Gesellschaft zur Forschung, Entwicklung
und Distribution von Diagnostika
im Blutspendewesen mbH

Instructions for use

PoET Negative Control

For use with PoET Instrument

In vitro diagnostic medical device

REF **P3A-500-30**

IVD CE

Table of contents

1. Intended use

1.1. Abstract

The kit *PoET Negative Control* from *Gesellschaft zur Forschung, Entwicklung und Distribution von Diagnostika im Blutspendewesen mbH* (hereinafter referred to as GFE) is a negative control for the quality monitoring of PCR reactions.

1.2. Intended use

Intended purpose

PoET Negative Control is an accessory for the *in vitro* testing for nucleic acids of infectious agents with the corresponding PCR kits of the PoET product line.

PoET Negative Control consists of an aqueous buffer solution and is prepared as a separate reaction. It is used as a PCR negative control to prove that the reagents involved in the amplification reaction are not contaminated with the nucleic acids to be detected.

PoET Negative Control serves exclusively as a no template control (NTC) in the PCR reaction and not as a negative control for certain analytes to be detected or for the overall process.

The processing of *PoET Negative Control* is carried out with *PoET Instrument* from GFE.

PoET Negative Control is a CE marked class A *in vitro* diagnostic accessory for professional use in accordance with Regulation (EU) 2017/746.

Intended users

The application must be carried out by pre-trained and qualified laboratory personnel who have been instructed and trained in *in vitro* diagnostic procedures and have successfully completed GFE's training.

2. Test principle

PoET system

The kit *PoET Negative Control* is a stand-alone reagent product in the PoET system, consisting of the *PoET Instrument* and the PoET reagent kits for fully automated extraction, amplification and detection of nucleic acids (nucleic acid amplification technology, NAT) of infectious agents.

Principle of PoET Negative Control

When used with the PoET PCR kits on *PoET Instrument*, *PoET Negative Control* fulfils the function of a ‘no template control’ (NTC) to prove that the reagents involved in the amplification reaction are not contaminated with the nucleic acids to be detected.

PoET Negative Control contains an aqueous buffer solution that is free of viral nucleic acids.

PoET Negative Control is used instead of the sample eluates to be examined in the PCR reaction. Since *PoET Negative Control* is free of viral nucleic acids (templates) and nucleases, the PCR reagents used (*enzyme mix* and *oligo mix*) can be tested for contaminating nucleic acid sequences. This allows *PoET Negative Control* to be used to evaluate the validity of the results of amplification and detection of PCR. Information on the exact procedure can be found in the instructions for use (IFU) of the PCR kits used in combination with *PoET Negative Control*.

By definition, the PCR negative controls must have a non-reactive test result. Reactive results lead to an invalidation of the results of the affected test parameter of a PCR plate in a PoET run.

The evaluation of the data after the PCR run on *PoET Instrument* is carried out fully automated by the software *Calliope*. Further details on the evaluation are described in the operator's manual of *PoET Instrument*.

3. Reagents

One kit *PoET Negative Control* contains 30 tubes of *negative control* (NC).

Table 1: Labelling and content

PoET Negative Control			
GFE Reference number	P3A-500-30		
Basic UDI-DI	42623533722M5		
UDI	(01)04262353370117(17)YYMMDD(10)3AYYXX		
Usable volume per test (test unit)	500 µL		
Number of tests per kit	30		
Total usable volume	15 mL		
Kit component	**Filling volume [µL]**	**Identifier**	**Primary packaging (closure type)**
negative control	650	NC v1	Screw tubes (white cap)

The UDI (Unique Device Identifier) consists of UDI-DI (Device Identifier) and UDI-PI (Production Identifier). It is composed as follows: (01) UDI-DI, (17) expiration date in YYMMDD format and (10) batch number in 3AJYXX format.

The symbols are explained in Chapter 12.

