3097-0020

chemagic™ DNA Plasma200 kit (MSM I)

Instructions for use. Reagents for 960 extractions.

Manufacturer:
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FOR *IN VITRO* DIAGNOSTIC USE

CE

revvity

SYMBOLS

	*In vitro* diagnostic medical device
	Batch code
	Packing number
	Catalog number
	Use by
	Temperature limitation
	Store in the dark
	Contains sufficient for <n> tests
	Consult instructions for use
	Manufacturer
	GHS02
	GHS08

GHS07

GHS05

This way up

Recyclable

Fragile, handle with care

Keep dry

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INTENDED PURPOSE

The chemagic™ DNA Plasma200 kit (MSM I) is intended for the extraction and purification of DNA from human plasma for analysis by PCR based *in vitro* diagnostic test systems. The disorder and determination of analytes are dependent on the PCR based downstream assay. The product is intended to be used with an automated workflow by trained laboratory personnel.

SUMMARY AND PRINCIPLE

The chemagic DNA Plasma200 kit (MSM I) is based on a magnetic bead technology platform proprietary to Revvity chemagen Technologie GmbH. Cells or other source of DNA present in plasma samples are lysed during the extraction process. The released nucleic acids bind to small magnetizable particles which are then magnetically separated from the sample material. During subsequent steps contaminants are removed and the purified nucleic acids are transferred into an elution buffer. The automated sample processing is performed using the chemagic Magnetic Separation Module I, MSM I (CMG-500) or the chemagic Magnetic Separation Module ND, MSM ND (CMG-533) with chemagic 96 Rod Head (CMG-536).

KIT CONTENTS

The kit contains reagents sufficient to perform 960 extractions.

The expiry date of the unopened kit is stated on the outer label. Do not use any component beyond the expiry date. Store at +2 to +25 °C.

Once opened, the kit components have a limited stability. The stability after opening is stated for each component separately in the reagent listing below. Note: Recap the bottles tightly immediately after use to prevent evaporation.

The bottles may discolor during storage. The discoloration of the bottles has no effect on the functionality of the assay.

The kit contains following items:

Component	Quantity
Magnetic Beads D	1 bottle, 31 mL
Lysis Buffer P	1 bottle, 210 mL
Binding Buffer P	1 bottle, 720 mL
Wash Buffer P	1 bottle, 550 mL
Wash Buffer E	1 bottle, 700 mL
Wash Buffer H	1 bottle, 700 mL
Elution Buffer	1 bottle, 115 mL
Proteinase K	5 bottles (lyophilized)
Poly(A)RNA	10 tubes (dried)
Poly(A)RNA buffer	10 tubes, 0.5 mL
Lot-specific quality control certificate	1 pc

Reagents

Component	Stability and storage
Magnetic Beads D	+2 to +25 °C until expiry date stated on the bottle label. Once opened, stable for 60 days in +2 to +25 °C.

Suspension of particles containing nanoparticular iron oxide encapsulated in a matrix of polyvinyl alcohol. Magnetic Beads (80 ± 4.8 mg/mL) bind the DNA during the extraction process.

Lysis Buffer P  DANGER	+2 to +25 °C until expiry date stated on the bottle label. Store in the dark. Once opened, stable for 60 days in +2 to +25 °C.

Ready-for-use aqueous buffer solution containing guanidinium thiocyanate (50–75%). Lysis Buffer is used to lyse the cells or other DNA source present in the sample in order to get the DNA in solution.

Lysis Buffer P contains guanidinium thiocyanate:
H302+H312+H332 Harmful if swallowed, in contact with skin or if inhaled.
H314 Causes severe skin burns and eye damage.
H412 Harmful to aquatic life with long lasting effects.
P260 Do not breathe dusts or mists.
P303+P361+P353 IF ON SKIN (or hair): Take off immediately all contaminated clothing. Rinse skin with water [or shower].
P305+P351+P338 IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
P310 Immediately call a POISON CENTER/doctor.
P362+P364 Take off contaminated clothing and wash it before reuse.
P405 Store locked up.
P501 Dispose of contents/container in accordance with local regulations.
EUH032 Contact with acids liberates very toxic gas.

