PoET Multiscreen

Qualitative nucleic acid test

for use with *PoET Instrument*

For *in vitro* diagnostic use

REF P2M-28-30

IVD CE 0123

Table of contents

1 Intended use

1.1 Intended purpose

PoET Multiscreen is a PCR kit for professional use for automated *in vitro* testing of human plasma specimens from blood donors.

PoET Multiscreen is used for the qualitative detection of hepatitis C virus (HCV) RNA, hepatitis B virus (HBV) DNA and human immunodeficiency virus 1 or 2 (HIV-1, HIV-2) RNA by real-time PCR in screening of individual specimens or pools of aliquots of individual specimens.

In addition, *PoET Multiscreen* is intended to confirm the results of samples tested in blood donor screening.

PoET Multiscreen is processed on *PoET Instrument*.

1.2 Intended users

The application has to be carried out by qualified laboratory personnel who have been instructed and trained in *in vitro* diagnostic procedures and have successfully completed the operator's training on *PoET Instrument*.

2 Background

2.1 Pathogen information

2.1.1 HCV

Hepatitis C virus (HCV; *Hepacivirus hominis*) is an enveloped, (+)ssRNA virus with a genome of about 9.6 kb and the causative pathogen of hepatitis C. HCV is taxonomically correctly referred to as *Hepacivirus hominis* (former *Hepacivirus C*) and is currently the only human pathogenic representative of the genus *Hepacivirus* in the *Flaviviridae* family (1) (2).

Currently, eight genotypes with various sub-genotypes and recombinant forms of HCV are known (3) (4) (5). The genetic diversity of the individual genotypes to each other is over 30 %. As an RNA virus, the genome of HCV is very variable. The virus is viewed as a quasispecies. This variability can be considered as one of the main reasons why no vaccine against HCV has been developed so far.

HCV is predominantly transmitted parenterally by blood-infected needles, *e.g.* during drug use and tattooing, more rarely also by sexual transmission pathways (1). Due to the introduction of serological HCV blood donation testing in Germany in 1991, the previously comparatively frequent transmission of HCV through blood transfusions and blood products has become very unlikely. The diagnostic window, which is unusually wide for HCV with an average of 60 days, was significantly shortened by the introduction of HCV nucleic acid amplification technology (NAT) testing (6). NAT testing for HCV was introduced in Germany in 1997.

Acute hepatitis, which can develop 6 to 8 weeks after infection with HCV, usually shows only a mild course of the disease. About 75 % of acutely HCV-infected persons develop a chronic HCV infection when left untreated. This chronic infection can often develop into liver cirrhosis and subsequently into primary liver cell carcinoma in the further course of the disease. Currently, there is no vaccination against HCV available. However, an effective antiviral therapy leads to a cure in most cases (1).

2.1.2 HBV

HBV, the hepatitis B virus, is an enveloped DNA virus with a circular, partially double-stranded, approximately 3.2 kb genome that predominantly infects the liver and causes liver inflammation. In addition to infectious viruses, spherical or filamentous virus particles are found that do not contain DNA and are not infectious (1). HBV belongs to the genus *Orthohepadnavirus* within the family *Hepadnaviridae* (7) (8) (9). Since HBV uses a reverse transcriptase for its replication cycle, the HBV genome is highly variable and the virus can generate quasispecies (10). Another specific characteristic of HBV is the appearance of virus particles with defective viral genomes (11).

For HBV, the human genotypes A-H and many recombinant forms derived from these are known, such as genotype 'I' (a recombinant form of A/C/G) or many B/C recombinants, as well as various genotypes from gibbons and apes that are not human pathogenic (9) (12) (13) (14). Another apparent human pathogenic genotype 'J' represents an isolated case, most closely related to a gibbon sequence and probably caused by a monkey-to-human transmission (12) (15). In Europe, the genotypes A and D are the most prevalent (16).

HBV is transmitted through virus-infected body fluids such as blood or blood products, saliva, breast milk or mucous membranes, *e.g.* at birth, or through sexual contact. The incubation period depends on the pathogen's dose, the route of infection and the immune status of the exposed person and can range between two and six months. About 65 % of all infections progress asymptomatically. Acute hepatitis persists for about 2-4 weeks. About 5-10 % of all infected people develop chronic hepatitis, which subsequently can lead to cirrhosis of the liver and to primary hepatocellular carcinoma.

In acute hepatitis, due to the high spontaneous healing rate, there is no indication for therapy. Patients with chronic hepatitis B are treated with antiviral drugs.

An effective prophylaxis of hepatitis B infection is possible by vaccination. Despite the availability of vaccination, hepatitis B infections continue to be an occupational infectious disease in the healthcare system (17).

2.1.3 HIV

Human immunodeficiency virus (HIV) is the causative pathogen of the acquired immunodeficiency syndrome AIDS. HIV forms a complex, enveloped virion equipped with two linear (+)ssRNA strands. HIV belongs to the genus of lentiviruses in the family *Retroviridae.* Two human species, HIV-1 and HIV-2, are currently known. The origin of both species is a transmission of the *Simian immunodeficiency virus* (SIV) from monkeys to humans (1) (18).

For HIV-1, four such independent transmissions from chimpanzees or gorillas to humans are currently known as subtypes M, N, O, and P (19). In particular, the subtype group M with a large number of subgenotypes and recombinant forms has spread and is responsible for over 90 % of all HIV infections worldwide. The most common subtypes of group M are subtype C in Asia and Africa and subtype B in Europe and the United States. Subtype O is mainly widespread in West Africa and only a few cases of subtypes N and P are known.

HIV-2 is predominantly endemic to West Africa and eight subtypes are currently known. Each subtype developed from independent transmissions from Mangabeys, a species of "Old World monkeys" (*Cercopithecidae*) often kept as pets, to humans (19). However, only subtypes A and B and recombinant forms derived thereof have a certain relevance for blood donation. So far, the other subtypes only represent endemic cases.

