kit.
- All reagents supplied in the *ipsogen* IDH1 RGQ PCR Kit are intended to be used solely with the other reagents supplied in the same *ipsogen* IDH1 RGQ PCR Kit. Do not substitute the reagents in the *ipsogen* IDH1 RGQ PCR Kit or between *ipsogen* IDH1 RGQ PCR Kits, as this may affect performance.
- Only use the Taq DNA polymerase (tube Taq) that is provided in the *ipsogen* IDH1 RGQ PCR Kit. Do not substitute with Taq DNA polymerase from other kits of the same or any other type, or with Taq DNA polymerase from another supplier.

	• Refer to the *Rotor-Gene Q MDx 5plex HRM Platform User Manual* for additional warnings, precautions, and procedures. • Placement of the Rotor-Gene Q MDx 5plex HRM instrument according to the Installation Procedures and site requirements. • Do not use expired or incorrectly stored components. • Use extreme caution to prevent contamination of the control and reaction mix reagents with the synthetic materials that are contained in the positive control reagent. • Use extreme caution to prevent cross-contamination between samples. Cap the tubes promptly after the addition of each sample. • Thoroughly decontaminate the loading block before using it for preparation of assay master mixes. The use of DNAZap PCR-degrading solutions, followed by Distel High Level Laboratory Disinfectant and an IPA wash, is recommended. The loading block must be dry before use. • Use individual, dedicated pipettes for setting up reaction mixes and adding positive control reagents. • Perform preparation and dispensing of reaction mixes in an area separate from the one used for the addition of the positive control. • Fluorescently labelled molecules included in the reaction mix reagents are light sensitive. Protect control and reaction mix reagents from light to avoid photo bleaching. • Do not open the Rotor-Gene Q MDx instrument until the run has finished. • Do not open Rotor-Gene Q tubes after the run has finished. If an error has occurred during the run, the samples in the Rotor-Gene Q MDx 5plex HRM instrument must be disposed of and not retested. • Caution must be exercised to ensure correct sample testing to avoid incorrect sample entry, loading errors and pipetting errors. • To minimize flags for the controls and samples, strict compliance with the *ipsogen IDH1 RGQ PCR Kit Instructions for Use* should be followed, including but not limited to:

	○ Correct reagent mixing must be ensured at each mixing step during assay setup.
5.3 Other relevant aspects of safety, including a summary of any field safety corrective action (FSCA including FSN), if applicable	Not applicable.
6. Summary of the performance evaluation and post-market performance follow-up (PMPF)	
6.1 Summary of scientific validity of the device	As this device is a companion diagnostic device, the demonstration of the scientific validity is twofold: 1) The association of the analyte (IDH1 mutations at R132) and the clinical condition, newly diagnosed AML. 2) The clinical utility of the therapeutic TIBSOVO (ivosidenib) in combination with azacitidine in the identified newly diagnosed AML patients with IDH1 R132C, R132H, R132G, R132S, and R132L variants. **Scientific validity on the association of the identified variants and AML** In summary, guidelines recommended screening for gene mutations in AML to establish diagnosis and identify actionable therapeutic targets. Mutational screening in AML is also required in minimal residual disease (MRD) follow-up by molecular techniques. IDH1 mutation is listed in all

	guidelines as one of the mutations of interest and it is recommended as an option for all patients. In the same way, IDH1 is identified as a relevant mutation in the clinical studies reviewed as it serves as prognostic for AML patients allowing earlier prediction of AML relapse and measuring the effectiveness of treatment. IDH1 mutation is observed in 6–10% of AML cases. The literature search also confirmed that IDH1 mutations affect amino acid residue 132, and that the most frequent alterations are in R132C and R132H. In addition, R132G, R132L and R132S are also detected. The patient sample types identified in the literature for screening for IDH1 mutations are bone marrow and peripheral blood. The literature confirms the adequacy of the IDH1 mutations selected in the *ipsogen* IDH1 RGQ PCR Kit, R132C, R132H, R132G, R132S, and R132L, as well as the patient sample type selected to screen the IDH1 mutation, WB or BMA specimens. The relevance of R132H mutation is further supported in Steinhäuser et al. 2023. Several techniques were identified as viable for detecting IDH1 mutations in AML. The literature focuses on more recent techniques, including NGS; however, the RT-PCR technique is also identified as relevant and is used in clinical practice, as it provides higher sensitivity levels as compared to NGS and multiparameter flow cytometry. This demonstrates the state-of-the-art nature of the IDH1 mutation assessment by the device in question. A similar device to the QIAGEN *ipsogen* IDH1 RGQ PCR assay is the Abbott® RealTime IDH1 assay, which can also be used for the qualitative detection of single nucleotide variants (SNVs) coding five IDH1 R132 mutations (R132C, R132H, R132G, R132S, and R132L) in DNA extracted from human blood (EDTA) or bone marrow (EDTA). The Abbott RealTime IDH1 assay exhibits advantages and limitations, including turnaround time, the number of samples assessable for each run, DNA or sample input necessary, lab experience necessary for sample processing workflows, coverage of mutations and limit of detection (LoD) differences. As shown in the literature (Dash et al. 2019), the Abbott RealTime IDH1 assay reliably detected IDH1 mutations at variant allele frequency (VAF) levels as low as 1% in patients with R/R AML. The Abbott RealTime IDH1 assay was more sensitive (100%) than the PCR-based Sanger sequencing assay and NGS panel, which had sensitivity limits of 20% and 10%, respectively.

