CE

IVD

For Professional Use Only

AmpliSens® All-screen-FRT

PCR kit

Instruction Manual

AmpliSens®

EC REP

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TABLE OF CONTENTS

1. INTENDED USE

AmpliSens® AII-screen-FRT PCR kit is an *in vitro* nucleic acid amplification test for qualitative detection and differentiation of RNA/DNA of *Shigella* spp., enteroinvasive *E.coli* (*EIEC*), *Salmonella* spp., thermophilic *Campylobacter* spp., group F *Adenoviruses* and group A *Rotaviruse*s, *Norovirus* genotype 2, and *Astroviruses* in the clinical material and environmental samples by using real-time hybridization-fluorescence detection.

The results of PCR analysis are taken into account in complex diagnostics of disease.

2. PRINCIPLE OF PCR DETECTION

Detection of acute intestinal infections (AII) by the polymerase chain reaction (PCR) is based on the multiplex amplification of the pathogen genome specific region in two tubes using specific primers. In real-time PCR, the amplified product is detected using fluorescent dyes. These dyes are linked to oligonucleotide probes which bind specifically to the amplified product during thermocycling. The real-time monitoring of fluorescence intensities during the real-time PCR allows the detection of accumulating product without re-opening the reaction tubes after the PCR run. **AmpliSens® AII-screen-FRT** PCR kit is a qualitative test that contains the Internal Control (IC). It must be used in the extraction procedure in order to control the extraction process of each individual sample and to identify possible reaction inhibition. **AmpliSens® AII-screen-FRT** PCR kit uses “hot-start,” which greatly reduces the frequency of nonspecifically primed reactions. “Hot-start” is guaranteed by separation of nucleotides and Taq-polymerase by using a chemically modified polymerase (TaqF). The chemically modified polymerase (TaqF) is activated by heating at 95 °C for 15 min.

3. CONTENT

AmpliSens® AII-screen-FRT PCR kit is produced in 1 form:

AmpliSens® AII-screen-FRT PCR kit variant FRT-50 F, **REF** R-B45(RG,iQ)-CE.

AmpliSens® AII-screen-FRT PCR kit variant FRT-50 F includes:

Reagent	*Description*	*Volume (ml)*	*Quantity*
PCR-mix-1-FEP/FRT *Shigella* spp. / *Salmonella* spp.	colorless clear liquid	0.6	1 tube
PCR-mix-1-FEP/FRT *Campylobacter* spp. / *Adenovirus*	colorless clear liquid	0.6	1 tube
RT-PCR-mix-1-FEP/FRT *Rotavirus* / *Astrovirus*	colorless clear liquid	0.6	1 tube
RT-PCR-mix-1-FEP/FRT *Norovirus* / STI	colorless clear liquid	0.6	1 tube
RT-PCR-mix-2-FEP/FRT	colorless clear liquid	0.3	5 tubes
Polymerase (TaqF)	colorless clear liquid	0.03	4 tubes
TM-Revertase (MMlv)	colorless clear liquid	0.015	4 tubes
RT-G-mix-2	colorless clear liquid	0.015	4 tubes
Positive Control DNA *Shigella sonnei* / *Salmonella* (C+$_{Shigella\ /\ Salmonella}$)	colorless clear liquid	0.1	1 tube
Positive Control DNA *Campylobacter jejuni* / *Adenovirus* F-Flu (C+$_{Campylobacter\ /\ Adenovirus}$)	colorless clear liquid	0.1	1 tube
Positive Control cDNA *Rotavirus*-Flu / *Astrovirus* (C+$_{Rotavirus\ /\ Astrovirus}$)	colorless clear liquid	0.1	1 tube
Positive Control cDNA *Norovirus* genotype 2-Flu / STI (C+$_{Norovirus\ genotype\ 2\ /\ STI}$)	colorless clear liquid	0.1	1 tube
DNA-buffer	colorless clear liquid	0.5	1 tube
Internal Control STI-87-rec (IC)*	colorless clear liquid	0.12	5 tubes
Negative Control (C–)**	colorless clear liquid	1.6	1 tube
RNA-eluent***	colorless clear liquid	1.2	5 tubes

* Internal Control STI-87-rec (IC) must be used in the extraction procedure. Add 10 µl to each sample if using RIBO-sorb, **REF** K2-1-Et-50-CE.

