bioeksen
MOLECULAR DIAGNOSTICS

March 6, 2024

LETTER OF AUTHORIZATION

By this means, the manufacturer Bioeksen AR GE Teknolojileri A.Ş, located in Huzur Mah. Metin Oktay Cad. Nurol Life Sitesi No:3/31 Sarıyer - İstanbul, authorizes the company SRL SANMEDICO to have a registered office at A. Corobceanu Street 7A, apt. 9, Chişinău MD-2012, Moldova.

As our representative and distributor carry out the necessary procedures in Moldova for the registration, importation, distribution, sales, and promotion of the products manufactured and/or assembled by Bioeksen AR GE Teknolojileri A.Ş in the Country of Moldova.

This authorization is valid for 1 year from the date of signature.

Bioeksen AR GE Teknolojileri A. Ş

Canan Ketre

Chair of the Board

Tel. : +90 (212) 285 10 17
Fax : +90 (212) 285 10 18

www.bioeksen.com.tr
info@bioeksen.com.tr

Merkez Ofis / Üretim Ofisi : Huzur Mah. Metin Oktay Cad.
Nurol Life Sitesi D Blok No:3/31 Sarıyer-İstanbul-TÜRKİYE

CERTIFICATE

BİOEKSEN AR-GE TEKNOLOJİLERİ ANONİM ŞİRKETİ

HQ: Huzur Mah. Metin Oktay Cad. Nurol Life Sitesi D Blok No:3/31, 34396 Sarıyer - İstanbul - Türkiye
Production: Huzur Mah. Metin Oktay Cad. Nurol Life Sitesi D Blok No:3/10, 34396 Sarıyer - İstanbul - Türkiye
R&D / Project: Maslak Mh. Büyükdere Cad. Noramin İş Merkezi No: 237/1, 34485
Maslak Sarıyer - İstanbul - Türkiye

Design, Production, Storage, Distribution, Installation and Technical Services of Molecular Based Analysis Kits and Devices

with a scope of

ISO 9001:2015

Has established a quality management system in accordance with international standard.

" Following elements of the standard are excluded "
"None"

Certificate No	: M 11839
Initial Certification Date	: 25 October 2019
Certification Date	: 12 October 2022
Expiration Date	: 11 October 2025

General Manager

TÜRKAK BDS NO
YS-BF5D-D46B

Kiwa Belgelendirme Hizmetleri A.Ş.
ITOSB 9. Cadde No. 15 Tepeören Tuzla
Istanbul / Turkey

Tel: + 90 216 593 25 75
Faks: + 90 216 593 25 74
info@kiwa.com.tr
www.kiwa.com.tr

Certificate is valid till expiration date, subject to successful completion of periodical surveillance audits.
Please contact above numbers for detailed information.

Last Modified : 12 October 2022 - R 00

CERTIFICATE

BİOEKSEN AR-GE TEKNOLOJİLERİ ANONİM ŞİRKETİ

HQ: Huzur Mah. Metin Oktay Cad. Nurol Life Sitesi D Blok No:3/31, 34396 Sarıyer - İstanbul - Türkiye
Production: Huzur Mah. Metin Oktay Cad. Nurol Life Sitesi D Blok No:3/10, 34396 Sarıyer - İstanbul - Türkiye
R&D / Project: Maslak Mh. Büyükdere Cad. Noramin İş Merkezi No: 237/1, 34485
Maslak Sarıyer - İstanbul - Türkiye

Design, Production, Storage, Distribution, Installation and Technical Services of Molecular Based Analysis Kits and Devices

with a scope of

EN ISO 13485:2016

Has established a management system in accordance
with international Medical Devices Quality Management System Standard

"Following elements of the standard are excluded"
"7.5.5" "7.5.7" " 7.5.9.2"

Certificate No	: M 11840
Initial Certification Date	: 25 October 2019
Certification Date	: 12 October 2022
Expiration Date	: 11 October 2025

General Manager

TÜRKAK BDS NO
YS-DCB8-88D2

Kiwa Belgelendirme Hizmetleri A.Ş.
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Istanbul / Turkey

Tel: + 90 216 593 25 75
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www.kiwa.com.tr

Certificate is valid till expiration date, subject to successful completion of periodical surveillance audits.
Please contact above numbers for detailed information.

Last Modified : 12 October 2022 - R 00

EC DECLARATION OF CONFORMITY

Directive 98/79/EC of the European Parliament and of the Council of 27 October 1998 on In Vitro Medical Diagnostic Devices

Bioeksen AR GE Teknolojileri A.Ş. hereby declares under its own responsibility that the products covered by this declaration conform with "Essential Requirements" listed in Annex I of EC Directive 98/79/EC (IVD Directive). Supporting documentation (technical documentation) is retained under the premises of the manufacturer.

Manufacturer	: Bioeksen AR GE Teknolojileri Anonim Şirketi
Central Office	: Huzur Mah. Metin Oktay Cad. Nurol Life Sitesi D Blok No:3/31, 34396 Sarıyer/İstanbul TÜRKİYE
Manufacturing Site	: Huzur Mahallesi Metin Oktay Caddesi Nurol Life No:3/10, Sarıyer/İstanbul TÜRKİYE
	Web: www.bioeksen.com.tr, E-mail: info@bioeksen.com.tr
Product(s) Name	: Bio-Speedy® Bordetella pertussis, B.parapertussis, B.bronchiseptica and B.holmesii Real-Time PCR Detection Kit
Description	: Bio-Speedy® Bordetella pertussis, B.parapertussis, B.bronchiseptica and B.holmesii Real-Time PCR Detection Kit
	Ref No: BS-DTC-103-25
	Ref No: BS-DTC-103-100
Classification	: Other (Neither listed in the Annex II, Nor Self-testing device), GMDN code: 50505 - Multiple Bordetella species nucleic acid IVD, kit, nucleic acid technique (NAT)
	Article 9, paragraph 1 of EC Council Directive
	98/79/EC on In Vitro Medical Diagnostic Devices
Conformity Assessment Route	: According to Annex III of the IVD Directive 98/79/EC
	EC declaration of conformity under manufacturer responsibility
Applied Standards	: All standards stated in the annex on the other page are strictly
	implemented in our company.

We hereby declare that the above-mentioned product/s meet the provisions of the EC Council Directive 98/79/EC for in vitro medical diagnostic devices. All supporting documentation is retained under the premises of the manufacturer and the manufacturer is exclusively responsible for the declaration of conformity.

BİOEKSEN AR GE TEKNOLOJİLERİ A.Ş.
Huzur Mah. Metin Oktay Cad. Nurol Life D Blok
No: 3/31 Sarıyer / İSTANBUL
Maslak V.D. 176 093 2853 Tic. Sicil No: 904277-0
Mersis No: 0176 0932 8530 0001
info@bioeksen.com.tr - www.bioeksen.com.tr

Signature:

Place of Issue: İstanbul

Valid from: 25.05.2022

Authorized Person: Canan Zöhre Ketre Kolukırık

Chairman of the Board

bioeksen

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EC DECLARATION OF CONFORMITY

Attachment
List of Applied Standards

No.	Title of standards	Contents
1	EN ISO 13485:2016	Medical devices - Quality management systems - Requirements for regulatory purposes
2	EN ISO 14971:2019	Medical devices – Application of risk management to medical devices
3	EN ISO 17511:2020	In vitro diagnostic medical devices - Measurement of quantities in biological samples - Metrological traceability of values assigned to calibrators and control materials
4	EN 13612:2002	Performance evaluation of in vitro diagnostic medical devices
5	EN ISO 23640:2015	In vitro diagnostic medical devices – Evaluation of stability of in vitro diagnostic reagents
6	EN ISO 18113-1:2011	In vitro diagnostic medical devices - Information supplied by the manufacturer (labelling) - Part 1: Terms, definitions, and general requirements
7	EN ISO 18113-2:2011	In vitro diagnostic medical devices - Information supplied by the manufacturer (labelling) - Part 2: In vitro diagnostic reagents for professional use
8	EN ISO 15223-1:2021	Medical devices - Symbols to be used with medical device labels, labelling and information to be supplied - Part 1: General requirements
9	IEC 62366-1:2015	Medical devices — Part 1: Application of usability engineering to medical devices
10	CLSI MM3 A3: 3ED 2015	Molecular Diagnostic Methods for Infectious Diseases
11	CLSI EP17 A2: 2ED 2012	Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures
12	CLSI EP07 3ED: 2018	Interference Testing in Clinical Chemistry, 3rd Edition
13	CLSI EP5 A3: 3ED 2014	Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline—Third Edition

EC DECLARATION OF CONFORMITY

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Manufacturer	: Bioeksen AR GE Teknolojileri Anonim Şirketi
Central Office	: Huzur Mah. Metin Oktay Cad. Nurol Life Sitesi D Blok No:3/31, 34396 Sarıyer/İstanbul TÜRKİYE
Manufacturing Site	: Huzur Mahallesi Metin Oktay Caddesi Nurol Life No:3/10, Sarıyer/İstanbul TÜRKİYE
	Web: www.bioeksen.com.tr, E-mail: info@bioeksen.com.tr
Product(s) Name	: Bio-Speedy® Bacillus anthracis Real-Time PCR Detection Kit
Description	: Bio-Speedy® Bacillus anthracis Real-Time PCR Detection Kit
	Ref No: BS-DTC-V-224-25
	Ref No: BS-DTC-V-224-100
Classification	: Other (Neither listed in the Annex II, Nor Self-testing device), GMDN code: 50432 - Bacillus anthracis nucleic acid IVD, kit, nucleic acid technique (NAT)
	Article 9, paragraph 1 of EC Council Directive
	98/79/EC on In Vitro Medical Diagnostic Devices
Conformity Assessment Route	: According to Annex III of the IVD Directive 98/79/EC
	EC declaration of conformity under manufacturer responsibility
Applied Standards	: All standards stated in the annex on the other page are strictly
	implemented in our company.

We hereby declare that the above-mentioned product/s meet the provisions of the EC Council Directive 98/79/EC for in vitro medical diagnostic devices. All supporting documentation is retained under the premises of the manufacturer and the manufacturer is exclusively responsible for the declaration of conformity.

Signature:

BİOEKSEN AR GE TEKNOLOJİLERİ A.Ş.
Huzur Mah. Metin Oktay Cad. Nurol Life D Blok
No: 3/31 Sarıyer / İSTANBUL
Maslak V.D. 176 093 2953 Tic. Sicil No: 904277-0
Mersis No: 0176 0932 8530 0001
info@bioeksen.com.tr - www.bioeksen.com.tr

Place of Issue: İstanbul

Valid from: 25.05.2022

Authorized Person: Canan Zöhre Ketre Kolukırık

Chairman of the Board

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No.	Title of standards	Contents
1	EN ISO 13485:2016	Medical devices - Quality management systems - Requirements for regulatory purposes
2	EN ISO 14971:2019	Medical devices – Application of risk management to medical devices
3	EN ISO 17511:2020	In vitro diagnostic medical devices - Measurement of quantities in biological samples - Metrological traceability of values assigned to calibrators and control materials
4	EN 13612:2002	Performance evaluation of in vitro diagnostic medical devices
5	EN ISO 23640:2015	In vitro diagnostic medical devices – Evaluation of stability of in vitro diagnostic reagents
6	EN ISO 18113-1:2011	In vitro diagnostic medical devices - Information supplied by the manufacturer (labelling) - Part 1: Terms, definitions, and general requirements
7	EN ISO 18113-2:2011	In vitro diagnostic medical devices - Information supplied by the manufacturer (labelling) - Part 2: In vitro diagnostic reagents for professional use
8	EN ISO 15223-1:2021	Medical devices - Symbols to be used with medical device labels, labelling and information to be supplied - Part 1: General requirements
9	IEC 62366-1:2015	Medical devices — Part 1: Application of usability engineering to medical devices
10	CLSI MM3 A3: 3ED 2015	Molecular Diagnostic Methods for Infectious Diseases
11	CLSI EP17 A2: 2ED 2012	Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures
12	CLSI EP07 3ED: 2018	Interference Testing in Clinical Chemistry, 3rd Edition
13	CLSI EP5 A3: 3ED 2014	Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline—Third Edition

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EC DECLARATION OF CONFORMITY

Directive 98/79/EC of the European Parliament and of the Council of 27 October 1998 on In Vitro Medical Diagnostic Devices

Bioeksen AR GE Teknolojileri A.Ş. hereby declares under its own responsibility that the products covered by this declaration conform with "Essential Requirements" listed in Annex I of EC Directive 98/79/EC (IVD Directive). Supporting documentation (technical documentation) is retained under the premises of the manufacturer.