	Therefore, the scientific validity of the analyte for the clinical condition has been demonstrated by clinical guidance, a systematic literature review and based on similar devices. **Clinical performance of the treatment in the identified population** For a companion diagnostic device, the scientific validity of the device needs to consider the stratification of the population and the outcome of the therapy in the selected population. For this device this will be treatment with TIBSOVO in combination with azacitidine in newly diagnosed AML patients with IDH1 R132C, R132H, R132G, R132S, and R132L variants. The European Medicines Agency (EMA) has approved TIBSOVO for use in AML and also biliary tract cancer (**note**: biliary tract cancer is out of scope for this SVR), although only for use in patients with an IDH1 R132 mutation. Therefore, the scientific validity for the use of the treatment of the clinical condition has been demonstrated by the state-of-the-art guidance from the EMA and is additionally supported by the literature reviewed above. The clinical evidence for the TIBSOVO treatment of AML patients is supported by Choe et al. 2020, Roboz et al. 2020, and NCT 02074839. Furthermore, QIAGEN in partnership with Servier (the Marketing authorization holder for TIBSOVO) have developed, provided and validated the ipsogen IDH1 RGQ PCR Kit as a companion diagnostic (CDx), as an alternative to the already FDA-approved and CE-marked (under IVDD) CDx Abbott Realtime IDH1 (CTA). The clinical bridging study demonstrates that in newly diagnosed AML patients the clinical efficacy in terms of event free survival (EFS) (and other clinical endpoints) were in line with the summary results in the drug AG120-C-009 study report. Furthermore, the PPA and NPA for the device in question vs the Abbott Realtime IDH1 device met the concordance requirements of PPA and NPA ≥95%. Therefore, the scientific validity for the treatment in the stratified population has been demonstrated.

	Conclusion Overall, the scientific validity in terms of the relevance of the stratified population to the clinical condition and the treatment efficacy of the therapeutic in this stratified population has been demonstrated. This will be maintained throughout the life cycle of the device.
6.2 Summary of performance data from the equivalent device, if applicable	Not applicable, no performance data from an equivalent device is utilized.
6.3 Summary of performance data from conducted studies of the device prior to CE-marking	Analytical Performance **Limit of Blank** The Limit of Blank (LoB) is defined in CLSI guideline EP17-A2 as "the highest measurement result that is likely to be observed (with a stated probability) for a blank sample". For the *ipsogen* IDH1 RGQ PCR Kit, this is the data point that corresponds to the upper 95th percentile in blank (wild type, i.e., R132 mutation negative) samples. The LoB has been determined by measuring the levels of breakthrough for each of the five IDH1 mutation assays of the *ipsogen* IDH1 RGQ PCR Kit, where breakthrough is defined as the non-specific, low-level amplification of a DNA template. For the *ipsogen* IDH1 RGQ PCR Kit, this refers to non-specific binding of a mutant probe to the wild type DNA.

Table 1. Summary of LoB results

IDH1 assay	LoB (Ct value)
R132H	No amplification
R132C	No amplification
R132S	No amplification
R132G	No amplification
R132L	No amplification

Based on this analysis, the LoB for the assay has been determined as the absence of a Ct value.

Limit of Detection

The LoD is defined as the lowest allele frequency of IDH1 R132 mutation (in a background of wild type DNA) that is possible to detect 95% of the time. Genomic DNA was extracted from WB and BMA specimens spiked with R132 mutant cell line DNA and was diluted into normalized DNA extracted from wild type clinical WB and BMA specimens. The genomic DNA was serially diluted to % MAF levels above, at, and below the estimated LoD for each assay.

At least 60 replicates of each % MAF dilution in the series at a low DNA input level were tested using three *ipsogen* IDH1 RGQ PCR Kit lots. The LoD for each assay was determined using a Probit model (Table 2).