Binding Buffer P

+2 to +25 °C until expiry date stated on the bottle label. Once opened, stable for 60 days in +2 to +25 °C.

DANGER

Ready-for-use Tris-HCl-buffered (pH 5.0–5.9) solution with sodium perchlorate (25–50%), acetic acid (1–2.5%) and ethanol (25–50%). Binding Buffer is used to create the appropriate conditions to get the DNA bound to the Magnetic Beads.

Binding Buffer P contains sodium perchlorate and ethanol:
H225 Highly flammable liquid and vapor.
H302 Harmful if swallowed.
H319 Causes serious eye irritation.
H373 May cause damage to organs through prolonged or repeated exposure.
P210 Keep away from heat, hot surfaces, sparks, open flames and other ignition sources. No smoking.
P241 Use explosion-proof [electrical/ventilating/lighting] equipment.
P303+P361+P353 IF ON SKIN (or hair): Take off immediately all contaminated clothing. Rinse skin with water [or shower].
P305+P351+P338 IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
P403+P235 Store in a well-ventilated place. Keep cool.
P501 Dispose of contents/container in accordance with local regulations.

Wash Buffer P

+2 to +25 °C until expiry date stated on the bottle label.
Once opened, stable for 60 days in +2 to +25 °C.

DANGER

Ready-for-use Tris-HCl-buffered (pH 4.6–5.8) solution with sodium perchlorate (15–25%), hydrogen chloride (<0.25%) and ethanol (25–50%). Used for removing non-DNA contaminants during washing step.

Wash Buffer P contains ethanol and sodium perchlorate:
H225 Highly flammable liquid and vapor.
H319 Causes serious eye irritation.
H373 May cause damage to organs through prolonged or repeated exposure.
P210 Keep away from heat, hot surfaces, sparks, open flames and other ignition sources. No smoking.
P241 Use explosion-proof [electrical/ventilating/lighting] equipment.
P303+P361+P353 IF ON SKIN (or hair): Take off immediately all contaminated clothing. Rinse skin with water [or shower].
P305+P351+P338 IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
P403+P235 Store in a well-ventilated place. Keep cool.
P501 Dispose of contents/container in accordance with local regulations.

Wash Buffer E

+2 to +25 °C until expiry date stated on the bottle label.
Once opened, stable for 60 days in +2 to +25 °C.

DANGER

Ready-for-use solution contains ethanol 50–75%. Used for removing last traces of non-DNA contaminants during washing step.

Wash Buffer E contains ethanol:
H225 Highly flammable liquid and vapor.
P210 Keep away from heat, hot surfaces, sparks, open flames and other ignition sources. No smoking.
P241 Use explosion-proof [electrical/ventilating/lighting] equipment.
P280 Wear protective gloves/protective clothing/eye protection/face protection.
P303+P361+P353 IF ON SKIN (or hair): Take off immediately all contaminated clothing. Rinse skin with water [or shower].
P403+P235 Store in a well-ventilated place. Keep cool.
P501 Dispose of contents/container in accordance with local regulations.

Wash Buffer H	+2 to +25 °C until expiry date stated on the bottle label. Once opened, stable for 60 days in +2 to +25 °C.

Ready-for-use ultra-filtered water solution. Used for removing possible residuals of ethanol.

Elution Buffer	+2 to +25 °C until expiry date stated on the bottle label. Once opened, stable for 60 days in +2 to +25 °C.

Ready-for-use 10 mM Tris-HCl-buffered (pH 7.8–8.4) solution.

Proteinase K	+2 to +25 °C until expiry date stated on the bottle label. Once reconstituted, stable for 28 days in +2 to +8 °C.