3.1. Transport and storage of reagents

The kit *PoET Negative Control* is shipped on dry ice. The product should be checked upon receipt (i.e. frozen state of reagents, integrity of packaging, completeness).

PoET Negative Control is stored at ≤ 18°C and is stable until the date stated on the label.

3.2. Handling of reagents

- Please check the filling of the tubes before use.
- Take care to ensure that no reagent drops have formed above the actual liquid level on the inner tube surface and/or caps of the tubes.
- After removing the cap, the frozen *negative control* (NC) can be loaded directly onto the reagent carrier of *PoET Instrument*. A separate thawing of the NC is not necessary.

	Expired reagents are recognized and excluded by *PoET Instrument* using the reagent barcodes.
	The reagents are intended for single use and not for repeated freezing and thawing. Any remaining reagents must be discarded after application.
	Within 5 hours after removal of the reagents from the freezer the analysis has to be started on *PoET Instrument*. If the tubes were stored without cap for several hours, the functionality is no longer guaranteed depending on the duration and degree of evaporation.

3.3. Disposal of reagents

- The component *negative control* (NC) of the kit *PoET Negative Control* contains no hazardous substances or biohazard substances. The material safety data sheet is available on request from GFE Customer service.
- The contents and containers of the reagents shall be disposed of in accordance with the relevant regional and national regulations.
- When using *PoET Negative Control*, PCR plates and PCR reagent residues as well as consumables that have come into contact with them are produced. These must be disposed of in accordance with the relevant regional and national regulations. Please refer to the instructions for use of the PoET PCR kits for further information.

4. Required equipment

4.1. Devices and software

Fully automated *PoET Instrument* including software *Calliope* and operator's manual.

4.2. Required consumables

The consumables for the application of *PoET Negative Control* on *PoET Instrument* are available separately from GFE.

The required consumables can be found in the corresponding instructions for use of the PoET extraction kits and PoET PCR kits as well as in the operator's manual of *PoET Instrument*.

	The use of other than the consumables specified in the operator's manual of *PoET Instrument* is not allowed.

5. Warnings and precautions

Good laboratory practice

- Wear personal protective equipment (laboratory coat, safety glasses, laboratory gloves).
- Do not eat, drink or smoke in the laboratory.
- Treat the samples as potentially infectious as described in '*Biosafety in Microbiological and Biomedical Laboratories*' [1] and CLSI document M29A4 [2].
- If sample material is spilled, immediately disinfect with a suitable agent. Treat contaminated materials as biologically hazardous.

- Disinfect and wash your hands thoroughly after handling the samples and reagents.
- Clean and disinfect all work surfaces with suitable disinfectants, e.g. listed by German Robert Koch Institute (RKI)[1]
- Eliminate potential nucleic acid contamination with DNA-ExitusPlus™ (AppliChem GmbH) or a comparably effective agent according to the manufacturer.

General information on use

- Use *PoET Negative Control* only with *PoET Instrument* and the associated reagent kits (PCR and accessory kits) and consumables.
- Use all reagents for *in vitro* diagnostics only.
- *PoET Instrument* shall only be operated by qualified personnel trained by GFE.
- In order to prevent cross-contamination of samples or controls, all material containing samples or controls must be handled in the laboratory in accordance with the regulations for safe work.
- Store samples, controls, and PCR kits separately.
- For the safe handling of the used and sealed *24well Extraction Plates* and *PCR Plates,* please follow the instructions in the operator's manual of *PoET Instrument*
- Dispose of all materials that have come into contact with potentially infectious samples, according to the relevant regional and national regulations.
- Use *PoET Negative Control* in the temperature range from +15°C to +30°C.