Table 2. Summary of LoD results

IDH1 assay	LoB (% MAF)
R132H	1.25
R132C	2.70
R132S	4.70
R132G	3.20
R132L	2.90

The LoD was verified across the validity range of the *ipsogen* IDH1 RGQ PCR Kit lots.

Assay cutoff

The assay cutoff is a specific ΔCt value used to determine whether a sample is classed as positive or negative for an IDH1 R132 mutation. Samples that generate ΔCt values at or below the cutoff are classified as R132 mutation-positive (i.e., R132 mutation detected) and ΔCt values generated above the cutoff are classified as R132 mutation negative (i.e., no mutation detected). The false-negative and false-positive rates for each IDH1 mutation-specific assay were used to determine a cutoff value for each mutation assay, such that a result equal to or less than the cutoff will result in an "IDH1 Mutation Detected" classification. The cutoff for each assay within the *ipsogen* IDH1 RGQ PCR Kit is shown in Table 3.

Table 3. Summary of assay cutoff values

IDH1 assay	Assay cutoff (ΔCt value)
R132H	14.75
R132C	14.75
R132S	14.75
R132G	14.75
R132L	14.75

Genomic DNA input range

The DNA input level is defined as the total quantity of amplifiable DNA in a sample, determined from the Ct value of the control reaction. To demonstrate that the performance of the *ipsogen* IDH1 RGQ PCR Kit is consistent across the control reaction working range (CWR) (21.54–25.25 Ct), a 7-level serial dilution of varying DNA input levels (with the highest and lowest levels being outside of the CWR) was tested. This was conducted

for wild type and for each of the five R132 mutations (at 1.5× LoD), and for both WB and BMA.

The evaluation was performed using three *ipsogen* IDH1 RGQ PCR Kit lots with six replicates tested per DNA input level (two replicates per kit lot). The data was analyzed using regression analysis to determine the linear range. For the assay to be determined as linear across the DNA input range, there should be no change across the range in ΔCt for mutation-positive samples, i.e., not statistically significant linear, quadratic, or cubic effect. For wild type sample, for the assay to be determined as linear across the DNA input range, there should be a statistically significant linear effect in control Ct with respect to dilution level, and no statistically significant quadratic or cubic effect.

Parameter estimates for the tested dilutions demonstrated linearity for all samples. A linear ΔCt and control Ct range was observed across the DNA input range tested for the assay.

Precision

The repeatability of the *ipsogen* IDH1 RGQ PCR Kit was assessed by testing contrived samples at two mutation levels (1× LoD and 2× LoD) at the standard DNA input of 5 ng/µL, and wild type samples at the standard (5 ng/µL) and low DNA input (3.5 ng/µL) levels were tested at one site (located in UK). The samples were tested in triplicate with four runs per day across multiple days, Rotor-Gene Q MDx instruments, and operators and using three lots of *ipsogen* IDH1 RGQ PCR Kit to generate a total of a minimum of 106 replicates per sample (Table 4 and Table 5).

Table 4. Assay repeatability for bone marrow aspirate samples*

Mutation	Level	Fractional proportion of valid results	Correct calls (%)	Lower two-sided 95% CI
Wild type	3.5 ng/µL	108 / 108	100.00	96.64
	5 ng/µL	106 / 106	100.00	96.58
R132H	1× LoD	106 / 108	98.15	93.47
	2× LoD	107 / 107	100.00	96.61
R132C	1× LoD	105 / 106	99.06	94.86
	2× LoD	108 / 108	100.00	96.64

R132S	1× LoD	99 / 106	93.40	86.87
	2× LoD	108 / 108	100.00	96.64
R132G	1× LoD	107 / 108	99.07	94.95
	2× LoD	108 / 108	100.00	96.64
R132L	1× LoD	107 / 108	99.07	94.95
	2× LoD	108 / 108	100.00	96.64

* Number of correct calls and lower two-sided 95% confidence limits for each IDH1 mutation at 1× and 2× LoD, and wild type samples tested across one site

Table 5. Assay repeatability for whole blood samples*

Mutation	Level	Fractional proportion of valid results	Correct calls (%)	Lower two-sided 95% CI
Wild type	3.5 ng/µL	107 / 107	100.00	96.61
	5 ng/µL	108 / 108	100.00	96.64
R132H	1× LoD	108 / 108	100.00	96.64
	2× LoD	107 / 107	100.00	96.61
R132C	1× LoD	107 / 108	99.07	94.95
	2× LoD	107 / 107	100.00	96.61
R132S	1× LoD	97 / 108	89.81	82.51
	2× LoD	107 / 107	100.00	96.61
R132G	1× LoD	106 / 107	99.07	94.90
	2× LoD	108 / 108	100.00	96.64
R132L	1× LoD	105 / 106	99.06	94.86
	2× LoD	106 / 106	100.00	96.58

* Number of correct calls and lower two-sided 95% confidence limits for each IDH1 mutation at 1× and 2× LoD, and wild type samples tested across one site.