HIV is transmitted mainly during sexual contacts with infectious body fluids, essentially sperm, vaginal secretions and the liquid film of the intestinal mucosa, with direct blood contact posing by far the greatest risk of transmission. The risk of infection after a transfusion of HIV-positive blood is over 90 %. However, the introduction of blood testing (in Germany serological testing since 1985, NAT since 1997, mandatory since 2004) has reduced the probability of an HIV-positive donation being transfused to a minimum (1:5,000,000 according to the German Robert Koch Institute, RKI).
The prevalence of HIV-2 in Germany is low, with four cases out of 2,818 new HIV diagnoses in Germany in 2018 (20). Compared to infections with HIV-1, the course of the disease in humans infected with HIV-2 is usually milder and slower and often even without recognizable symptoms (21).
The disease progression of a HIV infection is usually classified into three phases. The first phase is also called primary infection and often proceeds inapparently. The subsequent second phase is usually a symptom-free latency phase lasting several years, which, if left untreated, leads to the typical clinical picture of AIDS in the third phase. AIDS ultimately leads to the collapse of the immune defense and thus to death (18).
Currently, there is no vaccination against HIV available. However, it is possible to prevent the onset of AIDS almost completely by means of combined antiretroviral therapy (cART, *combined antiretroviral therapy*) (22).

2.2 Benefit of NAT tests

The safety of blood and blood products requires the determination of donor suitability and the testing of donated blood in order to minimize the risk of potential transmissions of viral pathogens during the transfusion of blood and blood components. Serological screening strongly reduces the risk of transmission of viral infections by transfusion, but cannot eliminate the risk completely. A residual transmission risk remains for blood donations drawn during the seroconversion window period, because serological tests may not detect the infection during this phase (23). Testing for viral nucleic acids using NAT shortens the diagnostic window and further reduces the risk of transmission substantially.
By surveying the current global use of blood donation NAT the study by Faddy *et al.* (24) was able to show that the use of NAT has increased over the last years. The percentage of NAT-positive donations, based on the total number of donations in 2019, was 0.0099 % for HIV, 0.0063 % for HCV and 0.0247 % for HBV. This clearly shows that NAT contributes to improving the safety of blood transfusions worldwide.

2.3 Test principle

The Multiplex PCR kit *PoET Multiscreen* is comprised of a real-time PCR (polymerase chain reaction) to detect HCV/HIV-specific RNA and HBV-specific DNA in human blood plasma.
Two target areas (X-tail and 5' UTR) are amplified in the PCR for HCV. A *dual-target design* (sequence overlap region of the P/X and C/P genes) has also been established for HBV. The detection of HIV-1 is ensured by a *triple-target design* (GAG, LTR and Pol3). For HIV-2, a conserved region of the LTR gene is amplified.
With *PoET Multiscreen*, the nucleic acids of HCV, HBV and HIV can be amplified simultaneously in one reaction and distinguished from each other using different fluorescent dyes. However, *PoET Multiscreen* does not differentiate between HIV-1 and HIV-2.

Very high concentrations of one virus can potentially impair the amplification of the other viruses. Limit values are stored in the *Calliope* software of *PoET Instrument* in order to take such cases into account accordingly.
All PoET PCR kits contain, in addition to the virus-specific oligonucleotides, another heterologous non-competitive amplification system for the Internal Control (*PoET Internal Control*, 'IC', available separately). The IC is added to each sample at the beginning of sample preparation and serves as an extraction and amplification control.

3 PoET system overview

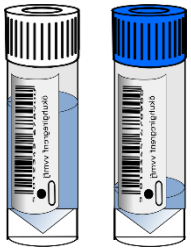
The PoET system provides a fully automated solution for the extraction, amplification and detection of nucleic acids of pathogens in human plasma specimens for applications in NAT high throughput screening or for testing individual samples. The PoET system consists of a line of different products which are available separately.

PoET system		
PoET Instrument	**PoET reagents**	**Disposables**
	▪ PoET PCR kits ▪ PoET controls ▪ PoET extraction reagents	▪ PCR plates ▪ Extraction plates ▪ Sample tubes ▪ Pipetting tips

4 Reagents

The PCR kit *PoET Multiscreen* consists of two components, one tube containing *enzyme mix v2* (EM v2) and one tube containing *oligo mix MSN* (O_M v1). Both tubes are required to use the test *PoET Multiscreen*.

PoET Multiscreen	
Reference number	P2M-28-30
Basic UDI-DI	42623533728MH
Total number of reactions	840 (30 x 28 reactions)



Kit component	**Identifier**	**Primary packaging**	**Reagent ingredients**	**Volume incl. dead volume per kit**
enzyme mix v2	EM v2	tube with screw cap (white)	H_2O, master mix containing < 1 % dUTP, dATP, dGTP, dCTP, dTTP and < 1 % Taq polymerase, < 0.001 % uracil-N-glycosylase, < 0.002 % MMLV reverse transcriptase, < 0.001 % RNase inhibitor	30 × 1210 µL
oligo mix MSN	O_M v1	tube with screw cap (blue)	Tris buffer, < 0.03 % forward and reverse HCV, HBV and HIV-1/2 and IC primers, < 0.004 % fluorescent-labeled HCV, HBV and HIV-1/2 and IC probes	30 × 250 µL

4.1 Reagent storage and handling conditions

Material	**Storage**	**Transport**	**Use**
PoET Multiscreen	≤ -18 °C	≤ -18 °C	+15 °C to +30 °C

The reagents are intended for single use.
Any reagents remaining in the tubes after use must be discarded.

The *oligo mix* is sensitive to light and should be stored protected from light during test preparation.

Start the analysis on *PoET Instrument* no later than 5 hours after removing the reagents from the storage locations. Do not open the reagents until shortly before starting the run.

Do not use expired reagents. *PoET Instrument* monitors reagent barcodes and will not allow to start a run with expired reagents.

4.2 Additional reagents and disposables required

Material	Reference number
PoET Extraction	P1A-24-04
PoET Prep Reagent	P1B-24-20
PoET Internal Control	P1C-1440-60
PoET Universal Positive Control	P3M-360-60
PoET Negative Control	P3A-500-30
1000 µL-CO-RE II Tips	235905
300 µL-CO-RE II Tips	235903
Extraction Plate Set	43001-0730
PCR Plate	SP-0362
*13 mL Tube & Cap**	60.541.004 & 65.714

*Optional. Refer to the operator's manual of *PoET Instrument* for additional information on primary and secondary tubes.

The use of other reagents and disposables on *PoET Instrument* is not permitted.