DANGER

The Proteinase K (Proteinase 50–90%) is reconstituted by adding 2.5 mL of purified water. Proteinase K is added to enhance the efficiency of the lysis step.

Proteinase K contains Proteinase, Tritirachium album serine:
H315 Causes skin irritation.
H319 Causes serious eye irritation.
H334 May cause allergy or asthma symptoms or breathing difficulties if inhaled.
H335 May cause respiratory irritation.
P261 Avoid breathing dust/fume/gas/mist/vapors/spray.
P280 Wear protective gloves / eye protection / face protection.
P284 [In case of inadequate ventilation] wear respiratory protection.
P305+P351+P338 IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
P405 Store locked up.
P501 Dispose of contents/container in accordance with local regulations.

Poly(A)RNA	+2 to +25 °C until expiry date stated on the tube label. Once reconstituted, stable for 30 days in +2 to +8 °C.

Poly(A)RNA is reconstituted by adding 440 µL of Poly(A)RNA Buffer. The Poly(A)RNA functions as a DNA carrier to enhance the efficiency of the extraction process.

Component	Quantity	Shelf life and storage
Poly(A)RNA buffer  DANGER	+2 to +25 °C until expiry date stated on the tube label.	

Ready-for-use aqueous buffer solution containing guanidinium thiocyanate (25–50%). Poly(A)RNA Buffer is used for reconstitution of Poly(A)RNA.

Poly(A)RNA buffer contains guanidinium thiocyanate:
H302+H332 Harmful if swallowed or if inhaled.
H314 Causes severe skin burns and eye damage.
H412 Harmful to aquatic life with long lasting effects.
P260 Do not breathe dusts or mists.
P303+P361+P353 IF ON SKIN (or hair): Take off immediately all contaminated clothing. Rinse skin with water [or shower].
P305+P351+P338 IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
P310 Immediately call a POISON CENTER/doctor.
P405 Store locked up.
P501 Dispose of contents/container in accordance with local regulations.
EUH032 Contact with acids liberates very toxic gas.

MATERIALS REQUIRED BUT NOT SUPPLIED WITH THE KIT

The chemagic DNA Plasma200 kit (MSM I) requires the following items, which are available from Wallac Oy or Revvity, Inc. and its distributors:

- chemagic Magnetic Separation Module I, MSM I (prod. no. CMG-500) or chemagic Magnetic Separation Module ND, MSM ND (prod. no. CMG-533) with chemagic 96 Rod Head (prod. no. CMG-536)
- chemagic consumables (tips, deep well plates and low well plates for chemagic, prod. no. 4155-0010)

Additional required items:

- pipettes and pipette tips with aerosol barriers
- molecular grade water

Additional optional items:

- chemagic™ Stand 96 (prod. no. CMG-301)

SPECIMEN COLLECTION AND HANDLING

Human plasma samples (200 µL) should be used, either fresh or stored typically for up to five days at +2 to +8 °C or stored frozen at -20 to -80 °C. Frozen samples must not be thawed more than once. The recommended sample stabilizers are EDTA or citrate. The use of heparin stabilized plasma samples can cause inhibition problems in PCR and is therefore not recommended.

The extraction efficiency using other types of sample material has not been determined.

Specimen Stability

The influence of storage time and temperature was studied[1] using several plasma specimens collected to collection tubes containing either EDTA or citrate as an anticoagulant. The specimens were stored at -20 °C and thawed specimens were spiked with PhiX 174 phage lysate as a viral model. The extracted DNA eluates were used as a template in Real Time PCR assay for PhiX, and two separate PCR runs were performed using each eluate once. The results fulfilled the pre-defined acceptance criteria.

WARNINGS AND PRECAUTIONS

The product is intended to be used by trained laboratory personnel.

To minimize irregularities in diagnostic results, the product is intended to be used with an internal control as well as positive and negative controls throughout the process of sample preparation, and sample amplification and detection according to the downstream assay used.