Intermediate precision

The precision of the *ipsogen* IDH1 RGQ PCR Kit within laboratory (repeatability) was assessed. The precision of ΔCt values (the difference in Ct values between a mutation reaction and the control reaction) for positive

test samples and control Ct values for negative test samples are reported in Table 6.

Table 6. Intermediate precision of ΔCt and control Ct*

Sample type	Analysis variable	Target mutation	Assay	N	Mean	Intermediate precision (SD)
BMA	ΔCt	R132C	RM1	108	6.17	0.8177
		R132G	RM2	108	7.22	0.6411
		R132H	RM1	107	5.92	0.6161
		R132L	RM2	108	6.54	0.3887
		R132S	RM1	108	7.68	0.5616
	Control Ct	WT	RM1	106	23.67	0.0903
			RM2	106	23.72	0.1277
WB	ΔCt	R132C	RM1	107	6.77	1.4127
		R132G	RM2	108	6.40	1.1413
		R132H	RM1	107	6.15	0.8026
		R132L	RM2	106	7.03	0.4312
		R132S	RM1	107	7.00	0.6764
	Control Ct	WT	RM1	108	23.67	0.0890
			RM2	108	23.76	0.1123

* Mean and standard deviation (intermediate precision) for the ΔCt of each mutation assay for 2× LoD mutation-positive samples, and for the control Ct for WT samples at 5 ng/µL DNA input, including both BMA and WB sample types.

Reproducibility

The reproducibility of the *ipsogen* IDH1 RGQ PCR Kit was assessed by testing contrived samples at two mutation levels (1× LoD and 2× LoD) at the standard DNA input of 5 ng/µL, and wild type samples at the standard (5 ng/µL) and low DNA input (3.5 ng/µL) levels were tested at three sites (one located in UK and two located in USA). The samples were tested in duplicate with six runs per sample across multiple days, Rotor-Gene Q MDx 5plex HRM instruments, and operators and using three lots of *ipsogen* IDH1 RGQ PCR Kit to generate a total of a minimum of 178 replicates per sample (Table 7 and Table 8).

Table 7. Assay reproducibility for bone marrow aspirate samples*

Mutation	Level	Fractional proportion of valid results	Correct calls (%0	Lower two-sided 95% CI
Wild type	3.5 ng/µL	179 / 179	100	97.96
	5 ng/µL	178 / 178	100	97.95
R132H	1× LoD	178 / 180	98.89	96.04
	2× LoD	179 / 179	100	97.96
R132C	1× LoD	177 / 178	99.44	96.91
	2× LoD	179 / 180	99.44	96.94
R132S	1× LoD	167 / 178	93.82	89.21
	2× LoD	179 / 180	99.44	96.94
R132G	1× LoD	179 / 180	99.44	96.94
	2× LoD	180 / 180	100	97.97
R132L	1× LoD	179 / 180	99.44	96.94
	2× LoD	180 / 180	100	97.97

* Number of correct calls and lower two-sided 95% confidence limits for each IDH1 mutation at 1× and 2× LoD, and wild type samples tested across three sites.

Table 8. Assay reproducibility for whole blood samples*

Mutation	Level	Fractional proportion of valid results	Correct calls (%)	Lower two-sided 95% CI
Wild type	3.5 ng/µL	179 / 179	100	97.96
	5 ng/µL	180 / 180	100	97.97
R132H	1× LoD	180 / 180	100	97.97
	2× LoD	179 / 179	100	97.96
R132C	1× LoD	178 / 180	98.89	96.04
	2× LoD	179 / 179	100	97.96

R132S	1× LoD	159 / 180	88.33	82.72
	2× LoD	179 / 179	100	97.96
R132G	1× LoD	178 / 179	99.44	96.93
	2× LoD	180 / 180	100	97.97
R132L	1× LoD	177 / 178	99.44	96.91
	2× LoD	178 / 178	100	97.95

* Number of correct calls and lower two-sided 95% confidence limits for each IDH1 mutation at 1× and 2× LoD, and wild type samples tested across three sites.

Lot interchangeability

The object of this study was to demonstrate that regardless of which lots of the QIAamp DSP DNA Blood Mini Kit and *ipsogen* IDH1 RGQ PCR Kit (IDH1 Kit) are used, the mutation call status for all samples, in both peripheral blood (PB) and bone marrow aspirate (BMA), is consistent for all targets.