** must be used in the extraction procedure as Negative control of extraction.

*** must be used in the extraction procedure.

AmpliSens® AII-screen-FRT PCR kit is intended for 55 reactions (including controls).

4. ADDITIONAL REQUIREMENTS

- RNA/DNA extraction kit.
- Disposable powder-free gloves and laboratory coat.
- Pipettes (adjustable).

- Sterile pipette tips with aerosol barriers (up to 200 µl).
- Tube racks.
- Vortex mixer.
- Desktop centrifuge with rotor for 2-ml reaction tubes.
- PCR box.
- Personal thermocyclers (for example, Rotor-Gene 3000 or Rotor-Gene 6000 (Corbett Research, Australia), Rotor-Gene Q (Qiagen, Germany), iQ5 (Bio-Rad, USA), Mx3000P (Stratagene, USA), or equivalent).
- Disposable polypropylene microtubes for PCR (0.1- or 0.2-ml; for example, Axygen, USA).
- Refrigerator for 2–8 °C.
- Deep-freezer for ≤ –16 °C.
- Waste bin for used tips.

5. GENERAL PRECAUTIONS

The user should always pay attention to the following:

- Use sterile pipette tips with aerosol barriers and use new tip for every procedure.
- Store and handle amplicons away from all other reagents.
- Thaw all components thoroughly at room temperature before starting detection.
- When thawed, mix the components and centrifuge briefly.
- Use disposable gloves, laboratory coats, protect eyes while samples and reagents handling. Thoroughly wash hands afterward.
- Do not eat, drink, smoke, apply cosmetics, or handle contact lenses in laboratory work areas.
- Do not use a kit after its expiration date.
- Dispose of all samples and unused reagents in compliance with local authorities' requirements.
- Samples should be considered potentially infectious and handled in a biological cabinet in accordance with appropriate biosafety practices.
- Clean and disinfect all sample or reagent spills using a disinfectant, such as 0.5 % sodium hypochlorite or another suitable disinfectant.
- Avoid contact with the skin, eyes and mucosa. If skin, eyes and mucosa contact, immediately flush with water, seek medical attention.
- Material Safety Data Sheets (MSDS) are available on request.
- Use of this product should be limited to personnel trained in the techniques of DNA

amplification.

- The laboratory process must be one-directional, it should begin in the Extraction Area and then move to the Amplification and Detection Areas. Do not return samples, equipment and reagents to the area in which the previous step was performed.

Some components of this kit contain sodium azide as a preservative. Do not use metal tubing for reagent transfer.

6. SAMPLING AND HANDLING

Obtaining samples of biological materials for PCR-analysis, transportation and storage are described in the manufacturer's handbook [1]. It is recommended that this handbook is read before starting work.

AmpliSens® AII-screen-FRT PCR kit is intended for the analysis of RNA/DNA extracted with RNA/DNA extraction kits from feces and concentrated water samples.

The clinical material must be taken according to state and local authorities' requirements.

7. WORKING CONDITIONS

AmpliSens® AII-screen-FRT PCR kit should be used at 18–25 °C.

8. PROTOCOL

8.1. RNA/DNA extraction

It is recommended to use the following nucleic acid extraction kits:

- RIBO-prep, **REF** K2-9-Et-50-CE.
- RIBO-sorb, **REF** K2-1-Et-50-CE.
- Other nucleic acid extraction kits.

Extract RNA/DNA according to the manufacturer's instructions.

RNA-eluent is additionally required for RNA/DNA extraction.

8.2. Preparing PCR

8.2.1. Preparing tubes for PCR with reverse transcription (RT-PCR)

The total reaction volume is **25 µl**, the volume of cDNA sample is **10 µl**.

Carry out all control amplification reactions even while testing only one RNA/DNA sample.

1. Prepare the required number of tubes including controls.
2. Mix in a sterile tube:

- **PCR-mix-1-FEP/FRT *Shigella* spp. / *Salmonella* spp.** or **PCR-mix-1-FEP/FRT *Campylobacter* spp. / *Adenovirus***
- **RT-PCR-mix-2-FEP/FRT**
- **Polymerase (TaqF)**

or

- **RT-PCR-mix-1-FEP/FRT *Rotavirus* / *Astrovirus*** or **RT-PCR-mix-1-FEP/FRT *Norovirus* / STI**
- **RT-PCR-mix-2-FEP/FRT**
- **Polymerase (TaqF)**
- **RT-G-mix-2**
- **TM-Revertase (MMlv)**

Mix reagents according to **Appendix 1**. Vortex the tubes thoroughly and sediment drops from walls of tubes.