Handle all patient specimens as potentially infectious. Nevertheless all recommended precautions for the handling of blood derivatives should be observed. Please refer to the U.S. Department of Health and Human Services publication "Biosafety in Microbiological and Biomedical Laboratories" or any other local or national regulation.

Lysis Buffer P contains guanidinium thiocyanate and is harmful if swallowed, in contact with skin or if inhaled, causes severe skin burns and eye damage and is harmful to aquatic life with long lasting effects. **Binding Buffer P contains sodium perchlorate and ethanol** and is highly flammable liquid and vapor and is harmful if swallowed, causes serious eye irritation and may cause damage to organs through prolonged or repeated exposure. **Wash Buffer P contains sodium perchlorate and ethanol** and is highly flammable liquid and vapor and causes serious eye irritation and may cause damage to organs through prolonged or repeated exposure. **Poly(A)RNA buffer contains guanidinium thiocyanate** and is harmful if swallowed or if inhaled, causes severe skin burns and eye damage and is harmful to aquatic life with long lasting effects. **Wash Buffer E contains ethanol** and is highly flammable liquid and vapor. **Proteinase K contains Proteinase, Tritirachium album serine** and causes skin irritation and serious eye irritation, may cause allergy or asthma symptoms or breathing difficulties if inhaled and may cause respiratory irritation. See specific precautions from the section “KIT CONTENTS”.

[1] Study performed at Revvity chemagen Technologie GmbH, Baesweiler, Germany.

To avoid injuries working with the kit components, always wear safety glasses, disposable gloves, and protective clothing. For detailed information, please refer to the corresponding safety data sheets (SDS).

Follow local regulations for handling of ethanolic solutions.

Disposal of all waste should be in accordance with local regulations.

For a patient/user/third party in the European Union and in countries with an identical regulatory regime (IVDR; EU 2017/746/EU); if, during the use of this device or as a result of its use, a serious incident has occurred, please report it to the manufacturer and to your national authority. The contact information for the manufacturer of this device to report a serious incident is stated on the cover page of these instructions for use.

PROCEDURE

Extraction protocol using the chemagic Magnetic Separation Module I (MSM I)

The duration of the automated extraction protocol is approximately 60 minutes.

The protocol is suitable for processing up to 96 samples in parallel (see protocol steps below). For detailed instructions on the use of the chemagic Magnetic Separation Module I (MSM I) or the chemagic Magnetic Separation Module ND (MSM ND), please refer to the respective instrument manual.

Samples and reagents must be brought to room temperature (+19 to +25 °C) before use.

NOTE: Recap the bottles tightly immediately after use. Binding Buffer P, Wash Buffer P and Wash Buffer E contain ethanol. If ethanol evaporates, the optimal yield or detection sensitivity cannot be guaranteed.

Processing Steps in Detail

Preparing Steps

1. Check all kit components for integrity. In case of damage, contact your supplier.

2. Before prefilling the plates mark each plate with material in position.

3. Reconstitute the Proteinase K and Poly(A)RNA components

    a. Proteinase K: Add 2.5 mL molecular grade water to Proteinase K bottle and mix gently until dissolved.
    b. Poly(A)RNA: Add 440 µL of Poly(A)RNA Buffer to the Poly(A)RNA tube and mix thoroughly until dissolved.

4. If Lysis Buffer P contains precipitate (formed during transfer or storage), the solution should be heated to 50 – 60 °C and thoroughly mixed until the solution is clear. The clarity of the Lysis Buffer P should be visually conformed always before use (visual inspection should be done followed by mixing and by opening the bottle cap).

5. Prefill the plates (using a multichannel pipette or a dispensing system) as described in the table in section “Protocol Steps”. **Please pay special attention to the prefilling order (Protocol Steps in MSM I instrument’s tracking system positions 3–7).** The process has to be started as soon as possible, at the latest 30 minutes after prefilling of the solutions to avoid evaporation of the solutions.