In order to assess the lot interchangeability of the kits, this study used five mutation samples (1 for each mutation target detected by the IDH1 Kit) and 1 WT sample, for each sample type (12 samples in total). Four extraction replicates for each sample were extracted using three independent extraction kit lots. DNA concentration for each replicate was quantified and subsequently normalized to 5 ng/µL (if not already within a range of 1–6 ng/µL). Each replicate was then assessed by PCR, one replicate per reaction mix using three independent IDH1 Kit lots.

In order to verify Lot Interchangeability, it was required that across all combinations of QIAamp DSP DNA Blood Mini and *ipsogen* IDH1 RGQ

	PCR Kit lots, that >90% correct call rate must be observed for each target in each sample type (PB and BMA). It was observed that all targets had a >90% correct call rate. Except for R132H in the PB sample type, a correct call rate of 100% (36/36) was obtained. The R132H PB sample type returned a correct call rate of 91.67% (33/36). This met the requirement for lot interchangeability of the QIAamp DSP DNA Blood Mini Kit and *ipsogen* IDH1 RGQ PCR Kit. **Cross-contamination / analytical carryover** The purpose of this study was to evaluate the *ipsogen* IDH1 RGQ PCR Kit for carryover when IDH1 mutation positive samples are tested adjacent to IDH1 mutation negative (wild type) samples. This study examined the entire IDH1 System from extraction to PCR amplification and investigated if carryover occurred between samples, extractions, and within or between runs. This study was performed with mutation-positive (either R132C or R132L) and wild type WB or BMA specimens. Two independent sets of samples were extracted following a predefined extraction matrix designed to introduce risk of sample cross-contamination. Extraction cross-contamination was tested across six extractions, and PCR cross-contamination was tested across six PCR runs, following a run matrix designed to introduce the risk of sample cross-contamination. Extraction and PCR runs were set up consecutively by the same operator (one operator per independent set of samples) using the same equipment, with no other runs set up using this instrument between these runs and separate instruments used for each sample set. One lot of the QIAamp DSP DNA Blood Mini Kit and one lot of the ipsogen IDH1 RGQ PCR Kit were used throughout this study. A total of 144 wild type replicates were tested, with no wild type replicate generating either an R132C or R132L mutation detected call. Therefore, demonstrating the absence of cross-contamination of the wild type samples

	by mutation positive samples sharing the same DNA extraction and run set up procedure. **Specimen handling** This study assessed sample handling variability during the DNA extraction process using the QIAamp DSP DNA Blood Mini Kit. Whole blood (WB) and bone marrow aspirate (BMA) samples were tested across three independent laboratories. Each of the three sites processed four extractions per sample (12 samples – five IDH1 mutation samples and one wild type sample, for both sample types), resulting in a total of 144 individual gDNA extracts. All samples were blinded before extraction. Each sample was extracted, quantified, and normalized at the respective sites, and then tested using the *ipsogen* IDH1 RGQ PCR Kit at QIAGEN Manchester. Across all mutation and WT samples, the proportion of correct calls was 100%, supporting the reproducibility and repeatability of the *ipsogen* IDH1 RGQ PCR Kit at the pre-analytical step of DNA extraction. **Interfering substances (analytical specificity)** The study aimed to evaluate the impact of exogenous and endogenous substances on the performance of the *ipsogen* IDH1 RGQ PCR Kit. The study included at least nine replicates for each sample type (whole blood and bone marrow aspirate) and mutation status (wild type, R132H, and R132G), in combination with each interferent. Exogenous substances present in the DNA extraction process were tested by spiking into the gDNA eluate after DNA extraction and normalization. Samples tested with potential exogenous interferents were spiked at concentrations representing the highest feasible level of the interfering substance carryover into a sample. The exogenous substances tested included: • K2-EDTA • Lysis buffer • QIAGEN Protease • Ethanol

	• Buffer AW1 • Buffer AW2 Endogenous substances, including pharmaceuticals and naturally occurring biological substances, were spiked into whole blood or bone marrow aspirate samples before DNA extraction. Test concentrations were determined based on C_{max} values (3x concentration of a substance expected in patient sample) or CLSI EP07-ED3 recommendations. The endogenous substances tested included: • Cytarabine • Decitabine • Etoposide • Idarubicin hydrochloride • Daunorubicin hydrochloride • Azacitidine • Fludarabine phosphate • Hemoglobin • Unconjugated bilirubin • Cholesterol • Albumin • Triglycerides Up to four exogenous or four endogenous substances were pooled using a single solvent, and spiked samples were compared to a solvent-only control sample. If required, individual substances from a pool that demonstrated an interfering effect were then tested in isolation. Cytarabine, decitabine, etoposide, idarubicin hydrochloride, daunorubicin hydrochloride, azacitidine, and triglycerides were noted to potentially reduce sample validity rates in low DNA input samples but did not lead to incorrect results. Fludarabine phosphate, hemoglobin, unconjugated bilirubin, cholesterol, albumin, and all exogenous substances tested met the acceptance criteria, demonstrating no significant impact on the performance of the *ipsogen* IDH1 RGQ PCR Kit.