4.3 Instrumentation and software required

Device	Reference number
PoET Instrument incl. software *Calliope* v2.0 or higher	P9A

5 Warnings and precautions

5.1 General precautions

- For *in vitro* diagnostics use only.
- Use only in combination with *PoET Instrument* and the associated reagent kits and disposables.
- Clean and disinfect all work surfaces according to the 'Guideline for Disinfection and Sterilization in Healthcare Facilities' (25) or comparable methods.
- Eliminate potential nucleic acid contaminations with DNA-ExitusPlus™ (AppliChem GmbH) or a comparably effective agent according to the manufacturer.
- Treat the specimens as potentially infectious as described in 'Biosafety in Microbiological and Biomedical Laboratories' (26) and CLSI document M29A4 (27). If specimen material is spilled, immediately disinfect with an appropriate agent. Treat contaminated materials as biologically hazardous.
- If spillages of samples or reagents occur on *PoET Instrument*, follow the instructions in the operator's manual of *PoET Instrument* in order to clean and decontaminate its surface.
- Dispose of all materials that have come into contact with potentially infectious specimens and/or reagents, according to the relevant regional and national regulations.
- Material safety data sheets (MSDS) are provided by GFE.
- Wear personal protective equipment (laboratory coat, eye protection, laboratory gloves). Do not eat, drink or smoke in designated work areas.

- Disinfect and wash your hands thoroughly after handling the specimens and reagents, and after removing the gloves. Gloves must be exchanged between handling of specimens, controls and reagents. Avoid contaminating gloves when handling specimens and controls.

5.2 Reagent handling

- Handle all reagents, controls, and specimens according to good laboratory practice in order to prevent carryover of specimens or reagents.
- Store specimens, controls and PCR kits separately.
- Store all reagents, controls and specimens upright and at specified temperatures.
- PoET PCR kits are shipped on dry ice. For safe handling and disposal of dry ice follow the local instructions and guidelines.
- After receipt, check the frozen state, the integrity of the packaging and the completeness of the product. If there is any evidence of thawed reagents or damage, do not use these products for testing.
- PCR reagents are photosensitive. Take care to store and handle them protected from light sources.
- Avoid interchanging tube caps to prevent cross-contamination.
- The reagents are designed for single use. Do not reuse reagent residues in the tubes.
- Do not combine different batches of the same reagents.
- Do not use reagents after their shelf life has expired.

6 Process description

The process with *PoET Instrument* consists of the following steps:

1. Sample preparation
2. PCR setup
3. Amplification and detection
4. Evaluation and report

6.1 Sample preparation

The specimen material to be used is human plasma with EDTA[1] or CPD[2] as anticoagulant.
Samples can be provided as individual donor specimens or as pooled specimens consisting of aliquots of individual donations.
PoET Instrument offers the possibility to generate pools of six individual donations. For more information on available sample formats and pooling options please refer to the operator's manual of *PoET Instrument* (Preanalytics and sample processing).

[1] Ethylenediaminetetraacetic acid (EDTA)
[2] Citrate-phosphate-dextrose (CPD)

Sample preparation consists of four steps:

Step	Description
Addition of IC	At the beginning of the process, *PoET Internal Control* (IC, available separately) is added to each sample as a process control for extraction and PCR amplification.
Lysis and binding	Virus particles are lysed to release the nucleic acids. In a second step the nucleic acids are adsorbed on magnetic particles.
Washing	Proteins and other impurities are removed by two washing steps.
Elution	The nucleic acids are released from the magnetic particles with elution buffer. The elution buffer then contains the RNA of the IC and, if present, the viral nucleic acids to be detected.

6.2 PCR setup

During PCR setup, the PCR master mix, the eluates and the PCR controls (positive and negative control) are pipetted into the PCR plate(s).

The PCR master mix consists of *enzyme mix v2* (EM v2, hereafter called EM) and *oligo mix MSN* (O_M v1, hereafter called OM). The OM contains virus-specific oligonucleotides (primers and probes) that bind to highly conserved regions of the viral nucleic acids. In addition, the OM contains another heterologous non-competitive amplification system with primers and probes for amplifying the sequence of Internal Control (IC). In the absence of the target virus a successful IC PCR reaction indicates correct PCR conditions and validates non-reactive target virus results.

To avoid contamination with PCR products of previous reactions, the EM contains a heat-labile *uracil DNA glycosylase* (UNG) and *deoxyuridine triphosphate* (dUTP) in the mixture of *deoxynucleotide triphosphates* (dNTPs). Any contaminating PCR products from previous reactions are degraded by the UNG at room temperature before the start of the current RT-PCR. Afterwards the UNG is inactivated by the elevated temperature during reverse transcription.

6.3 Amplification and detection

Before PCR amplification starts, the RNA of the IC and the RNA of HCV and HIV-1/2 undergo reverse transcription to generate cDNA copies of the RNA templates. Reverse transcription is carried out by a recombinant variant of the enzyme *Moloney Murine Leukemia Virus (M-MLV) reverse transcriptase*, which is contained in the EM. In the PCR reaction, the cDNA copies of the IC and of HCV and HIV-1/2 are then amplified in parallel with the DNA of HBV.

The amplification reaction is repeated over several cycles, with each cycle consisting of several steps. First, the reaction mixture is heated in order to split the double-stranded DNA into single-stranded DNA (“denaturation”). When cooling the mixture, probes and primers hybridize to the complementary DNA strands (“annealing”). In the presence of Mg^{2+} ions and excess dNTPs the primers are extended along the target sequences (“elongation”) by the enzyme *Thermus aquaticus* (Taq) *DNA polymerase*. During elongation, the hybridized probes are cleaved into their nucleotides by the 5’-3’-exonuclease activity of the Taq DNA polymerase.

In each cycle, new double-stranded DNA molecules are generated (“amplicons”). The PCR reaction is carried out for 50 cycles. Starting with the sixth PCR cycle, a fluorescence light measurement is taken for each cycle.

Probes add additional specificity to detection, since probe molecules can only hybridize to complementary DNA strands of the target region and probes are only cleaved by the Taq DNA polymerase, when hybridized to the complementary DNA strand.
To enable the detection of the number of amplicons produced, the probes are coupled with a fluorescent dye ("reporter") at the 5'-end and with a quencher at the 3'-end. While the probe molecules are intact, the reporter and the quencher are in close spatial proximity and the fluorescence signal is thereby strongly suppressed by fluorescence resonance energy transfer (FRET).
During elongation, the reporter dye is released, the FRET is interrupted and thus the fluorescence signal is emitted. The fluorescence signal increases in relation to the number of amplicons produced.
Different reporter dyes with specific fluorescence spectra are used for target viruses and the IC. Successful amplification of target viruses and the IC can therefore be detected by the signal increase in different fluorescence channels.

6.4 Evaluation and report

After the PCR run on *PoET Instrument*, the analysis and evaluation are carried out fully automatically by the software *Calliope*. Further details on the evaluation are described in chapter 7.10.