NOTE: The run must be started immediately after adding the Binding Buffer P and magnetic beads to the lysed sample wells. Hesitation may result in low yield and purity.

Protocol Steps

Position in tracking system*	Material in position	Protocol step in detail
		Select the protocol '**chemagic DNA Plasma200 IVD 140327.che**' and press [insert IDs] button. Follow the instructions given in the software. If the enhanced functions are deactivated, continue without pressing [insert IDs] button.
1	Rack with Disposable Tips	Use Disposable Tips according to the positions of the samples.
External step	Deep well plate 200 µL plasma (sample) 4 µL reconstituted Poly(A)RNA 10 µL reconstituted Proteinase K 200 µL Lysis Buffer P	Dispense up to 96 wells of the Sample Plate with 200 µL plasma. Add the reconstituted Poly(A)RNA and Proteinase K to the sample wells. Add Lysis Buffer P to the wells containing sample and incubate the samples in 50–60 °C for 10 minutes. The Proteinase K activity will decrease after incubation longer than 10 minutes in Lysis Buffer P. Ensure that all samples are mixed with Poly(A)RNA/Proteinase K/Lysis Buffer P during incubation.
2	650 µL Binding Buffer P 30 µL Magnetic Beads D	Add the Binding Buffer P and thoroughly resuspended Magnetic Beads D to each lysed sample well. Place the sample plate to rack position 2 and **start the MSM I run immediately.**
		Check all plates for accurate positioning and fitting. Close the cover and start the process by pressing [Start] button. **The process has to be started as soon as possible, at the latest 30 minutes after prefilling of the solutions** to avoid evaporation of the solutions.
3	Deep well plate 500 µL Wash Buffer P	Prefill **before starting the run** according to the positions of the samples.
4	Deep well plate 500 µL Wash Buffer E	Prefill **before starting the run** according to the positions of the samples.
5	Deep well plate 500 µL Wash Buffer H	Prefill **before starting the run** according to the positions of the samples.
6	Deep well plate 100 µL Elution Buffer	Prefill **before starting the run** according to the positions of the samples.
7	Deep well plate Empty	Empty deep well plate is for used Disposable Tips to be discarded.

* Numbers in tracking system refer to the positioning of the plate in MSM I instrument

PROCEDURAL NOTES

1. A thorough understanding of this package insert and the chemagic Magnetic Separation Module I (MSM I) or chemagic Magnetic Separation Module ND (MSM ND) instrument manual is necessary for successful use of the chemagic DNA Plasma200 kit (MSM I).

2. Do not use kit reagents after the expiry date printed on the kit label. Once opened, the reagents can be used for the time period stated in the reagent listing of this kit insert.

3. Any deviation from the protocol may affect the results.

LIMITATIONS OF THE PROCEDURE

In some cases traces of Magnetic Beads D may be left in the eluate. Though such particles will usually not interfere with PCR or most downstream applications, an additional separation step either using centrifugation or a magnetic separator (e.g. chemagic Stand 96, prod. no. CMG-301) is recommended, in order to separate any traces of particles.

The kit is not intended to be used for extraction and purification of human genomic or human cfDNA.

Extracted DNA should be used immediately after extraction in the desired *in vitro* diagnostic test.