Clinical Performance

Diagnostic sensitivity and specificity

The *ipsogen* IDH1 RGQ PCR Kit (IDH1 Kit) was compared with a next generation sequencing (NGS) reference test, the Archer VariantPlex Core Myeloid panel (validated by ICON) in newly diagnosed AML patients (Table 9) (using both BMA and PB samples). The overall diagnostic sensitivity was 98.48% (Clopper-Pearson (Exact) Binomial 95% Confidence Interval (CI): (91.84%, 99.96%), and diagnostic specificity was 100% (95% CI: (96.11%, 100%) (Table 10).

Table 9. *ipsogen* IDH1 RGQ PCR Kit vs Reference test (ICON NGS) for newly diagnosed AML – Analysis for all mutations

Frequency		Reference Test		
		IDH1 mutation detected	IDH1 mutation not detected	Total
ipsogen IDH1 RGQ PCR Kit	IDH1 mutation detected	65	0	65
	IDH1 mutation not detected	1	93	94
	Total	**66**	**93**	**159**

Table 10. Diagnostic sensitivity and specificity for newly diagnosed AML – Analysis for all mutations

	Frequencies	Clinical performance	Lower two-sided 95% CI	Upper two-sided 95% CI
Diagnostic sensitivity	65 / 66	98.48	91.84	99.96
Diagnostic specificity	93 / 93	100.00	96.11	100.00

The analysis of clinical performance was also performed on a per-mutation basis as presented in Table 11 and Table 12.

Table 11. *ipsogen* IDH1 RGQ PCR Kit vs reference test (ICON NGS) for newly diagnosed AML – Analysis per mutation

Frequency		Reference test							
		Mutation not detected	R132C	R132G	R132H	R132H and R132C	R132L	R132S	Total
ipsogen IDH1 RGQ PCR Kit	Mutation not detected	93	1	0	0	0	0	0	94
	R132C	0	39	0	0	0	0	0	39
	R132G	0	0	5	0	0	0	0	5
	R132H	0	0	0	16	0	0	0	16
	R132H and R132C	0	0	0	0	1	0	0	1
	R132L	0	0	0	0	0	1	0	1
	R132S	0	0	0	0	0	0	3	3
	Total	**93**	**40**	**5**	**16**	**1**	**1**	**3**	**159**

Table 12. Diagnostic sensitivity and specificity for newly diagnosed AML – Analysis per mutation

Mutation	Diagnostic sensitivity	Two-sided 95% CI	Diagnostic specificity	Two-sided 95% CI
R132C	97.6% (40 / 41)	87.1%, 99.9%	100.00% (118 / 118)	96.92%, 100.00%
R132G	100.0% (5 / 5)	47.8%, 100.0%	100.00% (154/154)	97.63%, 100.00%
R132H	100.0% (17 / 17)	80.5%, 100.0%	100.00% (142/142)	97.44%, 100.00%
R132L	100.0% (1 / 1)	2.5%, 100.0%	100.00% (158/158)	97.69%, 100.00%
R132S	100.0% (3 / 3)	29.2%, 100.0%	100.00% (156/156)	97.66%, 100.00%

Clinical Performance - Clinical utility/efficacy of the *ipsogen* IDH1 RGQ PCR Kit with TIBSOVO treatment in combination with azacitidine in newly diagnosed AML

Subjects screened in the AG120 C 009 clinical study who had available Abbott RealTime IDH1 CTA results were selected to evaluate concordance between the Abbott assay (CTA) and the IDH1 Kit (CDx). The maximum number of leftover samples positive for IDH1 mutations based on the CTA assay and meeting the study inclusion/exclusion criteria were included in the bridging analysis.

As of March 18, 2021 data cutoff, 146 IDH1 mutation-positive subjects (with the CTA) had been identified and randomized to receive either ivosidenib (TIBSOVO) + azacitidine (*N* = 72) or placebo + azacitidine (*N* = 74).

From this Full Analysis Set (FAS), subjects were excluded for the following reasons:

- Withdrawal from trial: 12 subjects, and lack of consent for future testing: 8 subjects
- Samples collected in China: 12 subjects, excluded due to export restrictions
- No leftover samples available: 2 subjects

After these exclusions, 112 samples remained available for the Bridging Study.