7 Performing the test

7.1 Requirements for performing the test

- Only personnel trained and qualified as proficient in the use of PoET products and in the handling of infectious materials should perform this procedure.
- Closely follow the procedures and guidelines provided to ensure that the test is performed correctly. Any deviation from the procedures and guidelines may affect test performance.
- Use this product only for its intended purpose.
- Use only the specified reagents and disposables.
- Use the product in a temperature range of +15 °C to +30 °C.

7.2 Specimen material

- In the validation studies for *PoET Multiscreen*, human EDTA and CPD plasma from living donors were used. All performance-related information is based on those materials, which are therefore recommended for the use of *PoET Multiscreen* with *PoET Instrument*.
- Blood specimens taken from heparin blood collection tubes, as well as specimens from heparinized persons, may not be used, as heparin can impair PCR (28).

Treat all specimens as potentially infectious.

7.3 Specimen drawing and preanalytics

7.3.1 EDTA plasma

- The blood specimen must be taken using commercially available EDTA blood collection tubes with or without gel barrier (*e.g.* Sarstedt or Becton Dickinson) according to the manufacturer's specifications.
- The whole blood specimens in the primary tubes have to be separated into the cellular and plasma components within 48 hours according to the manufacturer's specifications.
- Depending on the test method, *PoET Instrument* requires a volume of up to 1.5 mL per specimen. Further information can be found in the operator's manual of *PoET Instrument* (Preanalytics and sample processing).

The primary tubes must be filled sufficiently. Ensure that the plasma is free of visible impurities such as gel components or blood cells. Otherwise, this may lead to an impairment of test performance.

7.3.2 CPD plasma

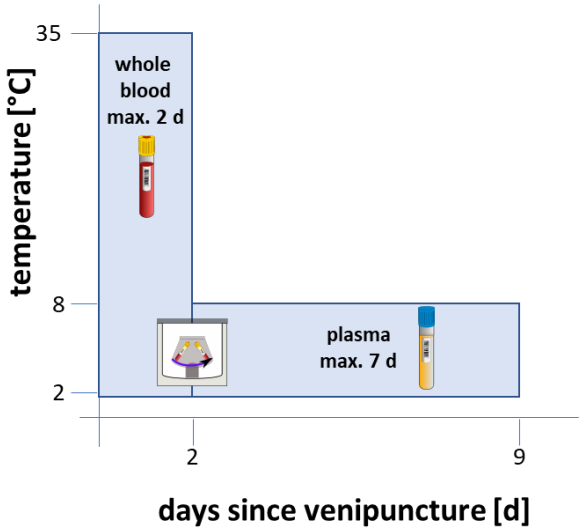
- Specimen drawing and CPD plasma production are carried out using blood bag collection systems (*e.g.* Fresenius-Kabi or Maco Pharma) following the bag collection system manufacturer's instructions.
- Depending on the test method, *PoET Instrument* requires a volume of up to 1.5 mL per specimen. Further information can be found in the operator's manual of *PoET Instrument* (Preanalytics and sample processing).

7.4 Specimen transport

Transport durations and temperatures have to comply with the conditions described in chapter 7.5).

7.5 Specimen storage

7.5.1 EDTA plasma



- Until separation the specimens can be transported and stored for 48 hours at +2 °C to +35 °C.
- After separation from the cells, EDTA plasma can be kept in primary or secondary tubes at +2 °C to +8 °C for up to 7 days without measurable change in the viral load of HCV, HBV and HIV-1/2.

Test performance may be impaired if the specified storage time of the EDTA plasma is exceeded.

7.5.2 CPD plasma

- CPD plasma bags can be transported frozen at ≤ -18 °C.
- The frozen CPD plasma bags can be stored at ≤ -20 °C for up to 3 years without measurable change in the viral load of HCV, HBV and HIV-1/2.

Test performance may be impaired if the specified storage time of the CPD plasma is exceeded.

7.6 Performing tests with *PoET Instrument*

The operation of *PoET Instrument* is described in detail in the operator's manual of *PoET Instrument* (Operation, *Calliope*).

The following is a summary of the test procedure:

Step	Action(s)
1	Prepare *PoET Instrument* for operation: • If necessary: Turn on *PoET Instrument* • If necessary: Unload samples, reagents and disposables from a previous run. Properly dispose of reagents and disposables. Either dispose of samples properly or store them as required. • If necessary: Carry out the maintenance program by following the instructions on the screen
2	Prepare the run: • Select the processing mode • Load samples onto the instrument • Assign testing orders (test types and test parameters) • Load reagents and consumables
3	Perform run
4	Unload *PoET Instrument*: • Unload samples, reagents and disposables. • Properly dispose of reagents and disposables. • Either dispose of samples properly or store them as required.

Depending on the chosen test parameters and number of samples, the PCR results of a sample batch are available about 3.5 hours after the start of the run.

7.7 Preparing samples for a *PoET Instrument* run

EDTA specimens stored in the refrigerator can be used and analyzed directly. Frozen CPD plasma bags have to be thawed and the specimen material transferred to secondary tubes. For information about primary and secondary tubes which can be used on the instrument please refer to the operator's manual of *PoET Instrument*.

7.8 Further preparations before starting the run

- In addition to the points described here, observe the instructions for use (IFU) of the other required PoET products.
- Completely thaw the required number of tubes of *PoET Internal Control* at +15 °C to +30 °C before use.
- PCR kits and PCR controls can be loaded on *PoET Instrument* frozen or thawed. Ensure that the duration of storage on the deck of the instrument does not exceed the duration specified in chapter 4.1.
- *PoET Extraction* and *PoET Prep Reagent* can be used directly.
- Before use, visually inspect each reagent container to ensure that there are no signs of leakage. If there is any sign of leakage, do not use for testing.
- Remove the caps of the reagent tubes and the peel-seal films of the extraction reagent troughs before positioning them on the carriers of *PoET Instrument*. *PoET Instrument* has no device for the automated removal of caps ('Decapper') or the piercing of films.

- In order to avoid evaporation of reagents, remove tube caps and peel-seal films only shortly before use. Remove the peel-seal films of the reagent troughs carefully to avoid spilling reagents.
- Take care that no liquid residues adhere to the tube caps or the tube walls.
- During positioning of the sample and reagent tubes on the carriers, make sure that the barcode labels are visible through the openings on the side of the carriers. Refer to the operator's manual of *PoET Instrument* for barcode specifications.
- Carry out the loading and unloading of the *PoET Instrument* reagent carriers as specified in the operator's manual of *PoET Instrument* (Operation).
- Disposables are for one time use only. Do not reuse.
- Please refer to the operator's manual of *PoET Instrument* for proper instrument maintenance.

Once the above points have been ensured, the run can be started.