Manufacturer	: Bioeksen AR GE Teknolojileri Anonim Şirketi
Central Office	: Huzur Mah. Metin Oktay Cad. Nurol Life Sitesi D Blok No:3/31, 34396 Sarıyer/İstanbul TÜRKİYE
Manufacturing Site	: Huzur Mahallesi Metin Oktay Caddesi Nurol Life No:3/10, Sarıyer/İstanbul TÜRKİYE
	Web: www.bioeksen.com.tr, E-mail: info@bioeksen.com.tr
Product(s) Name	: Bio-Speedy® Gastroenteritis RT-qPCR MX-5T Viral Panel
Description	: Bio-Speedy® Gastroenteritis RT-qPCR MX-5T Viral Panel
	Ref No: BS-GE-MX5T-25
	Ref No: BS-GE-MX5T-100
Classification	: Other (Neither listed in the Annex II, Nor Self-testing device), GMDN code: 66162 – Multiple gastrointestinal virus nucleic acid IVD, kit, nucleic acid technique (NAT)
	Article 9, paragraph 1 of EC Council Directive
	98/79/EC on In Vitro Medical Diagnostic Devices
Conformity Assessment Route	: According to Annex III of the IVD Directive 98/79/EC
	EC declaration of conformity under manufacturer responsibility
Applied Standards	: All standards stated in the annex on the other page are strictly
	implemented in our company.

We hereby declare that the above-mentioned product/s meet the provisions of the EC Council Directive 98/79/EC for in vitro medical diagnostic devices. All supporting documentation is retained under the premises of the manufacturer and the manufacturer is exclusively responsible for the declaration of conformity.

Place of Issue: İstanbul

Valid from: 25.05.2022

Signature:

BİOEKSEN AR GE TEKNOLOJİLERİ A.Ş.
Huzur Mah. Metin Oktay Cad. Nurol Life D Blok
No: 3/31 Sarıyer / İSTANBUL
Maslak V.D. 176 093 2853 Tic. Sicil No: 904277-0
Mersis No: 0176 0932 8530 0001
info@bioeksen.com.tr - www.bioeksen.com.tr

Authorized Person: Canan Zöhre Ketre Kolukırık

Chairman of the Board

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List of Applied Standards

No.	Title of standards	Contents
1	EN ISO 13485:2016	Medical devices - Quality management systems - Requirements for regulatory purposes
2	EN ISO 14971:2019	Medical devices – Application of risk management to medical devices
3	EN ISO 17511:2020	In vitro diagnostic medical devices - Measurement of quantities in biological samples - Metrological traceability of values assigned to calibrators and control materials
4	EN 13612:2002	Performance evaluation of in vitro diagnostic medical devices
5	EN ISO 23640:2015	In vitro diagnostic medical devices – Evaluation of stability of in vitro diagnostic reagents
6	EN ISO 18113-1:2011	In vitro diagnostic medical devices - Information supplied by the manufacturer (labelling) - Part 1: Terms, definitions, and general requirements
7	EN ISO 18113-2:2011	In vitro diagnostic medical devices - Information supplied by the manufacturer (labelling) - Part 2: In vitro diagnostic reagents for professional use
8	EN ISO 15223-1:2021	Medical devices - Symbols to be used with medical device labels, labelling and information to be supplied - Part 1: General requirements
9	IEC 62366-1:2015	Medical devices — Part 1: Application of usability engineering to medical devices
10	CLSI MM3 A3: 3ED 2015	Molecular Diagnostic Methods for Infectious Diseases
11	CLSI EP17 A2: 2ED 2012	Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures
12	CLSI EP07 3ED: 2018	Interference Testing in Clinical Chemistry, 3rd Edition
13	CLSI EP5 A3: 3ED 2014	Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline—Third Edition

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Bioeksen AR GE Teknolojileri A.Ş. hereby declares under its own responsibility that the products covered by this declaration conform with "Essential Requirements" listed in Annex I of EC Directive 98/79/EC (IVD Directive). Supporting documentation (technical documentation) is retained under the premises of the manufacturer.

Manufacturer	: Bioeksen AR GE Teknolojileri Anonim Şirketi
Central Office	: Huzur Mah. Metin Oktay Cad. Nurol Life Sitesi D Blok No:3/31, 34396 Sarıyer/İstanbul TÜRKİYE
Manufacturing Site	: Huzur Mahallesi Metin Oktay Caddesi Nurol Life No:3/10, Sarıyer/İstanbul TÜRKİYE
	Web: www.bioeksen.com.tr, E-mail: info@bioeksen.com.tr
Product(s) Name	: Bio-Speedy® Human Enterovirus (HEV) qPCR Detection Kit
Description	: Bio-Speedy® Human Enterovirus (HEV) qPCR Detection Kit
	Ref No: BS-HEV-DTC-304-25
	Ref No: BS-HEV-DTC-304-100
Classification	: Other (Neither listed in the Annex II, Nor Self-testing device), GMDN code: 48692 - Enterovirus nucleic acid (serotypes 68-71) IVD, kit, nucleic acid technique (NAT)
	Article 9, paragraph 1 of EC Council Directive
	98/79/EC on In Vitro Medical Diagnostic Devices
Conformity Assessment Route	: According to Annex III of the IVD Directive 98/79/EC
	EC declaration of conformity under manufacturer responsibility
Applied Standards	: All standards stated in the annex on the other page are strictly
	implemented in our company.

We hereby declare that the above-mentioned product/s meet the provisions of the EC Council Directive 98/79/EC for in vitro medical diagnostic devices. All supporting documentation is retained under the premises of the manufacturer and the manufacturer is exclusively responsible for the declaration of conformity.

Place of Issue: İstanbul

Valid from: 25.05.2022

Signature:

BİOEKSEN AR GE TEKNOLOJİLERİ A.Ş.
Huzur Mah. Metin Oktay Cad. Nurol Life D Blok
No: 3/31 Sarıyer / İSTANBUL
Maslak V.D. 176 093 2853 Tic. Sicil No: 904277-0
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Authorized Person: Canan Zöhre Ketre Kolukırık

Chairman of the Board

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EC DECLARATION OF CONFORMITY

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List of Applied Standards

No.	Title of standards	Contents
1	EN ISO 13485:2016	Medical devices - Quality management systems - Requirements for regulatory purposes
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3	EN ISO 17511:2020	In vitro diagnostic medical devices - Measurement of quantities in biological samples - Metrological traceability of values assigned to calibrators and control materials
4	EN 13612:2002	Performance evaluation of in vitro diagnostic medical devices
5	EN ISO 23640:2015	In vitro diagnostic medical devices – Evaluation of stability of in vitro diagnostic reagents
6	EN ISO 18113-1:2011	In vitro diagnostic medical devices - Information supplied by the manufacturer (labelling) - Part 1: Terms, definitions, and general requirements
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EC DECLARATION OF CONFORMITY

Directive 98/79/EC of the European Parliament and of the Council of 27 October 1998 on In Vitro Medical Diagnostic Devices

Bioeksen AR GE Teknolojileri A.Ş. hereby declares under its own responsibility that the products covered by this declaration conform with "Essential Requirements" listed in Annex I of EC Directive 98/79/EC (IVD Directive). Supporting documentation (technical documentation) is retained under the premises of the manufacturer.

Manufacturer	: Bioeksen AR GE Teknolojileri Anonim Şirketi
Central Office	: Huzur Mah. Metin Oktay Cad. Nurol Life Sitesi D Blok No:3/31, 34396 Sarıyer/İstanbul TÜRKİYE
Manufacturing Site	: Huzur Mahallesi Metin Oktay Caddesi Nurol Life No:3/10, Sarıyer/İstanbul TÜRKİYE
	Web: www.bioeksen.com.tr, E-mail: info@bioeksen.com.tr
Product(s) Name	: Bio-Speedy® Legionella pneumophila qPCR Kit
Description	: Bio-Speedy® Legionella pneumophila qPCR Kit Ref No: BS-LP-25 Ref No: BS-LP-100
Classification	: Other (Neither listed in the Annex II, Nor Self-testing device), GMDN code: 51060 - Legionella pneumophila nucleic acid IVD, kit, nucleic acid technique (NAT) Article 9, paragraph 1 of EC Council Directive 98/79/EC on In Vitro Medical Diagnostic Devices
Conformity Assessment Route	: According to Annex III of the IVD Directive 98/79/EC EC declaration of conformity under manufacturer responsibility
Applied Standards	: All standards stated in the annex on the other page are strictly implemented in our company.

We hereby declare that the above-mentioned product/s meet the provisions of the EC Council Directive 98/79/EC for in vitro medical diagnostic devices. All supporting documentation is retained under the premises of the manufacturer and the manufacturer is exclusively responsible for the declaration of conformity.

Place of Issue: İstanbul

Valid from: 25.05.2022

Signature:

BİOEKSEN AR GE TEKNOLOJİLERİ A.Ş.
Huzur Mah. Metin Oktay Cad. Nurol Life D Blok
No: 3/31 Sarıyer/İSTANBUL
Maslak V.D. 176 093 2853 Tic. Sicil No: 904277-0
Mersis No: 0176 0932 8530 0001
info@bioeksen.com.tr - www.bioeksen.com.tr

Authorized Person: Canan Zöhre Ketre Kolukırık

Chairman of the Board

bioeksen

CE IVD

EC DECLARATION OF CONFORMITY

Attachment
List of Applied Standards

No.	Title of standards	Contents
1	EN ISO 13485:2016	Medical devices - Quality management systems - Requirements for regulatory purposes
2	EN ISO 14971:2019	Medical devices – Application of risk management to medical devices
3	EN ISO 17511:2020	In vitro diagnostic medical devices - Measurement of quantities in biological samples - Metrological traceability of values assigned to calibrators and control materials
4	EN 13612:2002	Performance evaluation of in vitro diagnostic medical devices
5	EN ISO 23640:2015	In vitro diagnostic medical devices – Evaluation of stability of in vitro diagnostic reagents
6	EN ISO 18113-1:2011	In vitro diagnostic medical devices - Information supplied by the manufacturer (labelling) - Part 1: Terms, definitions, and general requirements
7	EN ISO 18113-2:2011	In vitro diagnostic medical devices - Information supplied by the manufacturer (labelling) - Part 2: In vitro diagnostic reagents for professional use
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Manufacturer	: Bioeksen AR GE Teknolojileri Anonim Şirketi
Central Office	: Huzur Mah. Metin Oktay Cad. Nurol Life Sitesi D Blok No:3/31, 34396 Sarıyer/İstanbul TÜRKİYE
Manufacturing Site	: Huzur Mahallesi Metin Oktay Caddesi Nurol Life No:3/10, Sarıyer/İstanbul TÜRKİYE
	Web: www.bioeksen.com.tr, E-mail: info@bioeksen.com.tr
Product(s) Name	: Bio-Speedy® Meningitis/Encephalitis qPCR MX-6T Bacterial Panel
Description	: Bio-Speedy® Meningitis/Encephalitis qPCR MX-6T Bacterial Panel
	Ref No: BS-ME-MX6T-25
	Ref No: BS-ME-MX6T-100
Classification	: Other (Neither listed in the Annex II, Nor Self-testing device), GMDN code: 61043 - Multiple-type meningitis pathogen nucleic acid IVD, kit, nucleic acid technique (NAT)
	Article 9, paragraph 1 of EC Council Directive
	98/79/EC on In Vitro Medical Diagnostic Devices
Conformity Assessment Route	: According to Annex III of the IVD Directive 98/79/EC
	EC declaration of conformity under manufacturer responsibility
Applied Standards	: All standards stated in the annex on the other page are strictly
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Place of Issue: İstanbul