Of these 112 samples, 111 were IDH1 mutation positive with the CTA and formed the positive Bridging set. One sample had been randomized based on a local test and was CTA negative, and therefore served as the negative Bridging sample. Note that two samples were non-evaluable and a further two samples were tested outside of the workflow, resulting in a total of 107 evaluable samples.

	In addition, a separate subset of CTA negative subjects was used to generate the negative sample set. A total of 148 CTA negative samples were available for testing with the IDH1 Kit. Note that of these samples, only 145 had a corresponding CDx result, so were evaluable and could be used in the concordance analysis. The Bridging Study was a non-interventional, retrospective analysis using leftover BMA and PB specimens from newly diagnosed AML patients. The primary objectives of the Bridging Study were to assess concordance between the IDH1 Kit and the Abbott CTA and to evaluate the ability of the IDH1 Kit to identify patients eligible for treatment with ivosidenib (TIBSOVO) plus azacitidine. Additionally, to determine the clinical efficacy using the IDH1 Kit, as shown by improved event-free survival (EFS) and other clinical outcomes consistent with the AG120-C-009 clinical study. The study population was representative with respect to demographics, disease characteristics, and sample type. No significant imbalances were observed between CDx evaluable and non-evaluable subjects. **Clinical Concordance** The Clinical Bridging Study demonstrated that Positive Percent Agreement (PPA) and Negative Percent Agreement (NPA) met the predefined concordance threshold of ≥95%, establishing concordance between the IDH1 Kit and the Abbott CTA. Concordance results were as follows: • PPA: 95.33% (102/107; 95% CI: 89.43–98.47) • NPA: 99.31% (144/145; 95% CI: 96.22–99.98) • Overall Percent Agreement (OPA): 97.62% (246/252; 95% CI: 94.89–99.12)

Table 13. Concordance between the IDH1 Kit (CDx) and the Abbott CTA with CTA as the reference method

CDx mutation status		CTA mutation status	
Frequency	**Mutation detected**	**No mutation detected**	**Total**
Mutation detected	102	1	**103**
No mutation detected	5	144	**149**
Total	**107**	**145**	**252**

Clinical efficacy

Clinical efficacy of the IDH1 Kit was assessed by evaluating treatment outcomes in newly diagnosed AML patients identified as IDH1-mutation-positive by the CDx. These outcomes, including event-free survival (EFS), were compared with the clinical efficacy observed in the AG120-C-009 study, in which patient selection was performed using the Abbott RealTime IDH1 CTA.

Table 14 shows the EFS for the two treatment groups of AG120-C-009 based on the clinical efficacy, and Table 15 for the two treatment groups of AG120-C-009 based on the CDx positive results.

Table 14. Clinical trial efficacy event-free survival results (AG120-C-009)

	Tibsovo + azacitidine (*N* = 72)	Placebo + azacitidine (*N* = 74)
Subjects (%) with events	**46 (63.9%)**	**62 (83.8%)**
EFS Rate (%) (95% CI)		
1 day	41.7% (30.2%, 52.7%)	20.3% (12.0%, 30.0%)
3 months	41.7% (30.2%, 52.7%)	20.3% (12.0%, 30.0%)
6 months	39.9% (28.6%, 51.0%)	20.3% (12.0%, 30.0%)

9 months	39.9% (28.6%, 51.0%)	20.3% (12.0%, 30.0%)
12 months	37.4% (25.9%, 48.9%)	12.2% (4.3%, 24.4%)
18 months	33.3% (20.9%, 46.2%)	6.1% (0.7%, 20.9%)
24 months	22.2% (6.6%, 43.4%)	0.0% (–, –) NE*
36 months	0.0% (–, –) NE	0.0% (–, –) NE*
Hazard ratio (relative to placebo + azacitidine) (Stratified)	0.33	
95% CI	(0.16, 0.69)	
p-value for HR=1 (one-sided)	0.0011	

* NE = Non-evaluable.

Table 15. Summary of overall event-free survival based on CDx results for Population 1

	Tibsovo + azacitidine (*N* = 50)	Placebo + azacitidine (*N* = 52)
Subjects (%) with events	32 (64%)	46 (88.5%)
Subjects (%) without events (censored)	18 (36.0%)	6 (11.5%)
EFS Rate (%) (95% CI)		
1 day	40.0% (26.5%, 53.1%)	13.5% (5.9%, 24.1%)
3 months	40.0% (26.5%, 53.1%)	13.5% (5.9%, 24.1%)
6 months	37.8% (24.5%, 51.0%)	13.5% (5.9%, 24.1%)
9 months	37.8% (24.5%, 51.0%)	13.5% (5.9%, 24.1%)
12 months	37.8% (24.5%, 51.0%)	9.0% (2.4%, 21.1%)

18 months	37.8% (24.5%, 51.0%)	9.0% (2.4%, 21.1%)
24 months	25.2% (7.4%, 48.2%)	0.0% (–, –) NE*
36 months	0.0% (–, –) NE	0.0% (–, –) NE*
Hazard Ratio (relative to Placebo + azacitidine) (Stratified)	0.438	
95% CI	(0.254, 0.757)	
p-value for HR=1 (one-sided)	0.0016	

* NE = Non-evaluable.