Handling of reagents

- Place the frozen *PoET Negative Control* on the appropriate position of the carrier of the *PoET Instrument*. A separate thawing of the NC is not necessary.
- Remove the caps of the reagents before positioning them onto the carrier of the *PoET Instrument. PoET Instrument* does not have a device for the automated removal of caps ('Decapper').
- Carry out the loading and unloading of the *PoET Instrument* reagent carriers with reagents according to the specifications in the operator's manual of *PoET Instrument*. This also applies to the correct preparation of samples and controls. Any deviation from the specified procedures may affect the test performance.
- Avoid mixing up tube caps, as this can lead to contamination.
- *PoET Negative Control* is designed for single use. Do not reuse reagent residues.
- Do not use reagents after their shelf life has expired.

[1] or other suitable guidelines, e.g. William A. Rutala, Ph.D., M.P.H., David J. Weber, M.D., M.P.H., and the Healthcare Infection Control Practices Advisory Committee (HICPAC): Guideline for Disinfection and Sterilization in Healthcare Facilities, 2008; Update: May 2019

6. Processing of samples on *PoET Instrument*

The operation of *PoET Instrument* is described in detail in the operator's manual of *PoET Instrument*. The NC is positioned on the device together with the other reagents when loading *PoET Instrument*. The NC is used automatically by *PoET Instrument*. For details on the procedure and the process overview, please refer to the instructions for use of the respective PoET extraction and PCR kits.

Depending on the test plan of a run on *PoET Instrument*, the PCR results are available about 3 hours after the start of the run.

7. Control procedures

The automated overall process consisting of sample preparation and PCR analysis is monitored by several controls. As a PCR negative control, NC represents a quality control of the PCR reactions.

Table 2: Control procedures

Control type	Product	Function
Internal control (IC)	*PoET Internal Control*	The IC indicates whether the processing from extraction to result was valid for each non-reactive[2] sample.
PCR positive control (PC)	Multiparameter control (*PoET Master Positive Control*) or single parameter PCR positive control kits	The PC contains nucleic acids of the parameters to be detected (e.g. multiparameter control *PoET Master Positive Control*: nucleic acids of HCV, HBV, HIV, HAV and B19V). It indicates whether the process on *PoET Instrument* from the setup of the PCR reaction, through the sealing of the *PCR Plates* to the execution of the PCR has been executed correctly.
PCR negative control (NC)	*PoET Negative Control*	*PoET Negative Control* indicates that the PCR reagents are free of contaminating nucleic acids. The NC corresponds to a 'no template control' (NTC).

8. Evaluation and validity of the results

The evaluation is carried out by the software *Calliope*. The software analyzes the fluorescence signals of all PCR reactions, including the controls, and evaluates whether the result is valid.

If the PCR controls do not meet the validity criteria, the PCR results of the samples of the affected test parameter on the PCR plate are evaluated as 'not valid'.

Depending on the number of samples and the test parameters with which the samples are analyzed, a predefined number of PCR negative controls (NC) per PCR plate is applied by *PoET Instrument*.

In order for NC results to be considered valid, the signals must not be reactive for the test parameters to be determined and the internal control (IC). If several NC are applied on one PCR plate, a maximum of one NC may be reactive for the respective test parameter or the IC.

[2] Additional function semi-quantification for *PoET B19V*: reactive samples above the cut-off value are evaluated with 'AboveCutOff', samples below the cut-off value with 'BelowCutOff'. Samples below the cut-off value are considered weakly reactive. For these samples, the validity assessment by the IC is applied. Further explanations on semi-quantification can be found in the instructions for use of *PoET B19V*.

The software *Calliope* applies the following case rules to the evaluation.

Table 3: Case rules for the evaluation of NC

Case	***Negative control* (NC) result for test parameters and IC**	**Assessment**
1	All NC per PCR plate non-reactive.	Overall NC result is valid
2	*Only in case of multiple NCs per test parameter on one PCR plate:* One NC is reactive.	Overall NC result is valid
3	Two or more / all NCs on the same PCR plate are reactive.	Overall NC result is **invalid**

9. Procedural limitations

PoET Negative Control is intended exclusively for use with the PCR kits of the PoET product line (e.g. *PoET HCV*, *PoET HBV*, *PoET HIV*, *PoET HAV*, *PoET B19V*, *PoET HEV, PoET WNV*) and the accessories and consumables specified therein as well as the *PoET Instrument*.