Valid from: 25.05.2022

Signature:

BİOEKSEN AR GE TEKNOLOJİLERİ A.Ş.
Huzur Mah. Metin Oktay Cad. Nurol Life D Blok
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Authorized Person: Canan Zöhre Ketre Kolukırık

Chairman of the Board

bioeksen

CE IVD

EC DECLARATION OF CONFORMITY

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List of Applied Standards

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5	EN ISO 23640:2015	In vitro diagnostic medical devices – Evaluation of stability of in vitro diagnostic reagents
6	EN ISO 18113-1:2011	In vitro diagnostic medical devices - Information supplied by the manufacturer (labelling) - Part 1: Terms, definitions, and general requirements
7	EN ISO 18113-2:2011	In vitro diagnostic medical devices - Information supplied by the manufacturer (labelling) - Part 2: In vitro diagnostic reagents for professional use
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13	CLSI EP5 A3: 3ED 2014	Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline—Third Edition

2017/746 In Vitro Diagnostic Medical Device Regulation (EU) Declaration of Conformity

EU DECLARATION OF CONFORMITY

Manufacturer	Bioeksen AR GE Teknolojileri A.Ş.
Manufacturer's Address	**Central Office:** Huzur Mah. Metin Oktay Cad. Nurol Life Sitesi D Blok No:3/31, 34396 Sarıyer/İstanbul TÜRKİYE **Manufacturing Site:** Huzur Mahallesi Metin Oktay Caddesi Nurol Life No:3/10, Sarıyer/İstanbul TÜRKİYE **Web:** www.bioeksen.com.tr, **E-posta:** info@bioeksen.com.tr
Manufacturer Individual Identification Number	TR-MF-000032826
Authorised Representative	-
Authorised Representative's Address	-
Authorized Representative Identification Number	-
Product(s) Name	*υ***NAT®** Transfer Tube
Product Catalog Number(s)	BS-NA-513m-100
Basic UDI-DI	868187745NAEXT0672
Intended Purpose	*υ***NAT®** Transfer Tube, 2 mL of viral nucleic acid extractive and preservative liquid. When clinical specimens suspected of respiratory tract infection are transferred in *υ***NAT®** Transfer Tube, the liquid inside the tube can be used directly in Real-Time PCR (qPCR) reactions. The nucleic acid extractive and preservative liquid inactivates all viral, bacterial, or eukaryotic pathogens in the sample, 1 minute after contact with the clinical specimen. The *υ***NAT®** Transfer Tube allows from sample to RT-qPCR in a minute.
Technical Documentation Number	TD.059
Risk Classification of Device and Classification Rule	Class A Device according to Annex VIII Article 2.5 (Rule 5), point c of 2017/746 In Vitro Diagnostic Medical Device Regulation (EU)
GMDN Code	62392- Oral/respiratory tract specimen container IVD, additive/medium
EMDN Code	-
Conformity Assessment Route	EU Declaration of Conformity, under the responsibility of the manufacturer, according to ANNEX IV (Annex II and Annex III) of 2017/746 In Vitro Diagnostic Medical Device Regulation (EU)

Bioeksen AR GE Teknolojileri A.Ş. declares that the above mentioned device meets the previsions of 2017/746 In Vitro Diagnostic Medical Device Regulation (EU). All supporting documentation is reserved under the premises of the manufacturer and the EU declaration of conformity is issued under sole responsibility of manufacturer.

Authorized Person: Canan Zöhre Ketre Kolukırık **Date of Issue:** 25.01.2023

Position: Chairman of the Board **Place of Issue:** İstanbul

Seal/Signature:

BİOEKSEN AR GE TEKNOLOJİLERİ A.Ş.
Huzur Mah. Metin Oktay Cad. Nurol Life D Blok
No: 3/31 Sarıyer / İSTANBUL
Maslak V.D. 176 093 2833 Tic. Sicil No: 904277-0
Mersis No: 0176 0932 8530 0001
info@bioeksen.com.tr - www.bioeksen.com.tr

EU DECLARATION OF CONFORMITY

ATTACHMENT
List of Applied Standards

	Standard Title	Content	Scope	Excluded Items
QMS	ISO 9001:2015	Quality management systems — Requirements	Covered	-
Harmonised Standard QMS	EN ISO 13485:2016 EN ISO 13485:2016/AC:2018 EN ISO 13485:2016/A11:2021	Medical devices — Quality management systems — Requirements for regulatory purposes	Partially covered.	– 7.5.5 Special Requirements for Sterile Medical Devices – 7.5.7 Special Requirements for Process Validation for Sterilization and Sterile Barrier Systems – 7.5.9.2 Special requirements for implantable medical devices
Harmonised Standard Risk Management	EN ISO 14971:2019 EN ISO 14971:2019/A11:2021	Medical devices — Application of risk management to medical devices	Covered	-
Risk Management	ISO/TR 24971:2020	Medical devices — Guidance on the application of ISO 14971	Covered	-
Performance Evaluation Metrological Traceability	EN ISO 17511:2020	In vitro diagnostic medical devices — Requirements for establishing metrological traceability of values assigned to calibrators, trueness control materials and human samples	Covered	-
Performance Evaluation	EN 13612:2002	Performance evaluation of in vitro diagnostic medical devices	Covered	-
Performance Evaluation Stability	EN ISO 23640:2015	In vitro diagnostic medical devices — Evaluation of stability of in vitro diagnostic reagents	Covered	-
Harmonised Standard Labelling	EN ISO 18113-1:2022	In vitro diagnostic medical devices — Information supplied by the manufacturer (labelling) — Part 1: Terms, definitions and general requirements	Covered	-
Harmonised Standard Labelling	EN ISO 18113-2:2012	In vitro diagnostic medical devices — Information supplied by the manufacturer (labelling) — Part 2: In vitro diagnostic reagents for professional use	Covered	-
Harmonised Standard Labelling	EN ISO 15223-1:2021	Medical devices — Symbols to be used with information to be supplied by the manufacturer — Part 1: General requirements	Covered	-
Post-Market Surveillance	ISO/TR 20416:2020	Medical devices — Post-market surveillance for manufacturers	Covered	-
Usability	IEC 62366-1:2015	Medical devices — Part 1: Application of usability engineering to medical devices	Covered	-
Performance Evaluation	ISO 20395:2019	Biotechnology — Requirements for evaluating the performance of quantification methods for nucleic acid target sequences — qPCR and dPCR	Partially covered.	Does not cover dPCR items.

Performance Evaluation	ISO 16142-2:2017	Medical devices — Recognized essential principles of safety and performance of medical devices — Part 2: General essential principles and additional specific essential principles for all IVD medical devices and guidance on the selection of standards	Partially covered.	Table B.1 — General principles for all medical devices 18.3 (l)
Clinical Studies	BS ISO 20916:2019	In vitro diagnostic medical devices — Clinical performance studies using specimens from human subjects — Good study practice	Covered	-
Stability	CLSI EP25-A	Evaluation of Stability of In Vitro Diagnostic Reagents; Approved Guideline, CLSI, Wayne, PA, 2009	Covered	-
Documentation	ISO 20417:2021	Medical devices — Information to be supplied by the manufacturer	Partially covered.	5.12 Sterile 6.5.3 (c) 6.6.2 (d) (7) 6.6.2 (g) 6.6.2 (h)
Performance Evaluation	MDCG 2021-21	Guidance on performance evaluation of SARS-CoV-2 in vitro diagnostic medical devices	Covered	-
Performance Evaluation	CLSI MM3 A3: 3ED 2015	Molecular Diagnostic Methods for Infectious Diseases	Covered	-
Performance Evaluation	CLSI EP17 A2: 2ED 2012	Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures	Covered	-
Performance Evaluation	CLSI EP07 3ED: 2018	Interference Testing in Clinical Chemistry, 3rd Edition	Not covered	-
Performance Evaluation	CLSI EP5 A3: 3ED 2014	Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline—Third Edition	Covered	-

EU DECLARATION OF CONFORMITY

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EC DECLARATION OF CONFORMITY

Directive 98/79/EC of the European Parliament and of the Council of 27 October 1998 on In Vitro Medical Diagnostic Devices

Bioeksen AR GE Teknolojileri A.Ş. hereby declares under its own responsibility that the products covered by this declaration conform with "Essential Requirements" listed in Annex I of EC Directive 98/79/EC (IVD Directive). Supporting documentation (technical documentation) is retained under the premises of the manufacturer.

Manufacturer	: Bioeksen AR GE Teknolojileri Anonim Şirketi
Central Office	: Huzur Mah. Metin Oktay Cad. Nurol Life Sitesi D Blok No:3/31, 34396 Sarıyer/İstanbul TÜRKİYE
Manufacturing Site	: Huzur Mahallesi Metin Oktay Caddesi Nurol Life No:3/10, Sarıyer/İstanbul TÜRKİYE
	Web: www.bioeksen.com.tr, E-mail: info@bioeksen.com.tr
Product(s) Name	: Bio-Speedy® Respiratory Tract Virus RT-qPCR Panel
Description	: Bio-Speedy® Respiratory Tract Virus RT-qPCR Panel Ref No: BS-RTV-S-25 Ref No: BS-RTV-S-100 Ref No: BS-RTV-T-25 Ref No: BS-RTV-T-100 Ref No: BS-RTV-L-25 Ref No: BS-RTV-L-100
Classification	: Other (Neither listed in the Annex II, Nor Self-testing device), GMDN code: 47922 - Multiple respiratory virus nucleic acid IVD, kit, nucleic acid technique (NAT) Article 9, paragraph 1 of EC Council Directive 98/79/EC on In Vitro Medical Diagnostic Devices
Conformity Assessment Route	: According to Annex III of the IVD Directive 98/79/EC EC declaration of conformity under manufacturer responsibility
Applied Standards	: All standards stated in the annex on the other page are strictly implemented in our company.

We hereby declare that the above-mentioned product/s meet the provisions of the EC Council Directive 98/79/EC for in vitro medical diagnostic devices. All supporting documentation is retained under the premises of the manufacturer and the manufacturer is exclusively responsible for the declaration of conformity.