When compared against the clinical trial efficacy population, an even split between the treatment groups was observed in the CDx+ subjects and the percentage of events between the groups was similar when compared against the clinical trial efficacy. The hazard ratio (HR) for the clinical trial was 0.33 and statistically significant (0.0011) (Table 14), the HR for the efficacy for the CDx + Population was 0.438 and statistically significant (0.0016) (Table 15). Although the CDx HR is higher than the clinical trial efficacy, there is still an improvement from placebo as both the CTA and CDx HRs are <1 which means that the treatment is working and both of them are statistically significant.

- EFS and secondary endpoints in CDx-positive patients were consistent with the main clinical trial results.

The *ipsogen* IDH1 RGQ PCR Kit demonstrated high concordance with the clinical trial assay and effectively identified ND AML patients eligible for targeted therapy.

6.4 Summary of performance data from other sources, if applicable	Not applicable.
6.5 An overall summary of the performance and safety	The performance and safety of the *ipsogen* IDH1 RGQ PCR Kit is based on: **Scientific validity** was demonstrated based on a systematic literature review, assessment of available data relevant to the *ipsogen* IDH1 RGQ PCR Kit and its intended purpose, the intended purpose of medical alternatives and consensus experts' opinions/positions from international guidelines. The scientific validity report concludes there is sufficient clinical evidence to demonstrate the scientific validity of the *ipsogen* IDH1 RGQ PCR Kit for its intended use. **Analytical performance** was demonstrated based on the investigations achieving the required analytical performance indicators (analytical specificity, accuracy of measurement (repeatability and reproducibility), Lot Interchangeability, Limit of Detection, Limit of Blank, Input Range/ Working Range, Cross-contamination, Criteria for Specimen Collection & Handling and Device Stability) as planned in the performance evaluation plan. The analytical performance report concluded that there is sufficient clinical evidence for the analytical performance of the *ipsogen* IDH1 RGQ PCR Kit for its intended use. **Clinical performance** was demonstrated based on clinical performance studies to determine the clinical performance indicators (diagnostic sensitivity, diagnostic specificity and the clinical utility of the therapeutic

	in the stratified population) as planned in the performance evaluation plan. A systematic literature review was also conducted; however, no clinical evidence was identified. The assessment of scientific validity, analytical performance, and clinical performance constitutes the clinical evidence for the *ipsogen* IDH1 RGQ PCR Kit. The clinical evidence also provides valid assurance that the relevant General Requirements (GR 1-20) of the General Safety and Performance Requirements (GSPR) as set out in Annex I in the IVDR 2017/746/EU are fulfilled when used as intended by the manufacturer (QIAGEN) and according to the Instructions for Use. Relevant harmonized standards and other relevant standards to demonstrate conformity with the GSPRs have been applied. The benefit-risk assessment based on systematic literature and database review, risk assessment activities (medical risk assessment, product and manufacturing process risk assessment), vigilance activities conducted by QIAGEN, and experience gained from routine diagnostic testing support a favorable benefit-risk ratio for the *ipsogen* IDH1 RGQ PCR Kit, taking into account the state-of-the-art. Overall, the performance evaluation of the *ipsogen* IDH1 RGQ PCR Kit when used as intended and according to the Instructions for Use identified no gaps for the *ipsogen* IDH1 RGQ PCR Kit. The analysis provided in the SVR and PER is in line with the current state of the art and no remaining unaddressed issues or gaps were identified for clinical evidence. No equivalency was claimed.

6.6 Ongoing or planned post-market performance follow-up	PMPF is a continuous process supporting the ongoing evaluation of device performance and contributes to the confirmation of safety, performance, and scientific validity throughout the device lifecycle. Ongoing and systematic monitoring of the device's clinical performance and safety is ensured through QIAGEN's established post-market surveillance framework. Based on the collected evidence which shows that this device meets the performance evaluation requirement's the assay is considered safe and effective for its intended use, and no unacceptable residual risks remain. It was concluded that no unaddressed issues or gaps have been identified for the device that require addressing through PMPF studies.
7. 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	
8.1 Suggested profile and training for users	The product is to be used only by trained personnel in a professional laboratory environment.

Revision History

SSP Revision Number	Date issued	Change description	Revision validated by the Notified Body
01	June 2026	CE certificate issued	×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)