PERFORMANCE CHARACTERISTICS

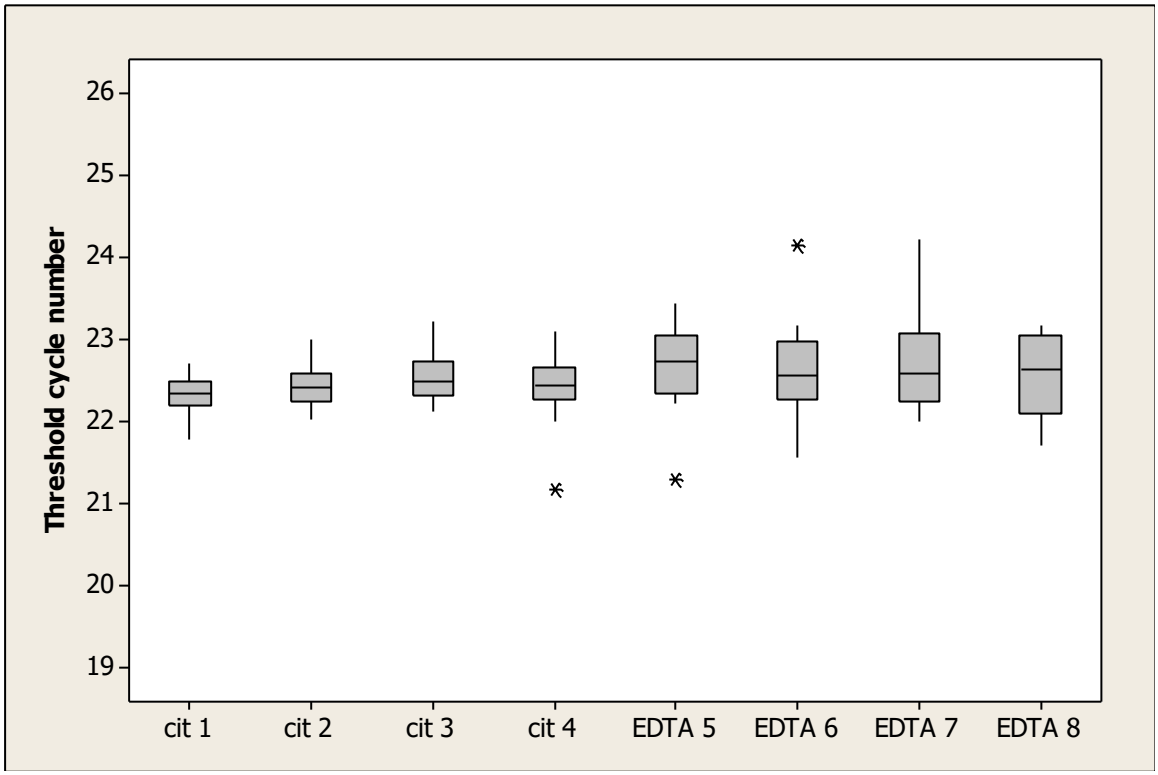
The performance of the chemagic DNA Plasma200 kit (MSM I) was established by conducting DNA extractions for human plasma samples spiked with bacteriophage or Cytomegalovirus (CMV).

The bacteriophage spiked in human plasma represents the virus from which the DNA is extracted during the process. The same amount of bacteriophage had been spiked to each sample. The descriptive statistics of the precision and repeatability testing is presented in table 1. In picture 1, the Ct -values (RT-PCR threshold cycle) from the samples are presented as Boxplot chart.

Table 1. The descriptive statistics of the precision and repeatability testing from the bacteriophage spiked plasma samples

Sample	N	Average Ct*	SD	Median Ct*	Min Ct*	Max Ct*
Citrate	80	22.43	0.30	22.43	21.16	23.23
EDTA	80	22.66	0.49	22.62	21.28	24.21