BİOEKSEN AR GE TEKNOLOJİLERİ A.Ş.
Huzur Mah. Metin Oktay Cad. Nurol Life D Blok
No: 3/31 Sarıyer/İSTANBUL
Maslak V.D. 476 088 2653 Tic. Sicil No: 904277-0
Mersis No: 0176 0932 8530 0001
info@bioeksen.com.tr - www.bioeksen.com.tr

Place of Issue: İstanbul

Signature:

Valid from: 25.05.2022

Authorized Person: Canan Zöhre Ketre Kolukırık
Chairman of the Board

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EC DECLARATION OF CONFORMITY

Attachment
List of Applied Standards

No.	Title of standards	Contents
1	EN ISO 13485:2016	Medical devices - Quality management systems - Requirements for regulatory purposes
2	EN ISO 14971:2019	Medical devices – Application of risk management to medical devices
3	EN ISO 17511:2020	In vitro diagnostic medical devices - Measurement of quantities in biological samples - Metrological traceability of values assigned to calibrators and control materials
4	EN 13612:2002	Performance evaluation of in vitro diagnostic medical devices
5	EN ISO 23640:2015	In vitro diagnostic medical devices – Evaluation of stability of in vitro diagnostic reagents
6	EN ISO 18113-1:2011	In vitro diagnostic medical devices - Information supplied by the manufacturer (labelling) - Part 1: Terms, definitions, and general requirements
7	EN ISO 18113-2:2011	In vitro diagnostic medical devices - Information supplied by the manufacturer (labelling) - Part 2: In vitro diagnostic reagents for professional use
8	EN ISO 15223-1:2021	Medical devices - Symbols to be used with medical device labels, labelling and information to be supplied - Part 1: General requirements
9	IEC 62366-1:2015	Medical devices — Part 1: Application of usability engineering to medical devices
10	CLSI MM3 A3: 3ED 2015	Molecular Diagnostic Methods for Infectious Diseases
11	CLSI EP17 A2: 2ED 2012	Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures
12	CLSI EP07 3ED: 2018	Interference Testing in Clinical Chemistry, 3rd Edition
13	CLSI EP5 A3: 3ED 2014	Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline—Third Edition

EC DECLARATION OF CONFORMITY

Directive 98/79/EC of the European Parliament and of the Council of 27 October 1998 on In Vitro Medical Diagnostic Devices

Bioeksen AR GE Teknolojileri A.Ş. hereby declares under its own responsibility that the products covered by this declaration conform with "Essential Requirements" listed in Annex I of EC Directive 98/79/EC (IVD Directive). Supporting documentation (technical documentation) is retained under the premises of the manufacturer.

Manufacturer	: Bioeksen AR GE Teknolojileri Anonim Şirketi
Central Office	: Huzur Mah. Metin Oktay Cad. Nurol Life Sitesi D Blok No:3/31, 34396 Sarıyer/İstanbul TÜRKİYE
Manufacturing Site	: Huzur Mahallesi Metin Oktay Caddesi Nurol Life No:3/10, Sarıyer/İstanbul TÜRKİYE
	Web: www.bioeksen.com.tr, E-mail: info@bioeksen.com.tr
Product(s) Name	: Bio-Speedy® Sepsis qPCR MX-30T Panel
Description	: Bio-Speedy® Sepsis qPCR MX-30T Panel
	Ref No: BS-SE-MX30T-25
	Ref No: BS-SE-MX30T-100
Classification	: Other (Neither listed in the Annex II, Nor Self-testing device), GMDN code: 62484 - Multiple-type bloodstream pathogen nucleic acid IVD, kit, nucleic acid technique (NAT)
	Article 9, paragraph 1 of EC Council Directive
	98/79/EC on In Vitro Medical Diagnostic Devices
Conformity Assessment Route	: According to Annex III of the IVD Directive 98/79/EC
	EC declaration of conformity under manufacturer responsibility
Applied Standards	: All standards stated in the annex on the other page are strictly
	implemented in our company.

We hereby declare that the above-mentioned product/s meet the provisions of the EC Council Directive 98/79/EC for in vitro medical diagnostic devices. All supporting documentation is retained under the premises of the manufacturer and the manufacturer is exclusively responsible for the declaration of conformity.

Place of Issue: İstanbul

Valid from: 25.05.2022

Signature:

BİOEKSEN AR GE TEKNOLOJİLERİ A.Ş.
Huzur Mah. Metin Oktay Cad. Nurol Life D Blok
No: 3/31 Sarıyer / İSTANBUL
Mersis No: 0176 0932 8530 0001
info@bioeksen.com.tr - www.bioeksen.com.tr

Authorized Person: Canan Zöhre Ketre Kolukırık

Chairman of the Board

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EC DECLARATION OF CONFORMITY

Attachment
List of Applied Standards

No.	Title of standards	Contents
1	EN ISO 13485:2016	Medical devices - Quality management systems - Requirements for regulatory purposes
2	EN ISO 14971:2019	Medical devices – Application of risk management to medical devices
3	EN ISO 17511:2020	In vitro diagnostic medical devices - Measurement of quantities in biological samples - Metrological traceability of values assigned to calibrators and control materials
4	EN 13612:2002	Performance evaluation of in vitro diagnostic medical devices
5	EN ISO 23640:2015	In vitro diagnostic medical devices – Evaluation of stability of in vitro diagnostic reagents
6	EN ISO 18113-1:2011	In vitro diagnostic medical devices - Information supplied by the manufacturer (labelling) - Part 1: Terms, definitions, and general requirements
7	EN ISO 18113-2:2011	In vitro diagnostic medical devices - Information supplied by the manufacturer (labelling) - Part 2: In vitro diagnostic reagents for professional use
8	EN ISO 15223-1:2021	Medical devices - Symbols to be used with medical device labels, labelling and information to be supplied - Part 1: General requirements
9	IEC 62366-1:2015	Medical devices — Part 1: Application of usability engineering to medical devices
10	CLSI MM3 A3: 3ED 2015	Molecular Diagnostic Methods for Infectious Diseases
11	CLSI EP17 A2: 2ED 2012	Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures
12	CLSI EP07 3ED: 2018	Interference Testing in Clinical Chemistry, 3rd Edition
13	CLSI EP5 A3: 3ED 2014	Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline—Third Edition

EC DECLARATION OF CONFORMITY

Directive 98/79/EC of the European Parliament and of the Council of 27 October 1998 on In Vitro Medical Diagnostic Devices

Bioeksen AR GE Teknolojileri A.Ş. hereby declares under its own responsibility that the products covered by this declaration conform with "Essential Requirements" listed in Annex I of EC Directive 98/79/EC (IVD Directive). Supporting documentation (technical documentation) is retained under the premises of the manufacturer.

Manufacturer	: Bioeksen AR GE Teknolojileri Anonim Şirketi
Central Office	: Huzur Mah. Metin Oktay Cad. Nurol Life Sitesi D Blok No:3/31, 34396 Sarıyer/İstanbul TÜRKİYE
Manufacturing Site	: Huzur Mahallesi Metin Oktay Caddesi Nurol Life No:3/10, Sarıyer/İstanbul TÜRKİYE
	Web: www.bioeksen.com.tr, E-mail: info@bioeksen.com.tr
Product(s) Name	: Bio-Speedy® Brucella spp. qPCR Kit
Description	: Bio-Speedy® Brucella spp. qPCR Kit
	Ref No: BS-SP-B-12-50
	Ref No: BS-SP-B-12-100
	Ref No: BS-SP-B-12-250
Classification	: Other (Neither listed in the Annex II, Nor Self-testing device), GMDN code: 50605 - Multiple Brucella species nucleic acid IVD, kit, nucleic acid technique (NAT)
	Article 9, paragraph 1 of EC Council Directive
	98/79/EC on In Vitro Medical Diagnostic Devices
Conformity Assessment Route	: According to Annex III of the IVD Directive 98/79/EC
	EC declaration of conformity under manufacturer responsibility
Applied Standards	: All standards stated in the annex on the other page are strictly
	implemented in our company.

We hereby declare that the above-mentioned product/s meet the provisions of the EC Council Directive 98/79/EC for in vitro medical diagnostic devices. All supporting documentation is retained under the premises of the manufacturer and the manufacturer is exclusively responsible for the declaration of conformity.

Signature:

BİOEKSEN AR GE TEKNOLOJİLERİ A.Ş.
Huzur Mah. Metin Oktay Cad. Nurol Life D Blok
No: 3/31 Sarıyer/İSTANBUL
Maslak V.D. 176 093 2853 Tic. Sicil No: 904277-0
Mersis No: 0176 0932 8530 0001
info@bioeksen.com.tr - www.bioeksen.com.tr

Place of Issue: İstanbul

Valid from: 25.05.2022

Authorized Person: Canan Zöhre Ketre Kolukırık

Chairman of the Board

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EC DECLARATION OF CONFORMITY

Attachment
List of Applied Standards

No.	Title of standards	Contents
1	EN ISO 13485:2016	Medical devices - Quality management systems - Requirements for regulatory purposes
2	EN ISO 14971:2019	Medical devices – Application of risk management to medical devices
3	EN ISO 17511:2020	In vitro diagnostic medical devices - Measurement of quantities in biological samples - Metrological traceability of values assigned to calibrators and control materials
4	EN 13612:2002	Performance evaluation of in vitro diagnostic medical devices
5	EN ISO 23640:2015	In vitro diagnostic medical devices – Evaluation of stability of in vitro diagnostic reagents
6	EN ISO 18113-1:2011	In vitro diagnostic medical devices - Information supplied by the manufacturer (labelling) - Part 1: Terms, definitions, and general requirements
7	EN ISO 18113-2:2011	In vitro diagnostic medical devices - Information supplied by the manufacturer (labelling) - Part 2: In vitro diagnostic reagents for professional use
8	EN ISO 15223-1:2021	Medical devices - Symbols to be used with medical device labels, labelling and information to be supplied - Part 1: General requirements
9	IEC 62366-1:2015	Medical devices — Part 1: Application of usability engineering to medical devices
10	CLSI MM3 A3: 3ED 2015	Molecular Diagnostic Methods for Infectious Diseases
11	CLSI EP17 A2: 2ED 2012	Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures
12	CLSI EP07 3ED: 2018	Interference Testing in Clinical Chemistry, 3rd Edition
13	CLSI EP5 A3: 3ED 2014	Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline—Third Edition

EC DECLARATION OF CONFORMITY

Directive 98/79/EC of the European Parliament and of the Council of 27 October 1998 on In Vitro Medical Diagnostic Devices

Bioeksen AR GE Teknolojileri A.Ş. hereby declares under its own responsibility that the products covered by this declaration conform with "Essential Requirements" listed in Annex I of EC Directive 98/79/EC (IVD Directive). Supporting documentation (technical documentation) is retained under the premises of the manufacturer.

Manufacturer	: Bioeksen AR GE Teknolojileri Anonim Şirketi
Central Office	: Huzur Mah. Metin Oktay Cad. Nurol Life Sitesi D Blok No:3/31, 34396 Sarıyer/İstanbul TÜRKİYE
Manufacturing Site	: Huzur Mahallesi Metin Oktay Caddesi Nurol Life No:3/10, Sarıyer/İstanbul TÜRKİYE
	Web: www.bioeksen.com.tr, E-mail: info@bioeksen.com.tr
Product(s) Name	: Bio-Speedy® COVID-19/Flu RT-qPCR
Description	: Bio-Speedy® COVID-19/Flu RT-qPCR
	Ref No: BS-SY-SI-100
	Ref No: BS-SY-SI-250
	Ref No: BS-SY-SI-500
	Ref No: BS-SY-SI-1000
Classification	: Other (Neither listed in the Annex II, Nor Self-testing device), GMDN code: 47922- Multiple respiratory virus nucleic acid IVD, kit, nucleic acid technique (NAT)
	Article 9, paragraph 1 of EC Council Directive
	98/79/EC on In Vitro Medical Diagnostic Devices
Conformity Assessment Route	: According to Annex III of the IVD Directive 98/79/EC
	EC declaration of conformity under manufacturer responsibility
Applied Standards	: All standards stated in the annex on the other page are strictly
	implemented in our company.

We hereby declare that the above-mentioned product/s meet the provisions of the EC Council Directive 98/79/EC for in vitro medical diagnostic devices. All supporting documentation is retained under the premises of the manufacturer and the manufacturer is exclusively responsible for the declaration of conformity.