3. Transfer **15 µl** of the prepared mixture to the prepared tubes.
4. Add **10 µl** of **RNA/DNA** obtained from clinical or control samples at the extraction stage to the prepared tubes using tips with aerosol barrier.

Dispose of the unused mixture.

When using RIBO-sorb, do not transfer the sorbent into the reaction mixture.

5. Carry out the control amplification reactions:

NCA - Add **10 µl** of **DNA-buffer** to the tube labeled NCA (Negative Control of Amplification).

C+*Shigella / Salmonella* - Add **10 µl** of **Positive Control DNA *Shigella sonnei* / *Salmonella*** for **PCR-mix-1-FEP/FRT *Shigella* spp. / *Salmonella* spp.** to the tube labeled C+*Shigella / Salmonella* (Positive Control of Amplification).

C+*Campylobacter / Adenovirus* - Add **10 µl** of **Positive Control DNA *Campylobacter jejuni* / *Adenovirus* F-Flu** for **PCR-mix-1-FEP/FRT *Campylobacter* spp. / *Adenovirus*** to the tube labeled C+*Campylobacter / Adenovirus* (Positive Control of Amplification).

C+*Rotavirus / Astrovirus* - Add **10 µl** of **Positive Control cDNA *Rotavirus*-Flu / *Astrovirus*** for **RT-PCR-mix-1-FEP/FRT *Rotavirus* / *Astrovirus*** to the tube labeled C+*Rotavirus / Astrovirus* (Positive

Control of Amplification).

C+*Norovirus* genotype 2 / STI - Add **10 µl** of **Positive Control cDNA *Norovirus* genotype 2-Flu/STI** for **RT-PCR-mix-1-FEP/FRT *Norovirus* / STI** to the tube labeled C+*Norovirus* genotype 2 / STI (Positive Control of Amplification).

8.2.2. Reverse transcription and amplification

Program the real-time amplification instrument according to manufacturer's manual and **Guidelines** [2].

1. Create a temperature profile on your instrument as follows:

Table 1

Amplification program

	Rotor-type Instruments[1]			Plate-type Instruments[2]		
Step	***Temperature, °C***	***Time***	***Cycles***	***Temperature, °C***	***Time***	***Cycles***
Hold 1	**50**	30 min	1	**50**	30 min	1
Hold 2	**95**	15 min	1	**95**	15 min	1
Cycling	**95**	10 s	45	**95**	10 s	45
	60	25 s		**60**	25 s	
	72	10 s		**72**	10 s	

Fluorescent signal is detected in the channels designed for the FAM/Green and JOE/Yellow/HEX fluorophores on the 2nd step of stage Cycling (60 °C).

2. Adjust the fluorescence channel sensitivity according to the *Important Product Information Bulletin.*

3. Insert tubes into the reaction module of the device.

4. Run the amplification program with fluorescence detection.

5. Analyze results after the amplification program is completed.

9. DATA ANALYSIS

The results are interpreted by the software of the instrument by the crossing (or not-crossing) of the fluorescence curve with the threshold line.

See **Guidelines** [2] for data analysis settings for the instrument.

9.1. Results interpretation for samples

[1] For example, Rotor-Gene 3000, Rotor-Gene 6000, Rotor-Gene Q or equivalent.
[2] For example, iCycler, iQ5, Mx3000P, Mx3000, or equivalent.

Table 2

Interpretation of results

Ct channel	PCR-mix-1-FEP/FRT ***Shigella*** **spp. / *Salmonella* spp.**	PCR-mix-1-FEP/FRT ***Campylobacter*** **spp. / *Adenovirus***	RT-PCR-mix-1-FEP/FRT ***Rotavirus*** **/ *Astrovirus***	RT-PCR-mix-1-FEP/FRT ***Norovirus*** **/ STI**
FAM/ Green	**Pos** (≤ boundary value*) **–** *Shigella* spp. DNA is **detected** **Neg –** *Shigella* spp. DNA is **not detected** **	**Pos** (≤ boundary value*) **–** *Campylobacter* spp. DNA is **detected** **Neg –** *Campylobacter* spp. DNA is **not detected** **	**Pos** (≤ boundary value*) **–** *Rotavirus* grA RNA is **detected** **Neg –** *Rotavirus* grA RNA is **not detected** **	**Pos** (≤ boundary value*) for **IC – valid results** **Neg – invalid results** ***
JOE/ Yellow/HEX	**Pos** (≤ boundary value*) **–** *Salmonella* spp. DNA is **detected** **Neg –** *Salmonella* spp. DNA is **not detected** **	**Pos** (≤ boundary value*) **–** *Adenovirus* grF DNA is **detected** **Neg –** *Adenovirus* grF DNA is **not detected** **	**Pos** (≤ boundary value*) **–** *Astrovirus* grA RNA is **detected** **Neg –** *Astrovirus* grA RNA is **not detected** **	**Pos** (≤ boundary value*) **–** *Norovirus* G2 RNA is **detected** **Neg –** *Norovirus* G2 RNA is **not detected** **