7.9 Calculation of results

The evaluation of the PCR raw data is performed by the *Calliope* software. Each amplification curve is analyzed individually using the analysis algorithm. "Positive points" (PP) are assigned to the amplification curves of reactive samples. As a second value for result evaluation, the algorithm calculates the "quotient value" (Q) for each individual curve. This value is calculated by dividing the highest fluorescence value of the last three cycles by the lowest fluorescence value of the first three cycles. It represents the signal strength of the individual curve.
Different fluorescence channels of the real-time PCR cycler are used to carry out and analyze the PCR, so that the three virus parameters of *PoET Multiscreen* and the IC can be distinguished:

Virus parameter	**Test parameter in *Calliope***	**Fluorescence channel**
HCV	HCVm	FAM
HBV	HBVm	ROX
HIV	HIVm	VIC
IC	IC	CY5

7.10 Quality control measures and validity of results

The entire process from sample preparation to PCR analysis is monitored by several controls:

Control type	Product	Function
Internal control (IC)	*PoET Internal Control*	IC is added to each sample at the beginning of the process. For each non-reactive sample, the IC indicates whether the processing from extraction to the result is valid.
PCR positive control (PC)	*PoET Universal Positive Control*	PC are set up as separate reactions. The PCR positive control contains synthetic nucleic acids of the amplicons of *PoET Multiscreen*. The PC is used to demonstrate that the reagents involved in the amplification of HCV, HBV and HIV are functional.
PCR negative control (NC)	*PoET Negative Control*	NC are set up as separate reactions. The PCR negative control is used to demonstrate that the reagents involved in the amplification reaction are not contaminated with the nucleic acids to be detected.

Based on the PP and Q values of the controls *Calliope* evaluates, whether the overall result is valid for the sample batch and for each individual sample.

7.10.1 Validation of PCR negative controls (NC)

The PCR negative control, *PoET Negative Control*, is set up as a separate reaction. The individual reaction is assessed as valid in *PoET Multiscreen* if neither the IC nor one of the three virus parameters to be detected is assigned a PP value.

Depending on the sample series, several PCR negative controls are prepared on one PCR plate. Whether the overall NC result is valid depends on the result constellation of the individual reactions.

Assessment	Number of NC on a PCR plate	Definition
NC overall result valid	1	This NC is not assigned a PP value.
NC overall result valid	≥ 2	All NC are not assigned any PP values.
		No more than one NC is assigned a PP value.
NC overall result invalid	1	This NC is assigned a PP value.
NC overall result invalid	≥ 2	More than one NC on a PCR plate is assigned a PP value.

In case of an overall invalid result of the NC, all results of the corresponding sample batch are automatically evaluated as invalid.

7.10.2 Validation of PCR positive controls (PC)

The PCR positive control, *PoET Universal Positive Control,* is set up as a separate reaction. The individual reaction is assessed as valid in *PoET Multiscreen* if the PP and Q values are within the limit values for all three virus parameters to be detected. The limit values are stored in the software *Calliope*.

Depending on the sample series, several PCR positive controls are prepared on one PCR plate. Whether the overall PC result is valid depends on the result constellation of the individual reactions.

Assessment	Number of PC on a PCR plate	Definition
PC overall result valid	1	PP and Q value of this PC are within the limit values.
PC overall result valid	≥ 2	PP and Q values of all PC are within the limit values.
		PP or Q value of no more than one PC is outside the limit values.
PC overall result invalid	1	PP or Q value of this PC is outside the limit values.
PC overall result invalid	≥ 2	PP or Q values of more than one PC is outside the limit values.

In case of an overall invalid result of the PC, all results of the corresponding sample batch are automatically evaluated as invalid.

7.10.3 Validation of internal control (IC)

PoET Internal Control is added to each sample before starting the processing. The samples thus contain an additional analyte which undergoes the entire sample processing. *PoET Internal Control* is used to evaluate the validity of the results of the samples tested.

As the IC runs through the entire process, it serves to functionally monitor the reagents used and the *PoET Instrument* employed. The analysis of IC validity is only performed if the overall results of the PCR controls (NC, PC) are valid for the corresponding sample batch.

The evaluation of the IC is carried out individually for each sample position on the PCR plate. An IC result is considered valid if the IC is within the specified limits.

Only if the IC result is assessed as valid, *not reactive* results for the virus parameters HCV, HBV or HIV can also be assessed as valid.

For virus parameters that receive the result *reactive*, the IC result is ignored and the result *reactive* remains valid for these virus parameters.

7.11 Interpretation of results

Sample results are only valid if the respective PCR controls (PC, NC) of the corresponding sample batch are valid and no processing errors or other malfunctions occurred. A valid sample batch in an individual *PoET Instrument* run may include both valid and invalid sample results. Invalid samples require repeat testing. Valid sample results can be either *reactive* or *not reactive*.

Depending on the configuration, *Calliope* either provides the results automatically to a laboratory information management system (LIS, LIMS) or the results have to be reviewed manually and then transmitted to a LIS. Please refer to the operator's manual of *PoET Instrument* (*Calliope*) for more details.

7.12 Procedural limitations

- The detection of viral nucleic acids is concentration dependent. Viral nucleic acids concentrations below the detection limit of the assay cannot be reliably detected by the PCR kit.
- Incorrect specimen collection, improper specimen storage and preparation can negatively affect the stability of the virus or the nucleic acids and impair the PCR results.
- If parts of the cellular sediment are visible in the plasma of EDTA tubes without a gel barrier or if it is suspected that the sediment has been stirred up, the tubes can be re-centrifuged.
- Blood specimens taken from heparin blood collection tubes, as well as specimens from heparinized individuals, shall not be used because heparin can impair the PCR.
- A reliable test result cannot be guaranteed for untested interfering substances and interfering substances above the concentrations specified in the performance data (see chapter 8.3.3 and 8.3.4).
- Pre-exposure prophylaxis compounds or other virostatic medication taken by blood donors can lead to low concentrations of viral nucleic acids that accordingly cannot be reliably detected (see above).
- Despite sequence alignment and comparison for verification of the primers in order to detect virus variants relevant for blood donation, mutations within the highly conserved regions of the viral genome may affect oligonucleotide binding and thus virus detection.
- For specimens with very high viral loads, carry-over during sample handling and processing cannot be ruled out. When detecting a PCR result with a very low PP value, samples in the same run can thus show weakly reactive results.