Signature:

BİOEKSEN AR GE TEKNOLOJİLERİ A.Ş.
Huzur Mah. Metin Oktay Cad. Nurol Life D Blok
No: 3/31 Sarıyer / İSTANBUL
Maslak V.D. 176 [illegible] Ticaret Sicil No: 904277-0
Mersis No: 0176 [illegible] 0001
info@bioeksen.com.tr - www.bioeksen.com.tr

Place of Issue: İstanbul

Valid from: 25.05.2022

Authorized Person: Canan Zöhre Ketre Kolukırık

Chairman of the Board

bioeksen

CE IVD

EC DECLARATION OF CONFORMITY

Attachment
List of Applied Standards

No.	Title of standards	Contents
1	EN ISO 13485:2016	Medical devices - Quality management systems - Requirements for regulatory purposes
2	EN ISO 14971:2019	Medical devices – Application of risk management to medical devices
3	EN ISO 17511:2020	In vitro diagnostic medical devices - Measurement of quantities in biological samples - Metrological traceability of values assigned to calibrators and control materials
4	EN 13612:2002	Performance evaluation of in vitro diagnostic medical devices
5	EN ISO 23640:2015	In vitro diagnostic medical devices – Evaluation of stability of in vitro diagnostic reagents
6	EN ISO 18113-1:2011	In vitro diagnostic medical devices - Information supplied by the manufacturer (labelling) - Part 1: Terms, definitions, and general requirements
7	EN ISO 18113-2:2011	In vitro diagnostic medical devices - Information supplied by the manufacturer (labelling) - Part 2: In vitro diagnostic reagents for professional use
8	EN ISO 15223-1:2021	Medical devices - Symbols to be used with medical device labels, labelling and information to be supplied - Part 1: General requirements
9	IEC 62366-1:2015	Medical devices — Part 1: Application of usability engineering to medical devices
10	CLSI MM3 A3: 3ED 2015	Molecular Diagnostic Methods for Infectious Diseases
11	CLSI EP17 A2: 2ED 2012	Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures
12	CLSI EP07 3ED: 2018	Interference Testing in Clinical Chemistry, 3rd Edition
13	CLSI EP5 A3: 3ED 2014	Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline—Third Edition

EC DECLARATION OF CONFORMITY

Directive 98/79/EC of the European Parliament and of the Council of 27 October 1998 on In Vitro Medical Diagnostic Devices

Bioeksen AR GE Teknolojileri A.Ş. hereby declares under its own responsibility that the products covered by this declaration conform with "Essential Requirements" listed in Annex I of EC Directive 98/79/EC (IVD Directive). Supporting documentation (technical documentation) is retained under the premises of the manufacturer.

Manufacturer	: Bioeksen AR GE Teknolojileri Anonim Şirketi
Central Office	: Huzur Mah. Metin Oktay Cad. Nurol Life Sitesi D Blok No:3/31, 34396 Sarıyer/İstanbul TÜRKİYE
Manufacturing Site	: Huzur Mahallesi Metin Oktay Caddesi Nurol Life No:3/10, Sarıyer/İstanbul TÜRKİYE
	Web: www.bioeksen.com.tr, E-mail: info@bioeksen.com.tr
Product(s) Name	: Bio-Speedy® Tropical Fever RT-qPCR Panel
Description	: Bio-Speedy® Tropical Fever RT-qPCR Panel Ref No: BS-TF-S-25 Ref No: BS-TF-S-100 Ref No: BS-TF-T-25 Ref No: BS-TF-T-100 Ref No: BS-TF-L-25 Ref No: BS-TF-L-100
Classification	: Other (Neither listed in the Annex II, Nor Self-testing device), GMDN code: 61053 - Multiple-type tropical pathogen nucleic acid IVD, kit, nucleic acid technique (NAT) Article 9, paragraph 1 of EC Council Directive 98/79/EC on In Vitro Medical Diagnostic Devices
Conformity Assessment Route	: According to Annex III of the IVD Directive 98/79/EC EC declaration of conformity under manufacturer responsibility
Applied Standards	: All standards stated in the annex on the other page are strictly implemented in our company.

We hereby declare that the above-mentioned product/s meet the provisions of the EC Council Directive 98/79/EC for in vitro medical diagnostic devices. All supporting documentation is retained under the premises of the manufacturer and the manufacturer is exclusively responsible for the declaration of conformity.

BİOEKSEN AR GE TEKNOLOJİLERİ A.Ş.
Huzur Mah. Metin Oktay Cad. Nurol Life D Blok
No: 3/31 Sarıyer / İSTANBUL
Maslak V.D. 176 093 2853 Ticaret Sicil No: 904277-0
Mersis No: 0176 0932 8530 0001
info@bioeksen.com.tr - www.bioeksen.com.tr

Signature:

Place of Issue: İstanbul
Valid from: 25.05.2022

Authorized Person: Canan Zöhre Ketre Kolukırık
Chairman of the Board

bioeksen

CE IVD

EC DECLARATION OF CONFORMITY

Attachment
List of Applied Standards

No.	Title of standards	Contents
1	EN ISO 13485:2016	Medical devices - Quality management systems - Requirements for regulatory purposes
2	EN ISO 14971:2019	Medical devices – Application of risk management to medical devices
3	EN ISO 17511:2020	In vitro diagnostic medical devices - Measurement of quantities in biological samples - Metrological traceability of values assigned to calibrators and control materials
4	EN 13612:2002	Performance evaluation of in vitro diagnostic medical devices
5	EN ISO 23640:2015	In vitro diagnostic medical devices – Evaluation of stability of in vitro diagnostic reagents
6	EN ISO 18113-1:2011	In vitro diagnostic medical devices - Information supplied by the manufacturer (labelling) - Part 1: Terms, definitions, and general requirements
7	EN ISO 18113-2:2011	In vitro diagnostic medical devices - Information supplied by the manufacturer (labelling) - Part 2: In vitro diagnostic reagents for professional use
8	EN ISO 15223-1:2021	Medical devices - Symbols to be used with medical device labels, labelling and information to be supplied - Part 1: General requirements
9	IEC 62366-1:2015	Medical devices — Part 1: Application of usability engineering to medical devices
10	CLSI MM3 A3: 3ED 2015	Molecular Diagnostic Methods for Infectious Diseases
11	CLSI EP17 A2: 2ED 2012	Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures
12	CLSI EP07 3ED: 2018	Interference Testing in Clinical Chemistry, 3rd Edition
13	CLSI EP5 A3: 3ED 2014	Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline—Third Edition

EU DECLARATION OF CONFORMITY

2017/746 In Vitro Diagnostic Medical Device Regulation (EU) Declaration of Conformity

Manufacturer	Bioeksen AR GE Teknolojileri A.Ş.
Manufacturer's Address	**Central Office:** Huzur Mah. Metin Oktay Cad. Nurol Life Sitesi D Blok No:3/31, 34396 Sarıyer/İstanbul TÜRKİYE **Manufacturing Site:** Huzur Mahallesi Metin Oktay Caddesi Nurol Life No:3/10, Sarıyer/İstanbul TÜRKİYE **Web:** www.bioeksen.com.tr, **E-posta:** info@bioeksen.com.tr
Manufacturer Individual Identification Number	TR-MF-000032826
Authorised Representative	-
Authorised Representative's Address	-
Authorized Representative Identification Number	-
Product(s) Name	Bio-Speedy® *ν*NAT® Viral Nucleic Acid Buffer
Product Catalog Number(s)	BS-NA-510-100 BS-NA-510-250 BS-NA-510-500 BS-NA-510-1000
Basic UDI-DI	868187745NAEXB013W
Intended Purpose	The *ν*NAT® Viral Nucleic Acid Buffer is a 10x concentrated viral nucleic acid extractive and preservative liquid for nasopharyngeal swab, oropharyngeal swab, oral/saliva swab samples. The nucleic acid extractive and preservative liquid inactivates all viral, bacterial, or eukaryotic pathogens in the sample within 1 minutes after contact with the clinical specimen. The *ν*NAT® Viral Nucleic Acid Buffer allows from sample to qPCR in a minute.
Technical Documentation Number	TD.016
Risk Classification of Device and Classification Rule	Class A Device according to Annex VIII Article 2.5 (Rule 5) point a of 2017/746 In Vitro Diagnostic Medical Device Regulation (EU)
GMDN Code	52521- Nucleic acid extraction/isolation kit IVD
EMDN Code	-
Conformity Assessment Route	EU Declaration of Conformity, under the responsibility of the manufacturer, according to ANNEX IV (Annex II and Annex III) of 2017/746 In Vitro Diagnostic Medical Device Regulation (EU)

Bioeksen AR GE Teknolojileri A.Ş. declares that the above mentioned device meets the previsions of 2017/746 In Vitro Diagnostic Medical Device Regulation (EU). All supporting documentation is reserved under the premises of the manufacturer and the EU declaration of conformity is issued under sole responsibility of manufacturer.

Authorized Person: Canan Zöhre Ketre Kolukırık

Position: Chairman of the Board

Seal/Signature: BİOEKSEN AR-GE TEKNOLOJİLERİ A.Ş.
Huzur Mah. Metin Oktay Cad. Nurol Life D Blok
No: 3/31 Sarıyer /İSTANBUL
Maslak V.D. 176 093 2858 Tic. Sicil No: 904277-0
Mersis No: 0176 0932 8530 0001
info@bioeksen.com.tr - www.bioeksen.com.tr

Date of Issue: 25.01.2023

Place of Issue: İstanbul

EU DECLARATION OF CONFORMITY

ATTACHMENT
List of Applied Standards

	Standard Title	Content	Scope	Excluded Items
QMS	ISO 9001:2015	Quality management systems — Requirements	Covered	-
Harmonised Standard QMS	EN ISO 13485:2016 EN ISO 13485:2016/AC:2018 EN ISO 13485:2016/A11:2021	Medical devices — Quality management systems — Requirements for regulatory purposes	Partially covered.	– 7.5.5 Special Requirements for Sterile Medical Devices – 7.5.7 Special Requirements for Process Validation for Sterilization and Sterile Barrier Systems – 7.5.9.2 Special requirements for implantable medical devices
Harmonised Standard Risk Management	EN ISO 14971:2019 EN ISO 14971:2019/A11:2021	Medical devices — Application of risk management to medical devices	Covered	-
Risk Management	ISO/TR 24971:2020	Medical devices — Guidance on the application of ISO 14971	Covered	-
Performance Evaluation Metrological Traceability	EN ISO 17511:2020	In vitro diagnostic medical devices — Requirements for establishing metrological traceability of values assigned to calibrators, trueness control materials and human samples	Covered	-
Performance Evaluation	EN 13612:2002	Performance evaluation of in vitro diagnostic medical devices	Covered	-
Performance Evaluation Stability	EN ISO 23640:2015	In vitro diagnostic medical devices — Evaluation of stability of in vitro diagnostic reagents	Covered	-
Harmonised Standard Labelling	EN ISO 18113-1:2022	In vitro diagnostic medical devices — Information supplied by the manufacturer (labelling) — Part 1: Terms, definitions and general requirements	Covered	-
Harmonised Standard Labelling	EN ISO 18113-2:2012	In vitro diagnostic medical devices — Information supplied by the manufacturer (labelling) — Part 2: In vitro diagnostic reagents for professional use	Covered	-
Harmonised Standard Labelling	EN ISO 15223-1:2021	Medical devices — Symbols to be used with information to be supplied by the manufacturer — Part 1: General requirements	Covered	-
Post-Market Surveillance	ISO/TR 20416:2020	Medical devices — Post-market surveillance for manufacturers	Covered	-
Usability	IEC 62366-1:2015	Medical devices — Part 1: Application of usability engineering to medical devices	Covered	-
Performance Evaluation	ISO 20395:2019	Biotechnology — Requirements for evaluating the performance of quantification methods for nucleic acid target sequences — qPCR and dPCR	Partially covered.	Does not cover dPCR items.