* For boundary values, see the *Important Product Information Bulletin*.

** If the Ct value in the FAM/Green channel for RT-PCR-mix-1-FEP/FRT *Norovirus* / STI is not more than the boundary value, the result is correct.

*** If the Ct value in the FAM/Green channel for RT-PCR-mix-1-FEP/FRT *Norovirus* / STI is absent or exceeds the boundary value, the negative result for other PCR-mixes-1 is considered to be invalid. It is necessary to repeat PCR starting from the extraction stage.

9.2. Interpretation of results for control samples

The result of the analysis is considered reliable only if the results obtained for positive and negative controls of amplification as well as for the negative control of extraction are correct.

Table 3

Results for controls

PCR-mixes-1	Control	Stage for control	Ct value in channel	
			FAM/Green	JOE/Yellow/HEX
PCR-mix-1 FEP/FRT *Shigella* spp. / *Salmonella* spp., PCR-mix-1-FEP/FRT *Campylobacter* spp. / *Adenovirus*, RT-PCR-mix-1-FEP/FRT *Rotavirus* / *Astrovirus*	C–	RNA/DNA extraction	Neg	Neg
RT-PCR-mix-1-FEP/FRT *Norovirus* / STI	C–	RNA/DNA extraction	Neg	Pos (≤ boundary value*)
PCR-mix-1 FEP/FRT *Shigella* spp. / *Salmonella* spp.	C+*Shigella / Salmonella*	Amplification	Pos (≤ boundary value*)	Pos (≤ boundary value*)
PCR-mix-1-FEP/FRT *Campylobacter* spp. / *Adenovirus*	C+*Campylobacter / Adenovirus*	Amplification	Pos (≤ boundary value*)	Pos (≤ boundary value*)
RT-PCR-mix-1-FEP/FRT *Rotavirus* / *Astrovirus*	C+*Rotavirus / Astrovirus*	Amplification	Pos (≤ boundary value*)	Pos (≤ boundary value*)
RT-PCR-mix-1-FEP/FRT *Norovirus* / STI	C+*Norovirus* genotype 2 / STI	Amplification	Pos (≤ boundary value*)	Pos (≤ boundary value*)
All mixes-1	NCA	Amplification	Neg	Neg

* For boundary values, see the *Important Product Information Bulletin*.

10. TROUBLESHOOTING

Results of analysis are not taken into account in the following cases:

- If the signal for C– (except for RT-PCR-mix-1-FEP/FRT *Norovirus* / STI) and/or the signal for NCA in JOE/Yellow/HEX or FAM/Green channel is less than the Ct boundary value, analysis should be repeated starting from the DNA extraction stage.
- If no signal is detected for the positive controls of amplification, it may suggest that the programming of the temperature profile of the used Instrument was incorrect, or that the configuration of the PCR reaction was incorrect, or that the storage conditions for kit components did not comply with the manufacturer's instruction, or that the reagent kit expired. Programming of the used instrument, storage conditions, and the expiration date of the reagents should be checked, and then PCR should be repeated.
- If a positive result (the fluorescence curve crosses the threshold line) is detected for a sample that has a fluorescence curve without the typical exponential growth phase (the curve is linear), this may suggest incorrect setting of the threshold line or incorrect calculation of baseline parameters. Such a result should not be considered as positive.

Once the threshold line has been set correctly, PCR analysis of the sample should be repeated (if iCycler iQ or iQ5 instruments are used).

If you have any further questions or if you encounter problems, please contact our Authorized representative in the European Community.

11. TRANSPORTATION

AmpliSens® AII-screen-FRT PCR kit should be transported at 2–8 °C for no longer than 5 days.