7.13 Disposal

- To prevent leaking of residue reagents from used extraction and PCR plates, the relevant plates are sealed automatically during the process.
- Dispose of all materials that have come into contact with reagents in accordance with the relevant regional and national regulations.
- Dispose of reagent residues in accordance with the relevant regional and national regulations.
- Dispose of all materials that have come into contact with potentially infectious specimens in accordance with the relevant regional and national regulations.
- For information on the disposal of the kits and consumables used in combination with the PCR kit, refer to the corresponding instructions for use and material safety data sheets.

8 Performance characteristics

The performance characteristics of *PoET Multiscreen* were determined using the following standards:

- 6th WHO International Standard for hepatitis C virus RNA for nucleic acid amplification techniques (NIBSC code: 18/184)
- 4th WHO International Standard for HBV DNA for NAT (NIBSC code: 10/266)
- 4th WHO HIV-1 International Standard (NIBSC code: 16/194)
- 2nd WHO International Standard for Human Immunodeficiency Virus type 2 RNA for Nucleic Acid Amplification Techniques (NIBSC code: 16/296)

8.1 Key test features

Specimen type	EDTA or CPD plasma
Required specimen volume range	200 – 1500 µL*
Processed sample volume range	40.5 – 1300 µL*
Limit of detection	
HCV	5.5 IU/mL
HBV	1.5 IU/mL
HIV-1	13.2 IU/mL
HIV-2	5.7 IU/mL
Specificity	
EDTA plasma with gel barrier	100 %
EDTA plasma without gel barrier	100 %
CDP plasma	100 %
Test duration	Depending on the test plan of the PoET run, results are available approximately 3.5 h after the start of the run.

* Depending on the required sensitivity for testing. Please refer to the operator's manual of *PoET Instrument*.

8.2 Analytical sensitivity

8.2.1 Limit of detection (LoD)

The determination of the 95 % limit of detection (95 % LoD) for HCV, HBV and HIV-1/2 with the PCR kit *PoET Multiscreen* was carried out with a sample volume of 1.3 mL using diluted virus standards in EDTA plasma from tubes with gel barrier. The LoD was determined by performing a PROBIT analysis (log10) with the software *IBM SPSS Statistics* on the basis of the hit rates of serial dilutions of virus standards.

	HCV	**HBV**	**HIV-1**	**HIV-2**
WHO International Standard: Version, NIBSC code	6th, 18/184	4th, 10/266	4th, 16/194	2nd, 16/296
95 % LoD	5.5 IU/mL	1.5 IU/mL	13.2 IU/mL	5.7 IU/mL
Confidence interval	4.5-7.1 IU/mL	1.2-1.9 IU/mL	10.4-20.2 IU/mL	3.4-22.5 IU/mL

For CPD plasma and EDTA plasma without gel barrier, the 95 % LoD was confirmed by determining hit rates at the corresponding virus concentrations. CPD plasma and EDTA plasma without gel barrier have no negative influence on the sensitivity of HCV, HBV, HIV-1/2.

8.2.2 LoD for smaller sample volumes

If samples with a plasma volume < 1.3 mL are used in the test, *PoET Instrument* automatically replenishes the volume to 1.3 mL total volume with *sample diluent* (SD), a component of *PoET Extraction*. The LoD of *PoET Multiscreen* is reduced by the dilution factor.

As part of the validation of the PCR kit *PoET Multiscreen*, it was confirmed that replenishing with SD instead of plasma has no effect on the performance data of HCV, HBV and HIV-1/2. Further information about sample input volumes can be found in the operator's manual of *PoET Instrument* (Preanalytics and sample processing).

8.2.3 Genotype verification

The detectability of all relevant genotypes and subtypes for HCV, HBV, HIV-1 and HIV-2 was ensured by alignments of the available sequences and primer selection based on them.

In addition, the analytical detection of relevant human pathogenic genotypes and subtypes, where available, was investigated in samples with known genotypes for HCV, HBV, HIV-1 and HIV-2. These samples represent a large proportion of the genotypes and subtypes known to date.

The genotype and subtype samples (where specified) were used and tested at 5-fold 95 % LoD.

HCV		
Genotype	**Number of samples***	**Hit rate [reactive / total]**
1	22	21 / 22
2	26	26 / 26
3	19	19 / 19
4	20	20 / 20
5	19	19/ 19
6	12	12/ 12

*Number including the subtypes

The genotypes 1-6 tested for HCV are comprehensively detected when using the PCR kit *PoET Multiscreen*. No samples are available for genotypes 7 and 8. Consequently, these genotypes were not tested. The available sequences are highly conserved in the target regions of the HCV PCR. The detection of genotype 7 and 8 is ensured on the basis of the sequence analyses and primer selection derived from these analyses.

HBV		
Genotype	**Number of samples***	**Hit rate [reactive / total]**
A	18	18 / 18
B	11	11/ 11
C	12	12 / 12
D	12	12 / 12
E	7	7 / 7
F	6	6 / 6
G	3	3/ 3
H	1	1 / 1

*Number including the sub-genotypes

HBV genotypes A-H are detected with the PCR kit *PoET Multiscreen*.

HIV-1		
Genotype	**Number of samples**	**Hit rate [reactive / total]**
A	9	9 / 9
B	9	9 / 9
C	9	9 / 9
D	10	10 / 10
E	3	3 / 3
F	9	9 / 9
G	9	9 / 9
H	5	5 / 5
J	2	2 / 2
K	1	1 / 1
N	4	4 / 4
O	10	10 / 10

HIV-1		
Genotype	**Number of samples**	**Hit rate [reactive / total]**
recombinant Subtype variants		
A, G, J, U	1	1 / 1
A1	7	6 / 7
AA-GH	1	1 / 1
AB	8	7 / 8
ADG	1	1 / 1
AE	10	10 / 10
AG	11	11 / 11
AG-GH	2	2 / 2
BG	1	1 / 1
BF	1	1 / 1
CC	1	1 / 1
CD	1	1 / 1
CPX	2	2 / 2
CRF01/CRF15	1	1 / 1
DF	3	3 / 3
GH	2	2 / 2
GJ	1	1 / 1

The HIV-1 genotypes/subtypes A-H, J, K, N and O as well as the tested recombinant subtypes are detected with the PCR kit *PoET Multiscreen*. No material was available for the very rare genotype P, so this genotype was not tested. The sequence in the target region of the HIV PCR is highly conserved and shows no genotype-specific variances, so that the detection of genotype P is ensured.

HIV-2		
Genotype	**Number of samples**	**Hit rate [reactive / total]**
A	9	9 / 9
B	3	3 / 3
AB	2	2 / 2

The HIV-2 genotypes A and B, as well as the recombinant form AB are detected with the PCR kit *PoET Multiscreen*. Genotypes C, D, E, F, G are described individual cases for which no patient samples are available.