* Ct = Threshold Cycle number



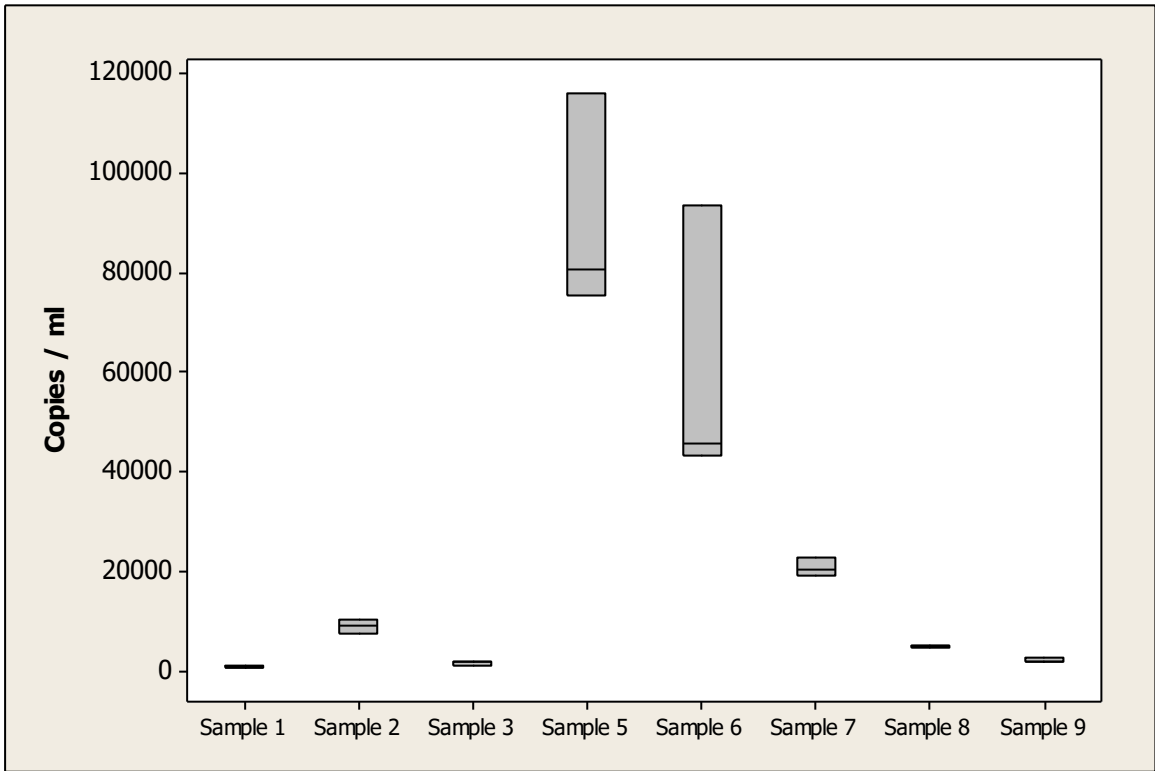
Picture 1. The Ct -values (RT-PCR threshold cycle) from the bacteriophage spiked plasma samples

The performance in clinical downstream application was tested with CMV spiked human EDTA plasma samples. The samples and the result targets were provided by an external test organizer. The results of the testing in clinical downstream application are presented in table 2. Boxplot chart from the results of CMV spiked plasma samples in presented in picture 2.

Table 2. The results of the testing in clinical downstream application (CMV testing)

	Test		Target		
Sample number	Average copies / mL	Result	Copies / mL	Result	Difference from the target %
Sample 1	892	positive	851	positive	-4.8%
Sample 2	8947	positive	8375	positive	-6.8%
Sample 3	1641	positive	1563	positive	-5.0%
Sample 4	0	negative*	0	negative	N/A
Sample 5	90767	positive	Not determined	positive	N/A
Sample 6	60833	positive	Not determined	positive	N/A
Sample 7	20933	positive	Not determined	positive	N/A
Sample 8	5063	positive	Not determined	positive	N/A
Sample 9	2183	positive	Not determined	positive	N/A

(* negative sample is not included in the Boxplot chart)



Picture 2. The results of RT-PCR run from CMV spiked EDTA plasma samples

WARRANTY

Any change or modification of the procedure not recommended by the manufacturer may affect the results, in which event Wallac Oy and its affiliates disclaim all warranties expressed, implied or statutory including the implied warranty of merchantability and fitness for use.

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No content changes between the current and previous version. Company name and logo updated.

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