12. STABILITY AND STORAGE

All components of the **AmpliSens® AII-screen-FRT** PCR kit (except for PCR-mixes-1 and RT-PCR-mixes-1, polymerase (TaqF), RT-G-mix-2, TM-Revertase (MMlv), and PCR-mix-2-FEP/FRT) are to be stored at 2–8 °C when not in use. All components of the **AmpliSens® AII-screen-FRT** PCR kit are stable until the expiration date on the label. The shelf life of opened reagents is the same as that of unopened reagents, unless otherwise stated.

PCR-mix-1-FEP/FRT *Shigella* spp. / *Salmonella* spp., PCR-mix-1-FEP/FRT *Campylobacter* spp. / *Adenovirus*, RT-PCR-mix-1-FEP/FRT *Rotavirus* / *Astrovirus*, RT-PCR-mix-1-FEP/FRT *Norovirus* / STI, RT-PCR-mix-2-FEP/FRT, polymerase (TaqF), TM-Revertase (MMlv), and RT-G-mix-2 are to be stored at temperature from minus 24 to minus 16 ºC when not in use.

PCR-mix-1-FEP/FRT *Shigella* spp. / *Salmonella* spp., PCR-mix-1-FEP/FRT *Campylobacter* spp. / *Adenovirus*, RT-PCR-mix-1-FEP/FRT *Rotavirus* / *Astrovirus*, and RT-PCR-mix-1-FEP/FRT *Norovirus* / STI are to be kept away from light.

13. SPECIFICATIONS

13.1. Sensitivity

Pathogen	Clinical material	Nucleic acid extraction kit	Sensitivity, GE/ml [3]
Shigella spp. and enteroinvasive *E. coli* (EIEC)	faeces	RIBO-prep	$1x10^3$
Salmonella spp.	faeces	RIBO-prep	$1x10^3$
Thermophilic *Campylobacter* spp.	faeces	RIBO-prep	$1x10^3$
Adenovirus F	faeces	RIBO-prep	$1x10^4$
Rotavirus A	faeces	RIBO-prep	$1x10^4$
Norovirus genotype 2	faeces	RIBO-prep	$5x10^3$
Astrovirus	faeces	RIBO-prep	$1x10^4$

[3] The quantity of genome equivalents of microorganism per 1 ml of the sample.

13.2. Specificity

The analytical specificity of **AmpliSens® AII-screen-FRT** PCR kit is ensured by selection of specific primers and probes as well as strict reaction conditions. The primers and probes were checked for possible homologies to all sequences deposited in gene banks by sequence comparison analysis. The clinical specificity of **AmpliSens® AII-screen-FRT** PCR kit was confirmed in laboratory clinical trials.

Specificity was checked in tests of DNA samples of the following microorganisms: *Enterovirus* (*Coxsakie* B1, B2, B3, B4, B5, B6; *Polio (Sabin)* I, II, III); *Adenovirus* strains of serogroups 5 and 7; *Influenza viruses* A (H13N2, H9N2, H8N4, H2N3, H4N6, H11N6, H12N5, H3N8, H1N1, H6N2, H10N7, H5N1), *Influenza virus B*; *Rhinovirus*; *RS virus*; human *Adenoviruses* of types 3, 5, 7, 37, and 40; *Salmonella enteritidis* S-6, *S.choleraesuis* 370, *S.typhimurium* 371, *S.dublin* 373, *S.typhi* C1, *S.abortusovis* 372, and *S.gallinarum-pullorum*; *Shigella flexneri* 851b; *Campylobacter fetus* ssp. *fetus* 25936, and *C.jejuni* ssp. *jejuni* 43435; *Clebsiella* K 65 SW4; *Listeria monocytogenes* USHC 19 and *L.monocytogenes* USHC 52; *Proteus vulgaris* 115/98; *Pseudomonas aeruginosa* DN c1; *Staphylococcus aureus* 653 and *S.aureus* 29112; *Morganella morganii* 619 c 01; *Enterobacter faecalis* 356; as well as 44 *Norovirus* isolates of different gene clusters of genotypes 1 and 2; 40 *Rotavirus* strains of different [P]G types; 19 *Astrovirus* strains of serogroups 1, 2, 4, 5, and 8; and 15 *Adenovirus* strains of different types and the following bacterial strains (see Table 4).