8.3 Analytical specificity

8.3.1 Experimental design cross-reactivity and interfering substances

Cross-reactivity and the influence of interfering substances on the PCR kit *PoET Multiscreen* was investigated by means of the extraction of different samples and detection of HCV, HBV and HIV. In one part of the samples, HCV, HBV and HIV-negative plasma was only spiked with the respective substance. Another part of the samples was additionally spiked with a HCV, HBV, HIV-1 and HIV-2 virus standard. Potential cross-reacting pathogens and endogenous and exogenous interfering substances were tested.

8.3.2 Cross-reactivity and clinical conditions

Sequence comparisons of the primers and probes with potentially cross-reactive human pathogenic virus sequences and an optimized PCR design minimize the risk of unwanted PCR by-products.
As part of the validation, the influence of genomic nucleic acids from selected viruses and bacteria on the PCR kit *PoET Multiscreen* was investigated. For this purpose, negative human EDTA plasma (NHP) was spiked with standards for the viruses or bacteria to be tested, extracted and amplified. In addition, HCV, HBV, HIV-1 and HIV-2-positive plasma was spiked with standards for the viruses/bacteria to be tested, extracted and amplified. The HCV, HBV, HIV-1 and HIV-2-positive samples, were spiked with HCV, HBV, HIV-1 and HIV-2 at 5-fold 95 % LoD.

Test results for cross-reactivity:

Species	**Domain**	**Nucleic acid**	**Observation**
Japanese Encephalitis Virus (JEV)	Virus	RNA	No Interference
St. Louis Encephalitis Virus (SLEV)	Virus	RNA	No Interference
West Nile Virus (WNV Lineage 1)	Virus	RNA	No Interference
Zika Virus (ZIKV)	Virus	RNA	No Interference
Yellow Fever Virus (YFV)	Virus	RNA	No Interference
Dengue Virus (DENV)	Virus	RNA	No Interference
Human T-lymphotropic Virus 1 (HTLV-1)	Virus	RNA	No Interference
Human T-lymphotropic Virus 2 (HTLV-2)	Virus	RNA	No Interference
Chikungunya Virus (ChikV)	Virus	RNA	No Interference
Hepatitis E Virus (HEV)	Virus	RNA	No Interference
Parvovirus B19 (B19V)	Virus	DNA	No Interference
Hepatitis A Virus (HAV)	Virus	RNA	No Interference
Hepatitis D Virus (HDV)	Virus	RNA	No Interference
Adenovirus	Virus	DNA	No Interference
BK Virus (BKV)	Virus	DNA	No Interference
Herpes Simplex Virus 1 (HSV-1)	Virus	DNA	No Interference
Herpes Simplex Virus 2 (HSV-2)	Virus	DNA	No Interference
Human Betaherpesvirus 6B (HHV-6B)	Virus	DNA	No Interference
Human betaherpesvirus 7 (HHV-7)	Virus	DNA	No Interference
Varicella Zoster Virus (VZV)	Virus	DNA	No Interference
Cytomegalovirus (CMV)	Virus	DNA	No Interference
Epstein-Barr Virus (EBV)	Virus	DNA	No Interference

Species	Domain	Nucleic acid	Observation
Serratia marcescens	Bakterium	DNA	No Interference
Klebsiella pneumoniae	Bakterium	DNA	No Interference
Streptococcus pyogenes	Bakterium	DNA	No Interference

No influence on the PCR performance of *PoET Multiscreen* was observed for the viruses/bacteria tested. All PCR reactions showed reactive results for IC and no false reactive or false non-reactive results for HCV, HBV or HIV.

In addition, it was shown that there is no cross-reactivity between HCV, HBV and HIV.

8.3.3 Endogenous interfering substances

To assess the influence of hemolysis and increased bilirubin, albumin and triglyceride content on *PoET Multiscreen*, plasma samples were spiked with the respective endogenous substance in several concentrations up to abnormally high levels. The test was carried out with CPD plasma.

Endogenous substance	Concentration	Observation
Bilirubin	≤ 50 mg/L	No influence
Hemoglobin	≤ 2000 mg/L	No influence
Triglycerides	≤ 40 g/L	No influence
Albumin	≤ 60 g/L	No influence
	> 60 g/L	Reliable test result not guaranteed

The tested endogenous potentially interfering substances (bilirubin, hemoglobin, triglycerides) did not show false non-reactive or false reactive results in CPD plasma at the test concentrations. No influence on the test results was observed. Albumin in high concentrations > 60 g/L in CPD plasma can interfere with the test. The reference range for healthy persons aged 20 to 60 years is between 30 and 50 g/L (29). Such high albumin concentrations can lead to invalid or, in some cases, false non-reactive results.

In addition, albumin was tested as an endogenous potentially interfering substance in EDTA plasma, as albumin can have the greatest influence on the results in the blood samples to be tested.

Endogenous substance	Concentration	Observation
Albumin	≤ 120 g/L	No influence

Albumin has shown no false non-reactive or false reactive results in EDTA plasma with *PoET Multiscreen*. There was no influence on the test results.

8.3.4 Exogenous interfering substances

The tests for assessing the influence of exogenous substances (medication taken before donating blood) were carried out on the basis of the information provided in the directive ‘EP7A2 Interference Testing in Clinical Chemistry’ (30). The selection of drugs and their concentrations are derived from this guideline. These validation tests were done with CPD plasma.

Exogenous substance	Effect	Concentration	Observation
Ascorbic acid	Antioxidant	60 µg/mL	No influence
Acetaminophen / Paracetamol	Painkiller	200 µg/mL	No influence
Aspirin	Painkiller	652 µg/mL	No influence
Ibuprofen	Painkiller	500 µg/mL	No influence
Naproxen	Painkiller	500 µg/mL	No influence
Phenylephrine HCl	Decongestant	82 µg/mL	No influence
Atrovastatin	Statin	335 µg/mL	No influence
Loratadine	Antihistamine	0.3 µg/mL	No influence
Fluoxetine	Antidepressant	3.5 µg/mL	No influence
Paroxetine	Antidepressant	1.0 µg/mL	No influence
Sertraline	Antidepressant	0.6 µg/mL	No influence

The investigated exogenous interfering substances did not show any influence on the analysis results with *PoET Multiscreen*, neither for HCV, HBV, HIV-1 or HIV-2-negative nor for HCV, HBV, HIV-1 or HIV-2-positive samples.