10. Performance characteristics

The performance characteristics of the kit *PoET Negative Control* can only be determined together with the associated PoET PCR kits. For detailed information, please refer to the instructions for use of the respective GFE PCR kits.

11. Changes in analytical procedure and performance

In the event of significant changes in the analytical procedure and / or in the analytical performance of the reagents, corresponding information will be passed on by the manufacturer to the users immediately. This also applies to the measures resulting from these changes. If necessary, this may include the recall of the *in vitro* diagnostic medical devices.

12. Explanation of symbols

LOT	Symbol for ‘Batch code’
REF	Symbol for ‘Reference number’
YYYY-MM	Symbol for ‘Use by date’ (year-month)
-18°C	Symbol for ‘Upper limit of temperature’
	Symbol for ‘Consult instructions for use’
	Symbol for ‘Caution’ Indication of safety-related information such as warning or precaution.
	Symbol for ‘Do not re-use’
	Symbol for ‘Keep away from sunlight’
IVD	Symbol for ‘*In vitro* diagnostic medical device’
CE	Symbol of conformity with Regulation (EU) 2017/746 on *in vitro* diagnostic medical devices
UDI	Symbol for ‘Unique Device Identification’
	Symbol for ‘Manufacturer’
	GFE manufacturer logo

13. List of abbreviations

B19V	Parvovirus B19
DNA	Deoxyribonucleic acid
GFE	Gesellschaft zur Forschung, Entwicklung und Distribution von Diagnostika im Blut-spendewesen mbH
HAV	Hepatitis A virus
HBV	Hepatitis B virus
HCV	Hepatitis C virus
HEV	Hepatitis E virus
HIV	Human immunodeficiency virus
IC	Internal control
IFU	Instruction for use
NC	*PoET Negative Control* (PCR negative control)
NTC	No template control
PC	PCR positive control
PCR	Polymerase chain reaction
UDI	Unique Device Identifier
UDI-DI	UDI device identifier
UDI-PI	UDI production identifier
WNV	West Nile virus

14. Contact

14.1. Technical service

Questions regarding the product *PoET Negative Control* can be addressed to GFE Customer service:

Email: service@gfeblut.de

Web: https://www.gfeblut.de

14.2. Reporting of serious incidents

Regulation (EU) 2017/746 requires all serious incidents involving the device to be reported to the manufacturer and the competent authority. Please send your notification in writing to us as manufacturer to the e-mail address given in Chapter 14.1.

15. References

[1] Lewis & Wilson, Deborah. (2009). Biosafety in Microbiological and Biomedical Laboratories, 5th Edition. HHS Publication No. (CDC) 21-1112 Revised December 2009

[2] Protection of Laboratory Workers From Occupationally Acquired Infections, 4th Edition; Clinical and Laboratory Standards Institute; May 2014; ISBN Number: 1-56238-962-9

16. Exclusion of liability and trademark protection

All registered names, trademarks, etc. used in this document are not to be considered legally unprotected, even if they are not specifically marked.

17. Version history

Version	Date [YYYY-MM-DD]	Remarks
1	2021-03-22	Initial release
2	2022-05-20	• Chapter 1 Intended use: Adaptation of intended use in accordance with Regulation (EU) 2017/746 • Chapter 2 Test principle: overview of PoET system inserted • Chapter 3 Reagents: UDI and reference to Chapter 12 (Explanation of symbols) inserted • Chapter 7 Control procedure: Insertion of a footnote explaining the assessment of the IC for the additional function 'semi-quantification' for B19V • Chapter 12 Explanation of symbols: reference to Regulation (EU) 2017/746 inserted at CE symbol; addition of UDI symbol • Chapter 14: Renamed to 'Contact', divided into Chapter 14.1: Technical service and newly added Chapter 14.2 Reporting of serious incidents

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