Table 4

Bacterial agents panel of Centers for Disease Control and Prevention (CDC, USA)

Strain ID	Organism	Strain ID	Organism
K2033	*Salmonella* ser. Grumpensis	K2015	*Salmonella* ser. Oranienburg
K1806	*Salmonella* ser. Newport	AM01144	*Salmonella* ser. Newport
K2077	*Salmonella* ser. Enteriditis	K1810	*Salmonella* ser. Anatum
83-99	*Salmonella* ser. Typhimurium	K1991	*Salmonella* ser. Typhimurium
PS505	*Shigella boydii*	K1898	*Salmonella* ser. Heidelberg
PS408	*Shigella sonnei*	PS555	*Shigella boydii*
B4003	*Shigella sonnei*	F6446	*Shigella dysenteriae*
PS801	*Shigella dysenteriae*	S821X1	*Shigella dysenteriae* type 1
C898	*Shigella dysenteriae* type1	S177X1	*Shigella dysenteriae* type 1
F2035	*Shigella flexneri*	S3314	*Shigella dysenteriae* type 2
E2539-C1	Enterotoxigenic *Escherichia coli* (*ETEC*)	PS071	*Shigella flexneri*
H10407	Enterotoxigenic *Escherichia coli* (*ETEC*)	PS050	*Shigella flexneri*
F1008	Enterotoxigenic *Escherichia coli* (*ETEC*)	F7862	*Shigella flexneri*
EDL 933	Shiga-toxin *E.coli* (*STEC*)	TX1	Enterotoxigenic *Escherichia coli* (*ETEC*)
3543-01	Shiga-toxin *E.coli* (*STEC*)	3525-01	Shiga-toxin *Escherichia coli* (*STEC*)
4752-71	*Proteus vulgaris*	25922	*Escherichia coli* O6:H1
QA/QC	*Citrobacter freundii*	621-64	*Citrobacter freundii*
QA/QC	*Aeromonas*	3910-68	*Aeromonas spp.*
3043-74	*Serratia marcescens*	E9113	*Vibrio cholerae*
QA/QC	*Serratia marcescens*	501-83	*Edwardsiella spp.*
F7894	*Vibrio vulnificus*	587-82	*Providencia stuartii*
F8515	*Yersinia enterocolitica*	27853	*Pseudomonas aeruginosa*
F8510	*Yersinia enterocolitica*	D4989	*Helicobacter cineadi*
K4299	*Vibrio parahaemolyticus*	D6827	*Helicobacter pullorum*
F9835	*Vibrio parahaemolyticus*	D5127	*Helicobacter pylori*
K2023	*Salmonella* ser. Kentucky	D2686	*Arcobacter butzleri*
K1684	*Salmonella* O-1, 4, 12 gr. B		

14. REFERENCES

1. Handbook “Sampling, Transportation, and Storage of Clinical Material for PCR Diagnostics”, developed by Federal Budget Institute of Science “Central Research Institute for Epidemiology” of Federal Service for Surveillance on Consumers’ Rights Protection and Human Well-Being, Moscow, 2008.
2. Guidelines to instruction manual AmpliSens® AII-screen-FRT, developed by Federal Budget Institute of Science “Central Research Institute for Epidemiology” of Federal Service for Surveillance on Consumers’ Rights Protection and Human Well-Being, Moscow.

15. QUALITY CONTROL

In compliance with Federal Budget Institute of Science “Central Research Institute for Epidemiology” ISO 13485-Certified Quality Management System, each lot of **AmpliSens® AII-screen-FRT** PCR kit has been tested against predetermined specifications to ensure consistent product quality.

16. KEY TO SYMBOLS USED

REF	Catalogue number		Caution
LOT	Batch code		Sufficient for
IVD	*In vitro* diagnostic medical device		Expiration Date
VER	Version		Consult instructions for use
	Temperature limitation		Keep away from sunlight
	Manufacturer	**NCA**	Negative control of amplification
	Date of manufacture	**C–**	Negative control of extraction
EC REP	Authorised representative in the European Community	**C+*Shigella / Salmonella*, C+*Campylobacter / Adenovirus*, C+*Rotavirus / Astrovirus*, C+*Norovirus* genotype 2 / STI**	Positive controls of amplification
FBIS CRIE	Federal Budget Institute of Science “Central Research Institute for Epidemiology”	**IC**	Internal control

List of Changes Made in the Instruction Manual

VER	Location of changes	Essence of changes
16.06.11 LA	Cover page, text	The name of Institute was changed to Federal Budget Institute of Science “Central Research Institute for Epidemiology”