Performance Evaluation	ISO 16142-2:2017	Medical devices — Recognized essential principles of safety and performance of medical devices — Part 2: General essential principles and additional specific essential principles for all IVD medical devices and guidance on the selection of standards	Partially covered.	Table B.1 — General principles for all medical devices 18.3 (l)
Clinical Studies	BS ISO 20916:2019	In vitro diagnostic medical devices — Clinical performance studies using specimens from human subjects — Good study practice	Covered	-
Stability	CLSI EP25-A	Evaluation of Stability of In Vitro Diagnostic Reagents; Approved Guideline, CLSI, Wayne, PA, 2009	Covered	-
Stability	ISO 20417:2021	Medical devices — Information to be supplied by the manufacturer	Partially covered.	5.12 Sterile 6.5.3 (c) 6.6.2 (d) (7) 6.6.2 (g) 6.6.2 (h)
Performance Evaluation	MDCG 2021-21	Guidance on performance evaluation of SARS-CoV-2 in vitro diagnostic medical devices	Covered	-
Performance Evaluation	CLSI MM3 A3: 3ED 2015	Molecular Diagnostic Methods for Infectious Diseases	Covered	-
Performance Evaluation	CLSI EP17 A2: 2ED 2012	Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures	Covered	-
Performance Evaluation	CLSI EP07 3ED: 2018	Interference Testing in Clinical Chemistry, 3rd Edition	Not covered	-
Performance Evaluation	CLSI EP5 A3: 3ED 2014	Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline—Third Edition	Covered	-

EU DECLARATION OF CONFORMITY

EC DECLARATION OF CONFORMITY

Directive 98/79/EC of the European Parliament and of the Council of 27 October 1998 on In Vitro Medical Diagnostic Devices

Bioeksen AR GE Teknolojileri A.Ş. hereby declares under its own responsibility that the products covered by this declaration conform with "Essential Requirements" listed in Annex I of EC Directive 98/79/EC (IVD Directive). Supporting documentation (technical documentation) is retained under the premises of the manufacturer.

Manufacturer	: Bioeksen AR GE Teknolojileri Anonim Şirketi
Central Office	: Huzur Mah. Metin Oktay Cad. Nurol Life Sitesi D Blok No:3/31, 34396 Sarıyer/İstanbul TÜRKİYE
Manufacturing Site	: Huzur Mahallesi Metin Oktay Caddesi Nurol Life No:3/10, Sarıyer/İstanbul TÜRKİYE
	Web: www.bioeksen.com.tr, E-mail: info@bioeksen.com.tr
Product(s) Name	: Bio-Speedy® Gastroenteritis RT-qPCR MX-24T Panel
Description	: Bio-Speedy® Gastroenteritis RT-qPCR MX-24T Panel
	Ref No: BS-GE-MX24T-25
	Ref No: BS-GE-MX24T-100
Classification	: Other (Neither listed in the Annex II, Nor Self-testing device), GMDN code: 61058 – Multiple-type gastrointestinal pathogen nucleic acid IVD, kit, nucleic acid technique (NAT)
	Article 9, paragraph 1 of EC Council Directive
	98/79/EC on In Vitro Medical Diagnostic Devices
Conformity Assessment Route	: According to Annex III of the IVD Directive 98/79/EC
	EC declaration of conformity under manufacturer responsibility
Applied Standards	: All standards stated in the annex on the other page are strictly
	implemented in our company.

We hereby declare that the above-mentioned product/s meet the provisions of the EC Council Directive 98/79/EC for in vitro medical diagnostic devices. All supporting documentation is retained under the premises of the manufacturer and the manufacturer is exclusively responsible for the declaration of conformity.

Place of Issue: İstanbul

Signature:

BİOEKSEN AR GE TEKNOLOJİLERİ A.Ş.
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Chairman of the Board

bioeksen

CE IVD

EC DECLARATION OF CONFORMITY

Attachment
List of Applied Standards

No.	Title of standards	Contents
1	EN ISO 13485:2016	Medical devices - Quality management systems - Requirements for regulatory purposes
2	EN ISO 14971:2019	Medical devices – Application of risk management to medical devices
3	EN ISO 17511:2020	In vitro diagnostic medical devices - Measurement of quantities in biological samples - Metrological traceability of values assigned to calibrators and control materials
4	EN 13612:2002	Performance evaluation of in vitro diagnostic medical devices
5	EN ISO 23640:2015	In vitro diagnostic medical devices – Evaluation of stability of in vitro diagnostic reagents
6	EN ISO 18113-1:2011	In vitro diagnostic medical devices - Information supplied by the manufacturer (labelling) - Part 1: Terms, definitions, and general requirements
7	EN ISO 18113-2:2011	In vitro diagnostic medical devices - Information supplied by the manufacturer (labelling) - Part 2: In vitro diagnostic reagents for professional use
8	EN ISO 15223-1:2021	Medical devices - Symbols to be used with medical device labels, labelling and information to be supplied - Part 1: General requirements
9	IEC 62366-1:2015	Medical devices — Part 1: Application of usability engineering to medical devices
10	CLSI MM3 A3: 3ED 2015	Molecular Diagnostic Methods for Infectious Diseases
11	CLSI EP17 A2: 2ED 2012	Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures
12	CLSI EP07 3ED: 2018	Interference Testing in Clinical Chemistry, 3rd Edition
13	CLSI EP5 A3: 3ED 2014	Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline—Third Edition

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For laboratory professional use only.

Cat No: BS-GE-MX24T-25/BS-GE-MX24T-100

Gastroenteritis RT-qPCR MX-24T Panel

Package Insert

1. Kit Content

Table 1. Kit Content

Oligo Mix Content					Positive Control Content		
Component	**Target**	**Channel**	**Quantity (20 µL/Rxn) 25 Rxns**	**Quantity (20 µL/Rxn) 100 Rxns**	**Component**	**Quantity (20 µL/Rxn) 25 Rxns**	**Quantity (20 µL/Rxn) 100 Rxns**
SA Oligo Mix	Sapovirus (GI/GII/GIV/GV)	FAM	1 x 125 µL	1 x 500 µL	PC-SA	1 x 100 µL	1 x 100 µL
	Internal Control (Human *RNase P* gene)	HEX					
	-	ROX					
	Adenovirus	CY5					
GCE Oligo Mix	*Giardia lamblia*	FAM	1 x 125 µL	1 x 500 µL	PC-GCE	1 x 100 µL	1 x 100 µL
	-	HEX					
	Entamoeba histolytica	ROX					
	Cryptosporidium spp.	CY5					
YPC Oligo Mix	*Yersinia enterocolitica*	FAM	1 x 125 µL	1 x 500 µL	PC-YPC	1 x 100 µL	1 x 100 µL
	Plesiomonas shigelloides	HEX					
	-	ROX					
	Cyclospora cayetanensis	CY5					
ANR Oligo Mix	Astrovirus	FAM	1 x 125 µL	1 x 500 µL	PC-ANR	1 x 100 µL	1 x 100 µL
	Norovirus (GI/GII)	HEX					
	Rotavirus (A)	ROX					
	-	CY5					
CVVS Oligo Mix	*Salmonella* spp.	FAM	1 x 125 µL	1 x 500 µL	PC-CVVS	1 x 100 µL	1 x 100 µL
	Campylobacter spp.	HEX					
	Vibrio parahaemolyticus	ROX					
	Vibrio cholerae	CY5					
ET1 Oligo Mix	*Shigella/Enteroinvasive E. coli* (EIEC)	FAM	1 x 125 µL	1 x 500 µL	PC-ET1	1 x 100 µL	1 x 100 µL
	-	HEX					
	Enteroaggregative *E. coli* (EAEC)	ROX					
	Shiga toxin producing *E. coli* (STEC)	CY5					
ET2 Oligo Mix	Enteropathogenic *E. coli* (EPEC)	FAM	1 x 125 µL	1 x 500 µL	PC-ET2	1 x 100 µL	1 x 100 µL
	-	HEX					
	-	ROX					
	Enterotoxigenic *E. coli* (ETEC)	CY5					
CTX Oligo Mix	*Clostridium difficile* toxin B	FAM	1 x 125 µL	1 x 500 µL	PC-CTX	1 x 100 µL	1 x 100 µL
	-	HEX					
	Clostridium difficile toxin A	ROX					
	Clostridium difficile Binary toxin A/B	CY5					

Component	**Intended Use**	**25 Rxns**	**100 Rxns**
2X Prime Script Mix	Optimized ready-to-use mix for RT-qPCR assay	2 x 1000 µL	7 x 1250 µL
NTC	Negative (No Template) Control (Nuclease-free Water)	1 x 1000 µL	1 x 1000 µL

Table 2. Storage Requirements and Shelf Life

Component	**Transport Condition**	**Storage Condition**	**Shelf Life**
2X Prime Script Mix	-22 °C to +8 °C	-22 to -18 °C	12 Months
Oligo Mix		-22 to -18 °C	
NTC		-22 to -18 °C / +2 to +8 °C	
PC		-22 to -18 °C before opening, +2 to +8 °C after first thaw	

Each reagent stored at storage temperature can be used until the expiration date indicated on the tube following the first opening. The expiration date of the kit is determined by the expiration date of the reagents.

2. Materials Required but Not Provided

Table 3. Components Required but not Included with The Test

Components Required but not Included with The Test	
1. Real-Time instrument with FAM, HEX, ROX, and CY5 channels, Ramp rate ≥3 °C/sec	**7.** Reaction tubes and their caps/seals compatible with the qPCR instruments and the reaction volume
2. Adjustable micropipettes and compatible pipette tips (nuclease-free)	**Extra components recommended to use:**
3. Centrifuge	**8.** Biosafety cabinet for PCR setup
4. Vortex	**9.** Cold tube rack (for microcentrifuge tubes and PCR tubes/strips)
5. Nuclease-free water/viral transport medium/serum physiologic	**10.** PPE (Personal Protective Equipment)
6. 1.5- or 2-mL microcentrifuge tubes (nuclease-free)	

3. Intended Use and Test Principle

Bio-Speedy® Gastroenteritis RT-qPCR MX-24T Panel is a one-step reverse transcription and real-time PCR (RT-qPCR) test intended for the presumptive qualitative detection of the viral, bacterial, and parasitic agents given in Table 1. The ***Bio-Speedy® Gastroenteritis RT-qPCR MX-24T Panel*** is applied to nucleic acid isolates obtained from the stool and rectal swab samples.

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Gastroenteritis is one of the best common health problems with high morbidity and mortality rates in children and the elderly. Therefore, a rapid and accurate diagnosis of the agent is essential for appropriate treatment.

Detection with the kit is achieved via rapid nucleic acid extraction from the stool and rectal swab samples followed by multiplex RT-qPCR targeting the genomic RNA and DNA regions specific to the target agents in real-time PCR instruments that are equipped with **FAM**, **HEX**, **ROX**, and **CY5** detection channels. **The kit allows to achieve RT-qPCR results in less than 60 minutes. (Run time may vary depending on the instrument)**

The oligonucleotide set targeting the human ***RNase P*** mRNA functions as a control of the sampling, nucleic acid extraction, reverse transcription, and qPCR since the oligonucleotide set targets the exon-exon junction. The kit also contains negative and positive control templates for testing the contamination and the RT-qPCR reagent stability, respectively.

Bio-Speedy® Gastroenteritis RT-qPCR MX-24T Panel is intended for use by laboratory personnel trained in the techniques of RT-qPCR and *in vitro* diagnostic procedures.

4. Analytical Specifications

Bio-Speedy® Gastroenteritis RT-qPCR MX-24T Panel is validated with ***Bio-Speedy® vNAT® Transfer Tube*** *(Catalog No: BS-NA-513-100),* ***vNAT® Transfer Tube*** *(Catalog No: BS-NA-513m-100)* for sample transfer, and ***Zybio EXM3000 Nucleic Acid Isolation System*** *(Model No: EXM3000)* for nucleic acids extracted from the stool and rectal swab samples.