8.4 Whole system failure rate

The determination of the whole system failure rate leading to false non-reactive results (in percent non-reactive samples) of the overall system (short 'failure rate') of the PCR kit *PoET Multiscreen* was carried out by testing 288 samples for HCV, HBV and HIV-1/2. For this test, negative human plasma was spiked with HCV, HBV and HIV-1/2 in 3-fold 95 % LoD.

All valid samples tested for the various virus parameters were reactive. A repeatability of 100 % was achieved and the failure rate was 0 %.

8.5 Clinical performance

8.5.1 Seroconversion panels

Ten commercially available seroconversion panels for each of the parameters HCV and HIV-1 and nine panels for HBV were tested. No seroconversion panels are available for HIV-2. The aim was to prove that *PoET Multiscreen* identifies samples as reactive that are in the phase before seroconversion. The comparison with the test results for pathogen-specific antibodies was carried out using the comparative tests specified in the panel documents. In all seroconversion panels tested, in the time course of the samples of a panel, reactive samples were detected with *PoET Multiscreen* before the reactive results of the antibody tests. As a NAT-based test, *PoET Multiscreen* can detect an infection prior to seroconversion.

In parallel to testing with the *PoET Multiscreen* PCR kit, additional data was collected using CE-labeled NAT reference tests. Both data sets were compared and evaluated. The consistency between the results of the NAT tests is 95 %. More samples were successfully detected with *PoET Multiscreen* than with the NAT reference tests.

8.5.2 Diagnostic sensitivity

Diagnostic sensitivity was determined by using available donor samples (samples positive in reference NAT test) as well as negative individual donations spiked with virus to simulate positive individual donations. Samples of the seroconversion panels were also considered as positive donor samples as long as the reference test also showed a reactive result.

Virus parameter	Number of tested samples	Number of reactive samples	Diagnostic sensitivity
HCV	153	152	99.3 %
HBV	111	111	100 %
HIV-1	168	166	98.8 %
HIV-2	14	14	100 %
Total	446	443	99.3 %

An average diagnostic sensitivity of 99.3 % was achieved for a total of 446 samples tested. The diagnostic sensitivity for HBV and HIV-2 was 100 %. For HIV-1 it was determined at 98.8 % and for HCV at 99.3 %. *PoET Multiscreen* therefore corresponds to the state of the art and can reliably detect the viruses mentioned.

8.5.3 Diagnostic specificity

To determine the diagnostic specificity of the PCR kit *PoET Multiscreen*, HCV, HBV and HIV-1/2-negative samples were examined using individual EDTA and CPD plasma donations.

Plasma	Number of valid non-reactive samples	Number of false reactive samples	Specificity
EDTA (with and without gel barrier)	668	0	100 %
CPD	96	0	100 %

No false reactive samples were observed in the samples tested. It can therefore be assumed that the specificity of the PCR kit *PoET Multiscreen* is approximately 100%.

9 Overview of reagents and materials

Material	Manufacturer	Reference number	Storage conditions
PoET Multiscreen	GFE	P2M-28-30	≤ -18 °C
PoET Universal Positive Control	GFE	P3M-360-60	≤ -18 °C
PoET Extraction	GFE	P1A-24-04	+2 °C to +8 °C
PoET Prep Reagent	GFE	P1B-24-20	+2 °C to +25 °C
PoET Internal Control	GFE	P1C-1440-60	≤ -18 °C
PoET Negative Control	GFE	P3A-500-30	≤ -18 °C

Material	Manufacturer	Reference number
PoET Instrument incl. software *Calliope*	GFE	P9A
1000 µL CO-RE II Tips	Hamilton Bonaduz AG	235905
300 µL CO-RE II Tips	Hamilton Bonaduz AG	235903
Extraction Plate Set	GFE	43001-0730
PCR Plate	Azenta Life Sciences	SP-0362
13 mL Tube & Cap	Sarstedt AG & Co.	60.541.004 & 65.714

Please refer to the operator's manual of *PoET Instrument* for additional information. All items are supplied by GFE.

10 Manufacturer and customer service

Gesellschaft zur Forschung, Entwicklung und Distribution von Diagnostika im Blutspendewesen mbH
Altenhöferallee 3, 60438 Frankfurt am Main, Germany
Phone: +49 (0) 69 / 400 5513 0

Questions concerning PoET products and training courses can be addressed to the local GFE representative:
Web: https://www.gfeblut.de/contact-us/

10.1 Reporting

Inform the local competent authority and GFE if any serious incidents occur when using this product. The summary of the safety and performance report of *PoET Multiscreen* can be found using the following link: https://ec.europa.eu/tools/eudamed. Until the EUDAMED database is fully functional, please contact the local GFE representative.

11 Trademarks and patents

- *PoET* and *Calliope* are registered names owned by GFE.
- The *SuperScript® III reverse transcriptase* included in the PCR kits is a product manufactured and licensed by Life Technologies by Thermo Fisher Scientific.
- During the application of the PCR kits, the PCR plates (*PCR Plates*) '*FrameStar® 96 (cut corner A12)' with barcode* [Reference number SP0362] are used. These are subject to the following license limitation: '*FrameStar® is covered by one or more of the following US patents or their foreign counterparts, owned by Eppendorf AG: US Patent Nos. 7,347,977 and 6,340,589. FrameStar® is a registered trademark owned by Azenta Life Sciences*'.
- Other registered names, trademarks etc. used in this document are not to be considered legally unprotected, even if they are not specifically marked.

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13 Symbols

The following symbols are used in labeling of GFE products:

LOT	Batch code	SN	Serial number
REF	Reference number	UDI	Unique device identifier
	GFE manufacturer logo		Manufacturer
 YYYY-MM	Use by date (year-month)		Date of manufacture
+X°C  +Y°C	Temperature limits	 -X°C	Upper temperature limit value
 n	Contains sufficient for <n> tests (n = total number of IVD tests)		Caution Indication of safety-related information such as warnings or precautions
	Protect from sunlight		Do not re-use
IVD	*In vitro* diagnostic medical device	 www.gfeblut.de	Consult instructions for use (Reference to eIFU)
CE	This device complies with the applicable regulations for CE marking of an *in vitro* diagnostic medical device	CE 0123	CE marking and identification number of the Notified Body (0123)

14 Revision history

Version	Document ID	Date [YYYY-MM-DD]	Remarks
1	IFU-0030	2025-07-03	First release Document template: FB-0119 V04
2	IFU-0030	2025-12-17	- Error correction reference number *Extraction Plate Set* - Generalization of keywords for operator's manual of *PoET Instrument* Document template: FB-0119 V04