Limit of Detection (LoD) of the kit is between 28-100 copies/mL for stool and rectal swab samples extracted using the ***Zybio EXM3000 Nucleic Acid Isolation System***.

Table 4. Summary of LoD results based on the specimen type and extraction method.

NO	Specimen Type	Sample Transfer Method		Extraction Method	LOD (cp/mL)
		Sterile Container	***vNAT®*** Transfer Tube	***Zybio*** *EXM3000 Nucleic Acid Isolation System*	
1	Rectal swab	-	✓	✓	28-100
2	Stool	✓	-	✓	28-100

The RT-qPCR is carried out in 20 µL reaction volume using the ***CFX96 Touch™/CFX96™ Dx/CFX Opus 96™/CFX Opus 96™ Dx (Bio-Rad)***, and ***Magnetic Induction Cycler (Mic) (Bio Molecular System - BMS)*** Real-Time PCR systems equipped with the **FAM**, **HEX**, **ROX**, and **CY5** detection channels.

The exclusivity of the kit was tested on different viral, bacterial, and parasitic agents. No cross-reaction was observed in analytical specificity studies performed on reference strains and field isolates. The sensitivity and specificity of the kit were determined as 98.93% and 99.14%, respectively.

5. Collection, Storage, and Shipment of Clinical Specimens

Clinical stool samples collected from individuals are transferred into a 1-5 ml in a sterile, leak-proof, screw cap container. No preservative is required. Clinical rectal swab samples collected from individuals are transferred into a sterile empty tube with a screw cap if the swab is to be processed within 2 hours. If it is to be kept for longer than 2 hours, it should be inoculated into a transport medium. Samples should be stored and transported at 2 °C to 8 °C until they arrive at the laboratory. Samples should be transferred within maximum 2 days. Nucleic acid from samples should be extracted and frozen at -70 °C and shipped with dry ice.

6. Warnings

1. Specimen processing should be performed in accordance with national biological safety recommendations.
2. Immediately clean up any spill containing potentially infectious material with 0.5-1% (w/v) sodium hypochlorite (10-20% v/v bleach). Dispose of cleaning materials in a biohazard waste stockpot.
3. All personnel who perform aspects of the testing procedures should be trained to work with PCR and microbiology as appropriate. Sampling should be carried out by personnel with sufficient knowledge and experience.
4. The kit should be stored away from nucleic acid sources and PCR amplicons.
5. Except for fluid transfers, nucleic acid, and positive control tubes should always be kept closed.
6. To prevent contamination of the reaction mixture by previously amplified target sequences, maintain separate work areas, and dedicated equipment.
7. Different sets of laboratory coats should be worn in pre- and post-PCR areas.
8. The micropipettes used for pipetting PCR mixes and template nucleic acids should be separate. Filtered and nuclease-free tips should be used.
9. Cotton or calcium alginate swabs or swabs with wooden sticks should not be used since they may contain substances that inactivate some pathogens and inhibit PCR.
10. The components in the kit should not be mixed with different lot numbers or chemicals of the same name but from different manufacturers.
11. Master stock reagents should be kept on the cold block during the PCR setup.
12. Kit components should be mixed by gently shaking before use.
13. Maintenance/calibration interval should be determined for all instruments and equipment used with the kit.
14. Immediately after each RT-qPCR run, dispose of the qPCR tubes in closed bags to avoid the PCR amplicon contamination in the lab.
15. The wipeable surfaces of the rooms, benches and devices should be cleaned regularly with freshly diluted 10% bleach solution (0.5% NaClO).
16. Dispose of waste in a designated matter in accordance with local, regional, and federal regulations.

7. RT-qPCR Application Protocol

Before starting the assay, please consider the following:

1. The kit was validated only for the template nucleic acid volume that is 25% of the total qPCR volume.
2. The kit cannot be used with real-time PCR instruments without the periodic maintenance records.
3. **It is recommended to use a validated qPCR plate/strip with the kit!** The specified analytical performance of the kit can only be achieved using the validated tubes.
4. **For testing the contamination, set up two different negative control reactions with and without the addition of NTC.**

Program the qPCR device as follows and add the reagents into the qPCR tubes, close the tubes, place them into the qPCR instrument and start the run (Table 5).

Table 5. Real-Time PCR Program

Reaction Setup		RT-qPCR Program				QR Code for Thermal Protocol
		CFX96 Touch™/CFX96™ Dx/CFX Opus 96™/CFX Opus 96™ Dx (Bio-Rad) and *Magnetic Induction Cycler (Mic) (Bio Molecular System - BMS)*				
Reagent	**Volume/Rxn**	**Step**	**Cycle No.**	**Temperature**	**Duration**	
2X Prime Script Mix	10 µL	**Reverse Transcription**	1 Cycle	52 °C	5 min	
		Pre-Incubation	1 Cycle	95 °C	10 sec	
Oligo Mix	5 µL	**Denaturation**	12 Touch Down Cycles: 1 °C decrement in annealing temperature per cycle	95 °C	1 sec	
		Annealing and Extension		67 °C to 56 °C	30 sec	
Template Nucleic Acid	5 µL	**Denaturation**	35 Cycles	95 °C	1 sec	
		Annealing and Extension		55 °C	30 sec	
Total Reaction Volume	20 µL	**Detection (Reading)**		*FAM/HEX/ROX/CY5*		www.bioeksen.com.tr/files/gastroenteritis_mx-24t_panel/

8. Interpretation of the Assay Results

- All default analysis options (e.g. **auto-calculated threshold**) in the related software of ***CFX96 Touch™/CFX96™ Dx/CFX Opus 96™/CFX Opus 96™ Dx (Bio-Rad)*** and ***Magnetic Induction Cycler (Mic) (Bio Molecular System - BMS)*** instruments should not be changed to calculate Cq values.
- Shape of the amplification curves obtained in the FAM/HEX/ROX/CY5 channels should be examined for all reaction wells returning with Cq values. All the **sigmoidal curves above the threshold** should be recorded as "**positive**" and their Cq values should be recorded. **Non-sigmoidal curves** should be recorded as "**negative**".
- For samples with a sigmoidal curve below the auto-calculated threshold for the ***CFX96 Touch™/CFX96™ Dx (Bio-Rad) and CFX Opus 96™/CFX Opus 96™ Dx (Bio-Rad)*** instruments, **the threshold level should be manually set to 200 RFU**. **If the sigmoidal curve exceeds the threshold, the Ct value should be recorded as "35"** and the sample should be reported as **positive**. For samples with a sigmoidal curve below the auto-calculated threshold for ***Magnetic Induction Cycler (Mic) (Bio Molecular System - BMS)*** should be reported as **positive** and **their Ct values should be recorded as "35"**.
- Because touch down cycles without the fluorescence read were used in the kit, conversion of the detected Ct values to standard cycling values is needed for the reporting. Based on the correlation studies, 12 touchdown cycles between 67-56 °C equals to 7 cycles at 55 °C. **Add 7 cycles to the detected Ct value before reporting the Ct values**.

The data produced by the instruments can manually be evaluated and reported using their software or can automatically be evaluated and reported using the online FastFinder software: https://www.ugentec.com/fastfinder. In case the online ***FastFinder*** software is used for the interpretation, the Ct values provided by the software shouldn't be changed and must be reported as they are obtained on the software.

Table 6. Expected Performance of the Kit Controls

Control Type	Control Name	Purpose	Expected Results and Cq Values	
			***RNase P* (HEX)**	***Target* (FAM, HEX, ROX, and CY5)**
Negative Control	NTC	Contamination control during RT-qPCR	**Not Detected** (No Cq)	**Not Detected** (No Cq)
No template addition	NRC	Reagent contamination control	**Not Detected** (No Cq)	**Not Detected** (No Cq)
Positive Control	PC	Reagent integrity	**Detected** (Cq≤33)	**Detected** (Cq≤33)
Internal/Extraction Control	IC	To monitor the integrity of nucleic acid extraction and RT-qPCR from each sample	**Detected** (Cq≤33) If IC Cq>33 check the target Cq	If target Cq≤35, conclude it as IC is valid

If any control does not perform as described above, the run is considered invalid, and the test is repeated.

1. **Invalid PC (Cq>33 in any channel):** It is recommended to contact the manufacturer, renew the reagents, and repeat the reaction.
2. **Invalid NTC (No Cq in any channel):** Repeat the analysis by paying attention to the "**Warnings**" section.
3. **Invalid NRC (No Cq in any channel):** Contact the manufacturer, renew the reagents, and repeat the reaction.
4. **Invalid IC (Cq>33 in HEX channel and no Cq in the other channels):** Repeat the analysis. If the problem continues, then conclude it as an invalid PCR template.

If all the controls are valid, proceed to the analysis of the results (Table 7).

Table 7. Analysis of Results

Target	Internal Control	Report	
Positive (+)	**Positive (+)**	Report it as **POSITIVE** for the target	25≤Cq≤35 = Low positive 18≤Cq<25 = Positive 11≤Cq<18 = High positive Cq<11 = Very high positive
Positive (+)	**Negative (-)**	Report it as **POSITIVE** for the target	
Negative (-)	**Positive (+)**	Report it as **NEGATIVE** for the target	
Negative (-)	**Negative (-)**	**INVALID** Result: Sampling/extraction/inhibition problem Re-extract the specimen and perform testing again. If the result is still invalid, a new specimen should be obtained. If an additional clinical sample is unavailable, report it as **INVALID.**	

WARNING: On the web page linked with the QR code, examples of the sigmoidal amplification curves are given. The results obtained with this kit should NOT be interpreted without examining these samples.

9. Limitations

- ***Bio-Speedy® Gastroenteritis RT-qPCR MX-24T Panel*** is intended for use by laboratory personnel trained in the techniques of RT-qPCR and *in vitro* diagnostic procedures.
- The clinical specimens shall be collected by a healthcare provider in accordance with the specimen collection guidelines.
- A false-negative result may occur if a specimen is improperly collected, transported, or handled.
- The use of cotton or calcium alginate swabs or swabs with wooden sticks can lead to false-negative results since they may contain substances that inactivate some pathogens and inhibit PCR.
- Mutations within the target regions of the ***Bio-Speedy® Gastroenteritis RT-qPCR MX-24T Panel*** could affect primer and/or probe binding resulting in failure to detect the presence of the virus, bacteria, and parasite.
- Inhibitors or other types of interference may produce a false-negative result. False-negative results may also occur if inadequate numbers of organisms are present in the specimen.

10. Explanation of Symbol

Symbol	Title of Symbol	Symbol	Title of Symbol	Symbol	Title of Symbol
CE	European Conformity CE Mark	LOT	Batch code		Keep away from sunlight
IVD	*In vitro* diagnostic *medical device*	REF	Catalogue number		Protect from heat and radioactive sources
	Manufacturer	NON STERILE	Non-*sterile*		Do not use if package is damaged and consult *instructions for use*
	Use-by date		Consult *instructions for use* or consult electronic *instructions for use*		Keep dry
CONTROL -	Negative control		Caution		Keep upright
CONTROL +	Positive control		Temperature limit	Σ	Contains sufficient for *<n>* tests
CONTROL	Control				

11. Manufacturer and Technical Support

Bioeksen R&D Technologies Incorporated Company
Address: Resitpasa Mh. Katar Cd., 4/B-105. 34467, Sariyer, Istanbul, TURKEY.
Phone: +90 (212) 285 10 17, **Fax:** +90 (212) 285 10 18
Web: www.bioeksen.com.tr, **e-mail:** info@bioeksen.com.tr,
Technical Support: support@bioeksen.com.tr

Notice to User: Please inform us about product-related incidents at " **vigilance@bioeksen.com.tr** " within 24 hours.

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For professional use only.

Cat No: BS-NA-513m-100

*v*NAT® Transfer Tube

Instructions for Use (IFU)

1. PRODUCT DESCRIPTION

Table 1. Product overview

Product Name	*v*NAT® Transfer Tube
Catalog No	BS-NA-513m-100
Basic UDI	868187745NAEXT0672
Intended Use	The *v*NAT® Transfer Tube contains 2 ml of *v*NAT® reagent, which lyses cells, releases nucleic acids, and preserves them. The *v*NAT® reagent also inactivates viral and bacterial pathogens within 1 minute of contact with the clinical specimen. When clinical specimens suspected of respiratory tract infection are transferred into the *v*NAT® Transfer Tube, the liquid inside the tube can be directly used in Real-Time PCR (qPCR) reactions without the need for nucleic acid extraction.
Intended Users	Professional use with training in the sampling process.
Intended environment of use	Near-patient testing in non-laboratory conditions.
Special Conditions for Use Statements	For in vitro diagnostic use only.
Test Principle	The *v*NAT® reagent contains a combination of quaternary ammonium compound (QAC) and tween-20, which work together to effectively lyse cells and release the genomic material present in the sample. The QAC and NaN_3 in the reagent also play a crucial role in preserving the integrity of the released genomes.
Analyte	Respiratory tract pathogens.
Specimen Type (s)	Nasopharyngeal, oropharyngeal, and nasal, and oral/saliva swab samples from the respiratory tract.

Table 2. Product content

Component	Description	Amount
*v*NAT® *Transfer Tube*	Cell lysis and nucleic acid storage	100 tubes each containing 2 mL of *v*NAT® reagent

Table 3. Storage requirements and shelf life

Component	Transport Conditions	Storage Conditions	Shelf Life
*v*NAT® *Transfer Tube*	+2 °C to +50 °C	+2 °C to +30 °C	60 months

Table 4. Materials required but not included with the product.

Component	Intended use	Specifications
Vortex mixer	Sample homogenization	Speed up to 3000 rpm
Micropipettes	Liquid transfer	Adjustable volume; 10-100 µL or 0.1-10 µL
Micropipettes tips	Liquid transfer	Compatible with the micropipettes, filtered, nuclease-free

2 APPLICATION PROTOCOL

The collection of nasopharyngeal, oropharyngeal, nasal, and oral/saliva swab samples should be performed by a healthcare provider following the guidelines outlined in national and international clinical specimen collection regulations. These regulations include adherence to protocols such as the updated version of the CDC Interim Guidelines for Collecting, Handling, and Testing Clinical Specimens for COVID-19, which can be found at the following link: https://www.cdc.gov/coronavirus/2019-ncov/lab/guidelines-clinical-specimens.html.

Once the swab samples are collected, it is important to immediately place them into the *v*NAT® Transfer Tube.

One minute after the sampling, the sample in the *v*NAT® ***Transfer Tube*** can be used directly in RT-qPCR. Vortex the tube at the highest speed for 3 seconds before adding the sample into the RT-qPCR.

Store the specimens at +2 °C to +8 °C and ship them to the laboratory on the ice pack. Specimens in the *v*NAT® ***Transfer Tube*** can be stored at +2 °C to +30 °C for up to 72 hours and +2 °C to +8 °C for up to 3 months after the collection.

3 PERFORMANCE CHARACTERISTICS

The *v*NAT® ***Transfer Tube*** has been validated specifically for use with RT-qPCR-based test kits manufactured by Bioeksen AR GE Teknolojileri A.Ş. The performance characteristics of the *v*NAT® ***Transfer Tube***, when used in conjunction with these specific kits for the in vitro diagnosis of targeted pathogens, are provided in the Instructions for Use (IFUs) of the respective RT-qPCR kits.

3.1 Shelf-life and shipping stability

Since the swab samples are placed into the *v*NAT® Transfer Tube immediately after its initial opening, stability studies were carried out only for the unopened *v*NAT® Transfer Tubes. Separate shelf-life stability studies for the components prepared in bulk and stored before use in different lots were not conducted since the components of the *v*NAT® Transfer Tube are always freshly prepared.

The shelf-life and shipping stability test involved three different lots all manufactured under routine production conditions. The stability study was initiated within one week after production. The *v*NAT® Transfer Tubes were stored for 113 weeks (26 months) in a stability chamber set at 2 °C, 30 °C and 50 °C to mimic all possible storage and shipping conditions. The stability chamber was set at 85% relative humidity for a worst-case scenario.

The Bio-Speedy® Respiratory ID-3 Panel (Cat No: BS-RIDP-3) was used to evaluate the stability of the stored *v*NAT® Transfer Tubes. Negative clinical samples were collected using freshly produced *v*NAT® Transfer Tubes. Subsequently, the samples were pooled together and subjected to 24 tests using the Bio-Speedy® Respiratory ID-3 Panel to confirm the absence of any positive results in the negative sample matrix. All tests yielded negative results for the analyte and positive results for the internal control (IC), with an average Cq value of 18.31 ± 0.74. Subsequently, reference materials of Group A *Streptococcus* (Zeptometrix, #0801512), *Streptococcus pneumoniae* (Zeptometrix, 0801439), *Mycoplasma pneumoniae* (Zeptometrix, 0801579), *Chlamydophila pneumoniae* (ATCC, VR-2282), *Haemophilus influenzae* (Zeptometrix, 0801679), *SARS-CoV-2* (Zeptometrix, 0810589CFHI), Influenza A (Zeptometrix, 0810036CF), RSV A (Zeptometrix, 0810040ACF), Adenovirus (Zeptometrix, 0810050CF), Rhinovirus (Zeptometrix, 0810012CFN), and Parainfluenza virus 3 (Zeptometrix, 0810016CF) were diluted in the negative clinical sample matrix to reach an analyte concentration that is 11x higher than the Limit of Detection (LoD) of the Bio-Speedy® Respiratory ID-3 Panel, which is 250 copies/mL.

Weekly testing was conducted on five *v*NAT® Transfer Tubes from each lot involved in the stability study, resulting in a total of 15 tubes (3 lots x 5 tubes) tested for each condition every week. The *v*NAT® Transfer Tubes were spiked with 0.2 mL of the sample matrix containing the analytes, leading to a final concentration of 250 copies/mL for each analyte. These spiked tubes were then subjected to testing using the Bio-Speedy® Respiratory ID-3 Panel.

For the study, a baseline was established by defining a 5% deterioration from the initial Cq value. The stability of the tube was determined by selecting the time point prior to the last time point at which it met the acceptance criteria. The results of the stability tests are presented in Table 5-7.

The results of the stability study indicated that the *v*NAT® Transfer Tubes remained stable at 2°C, 30 °C, and 50 °C even after 26 months of testing. To calculate the theoretical shelf-life at 30 °C, the data obtained from the tubes stored at 50 °C was analyzed using the Arrhenius equation, which establishes a relationship between the rate of product degradation and the storage temperature. The calculated theoretical shelf-life for the *v*NAT® Transfer Tubes was determined to be 105 months at 30 °C.

Table 5. Stability study results at 50 °C.

Analyte	t = 0					t = Week 113				
	Analyte		IC		Detection Rate	Analyte		IC		Detection Rate
	Cq	± SD	Cq	± SD		Cq	± SD	Cq	± SD	
Group A *Streptococcus*	25.33	0.66	18.58	0.47	15/15	25.17	0.82	18.14	0.49	15/15
Streptococcus pneumoniae	25.47	0.62	18.48	0.87	15/15	25.72	0.65	18.34	0.71	15/15
Mycoplasma pneumoniae	24.25	0.54	18.42	0.8	15/15	24.12	0.64	18.8	0.46	15/15
Chlamydophila pneumoniae	25.97	0.54	18.89	0.81	15/15	25.82	0.75	18.71	0.61	15/15
Haemophilus influenzae	24.86	0.75	18.78	0.49	15/15	24.57	0.6	18.49	0.79	15/15
SARS-CoV-2	24.20	0.79	18.6	0.56	15/15	25.63	0.47	18.14	0.73	15/15
Influenza A	25.19	0.47	18.67	0.53	15/15	24.76	0.47	18.94	0.43	15/15
RSV A	25.71	0.52	18.19	0.6	15/15	25.95	0.49	18.53	0.61	15/15
Adenovirus	24.77	0.62	18.37	0.65	15/15	25.38	0.81	18.24	0.64	15/15
Rhinovirus	24.42	0.45	18.38	0.53	15/15	24.76	0.66	18.15	0.59	15/15
Parainfluenza virus 3	25.55	0.76	18.18	0.45	15/15	25.24	0.66	18.44	0.72	15/15

Table 6. Stability study results at 30 °C.

Analyte	t = 0					t = Week 113				
	Analyte		IC		Detection Rate	Analyte		IC		Detection Rate
	Cq	± SD	Cq	± SD		Cq	± SD	Cq	± SD	
Group A *Streptococcus*	25.33	0.66	18.58	0.47	15/15	25.58	0.81	18.54	0.72	15/15
Streptococcus pneumoniae	25.47	0.62	18.48	0.87	15/15	25.72	0.56	18.69	0.68	15/15
Mycoplasma pneumoniae	24.25	0.54	18.42	0.8	15/15	24.68	0.69	18.96	0.69	15/15
Chlamydophila pneumoniae	25.97	0.54	18.89	0.81	15/15	24.81	0.78	18.86	0.51	15/15
Haemophilus influenzae	24.86	0.75	18.78	0.49	15/15	24.88	0.47	18.7	0.45	15/15
SARS-CoV-2	24.20	0.79	18.6	0.56	15/15	25.66	0.81	18.4	0.56	15/15
Influenza A	25.19	0.47	18.67	0.53	15/15	25.94	0.89	18.28	0.77	15/15
RSV A	25.71	0.52	18.19	0.6	15/15	24.28	0.45	18.59	0.5	15/15
Adenovirus	24.77	0.62	18.37	0.65	15/15	24.63	0.5	18.86	0.52	15/15

Rhinovirus	24.42	0.45	18.38	0.53	15/15	25.64	0.76	18.75	0.66	15/15
Parainfluenza virus 3	25.55	0.76	18.18	0.45	15/15	25.73	0.44	18.32	0.69	15/15

Table 7. Stability study results at 2 °C.

Analyte	t = 0					t = Week 113				
	Analyte		IC		Detection Rate	Analyte		IC		Detection Rate
	Cq	± SD	Cq	± SD		Cq	± SD	Cq	± SD	
Group A *Streptococcus*	25.33	0.66	18.58	0.47	15/15	25.65	0.62	18.49	0.6	15/15
Streptococcus pneumoniae	25.47	0.62	18.48	0.87	15/15	25.38	0.53	18.79	0.63	15/15
Mycoplasma pneumoniae	24.25	0.54	18.42	0.8	15/15	24.71	0.48	18.46	0.67	15/15
Chlamydophila pneumoniae	25.97	0.54	18.89	0.81	15/15	24.86	0.82	18.18	0.86	15/15
Haemophilus influenzae	24.86	0.75	18.78	0.49	15/15	25.27	0.65	18.68	0.45	15/15
SARS-CoV-2	24.20	0.79	18.6	0.56	15/15	25.57	0.49	18.15	0.62	15/15
Influenza A	25.19	0.47	18.67	0.53	15/15	24.44	0.66	18.18	0.86	15/15
RSV A	25.71	0.52	18.19	0.6	15/15	25.81	0.45	18.38	0.44	15/15
Adenovirus	24.77	0.62	18.37	0.65	15/15	25.35	0.52	18.65	0.6	15/15
Rhinovirus	24.42	0.45	18.38	0.53	15/15	25.73	0.55	18.34	0.69	15/15
Parainfluenza virus 3	25.55	0.76	18.18	0.45	15/15	24.72	0.75	18.53	0.56	15/15

3.2 Stability of specimens in the *v*NAT® Transfer Tube

The Bio-Speedy® Respiratory ID-3 Panel (Cat No: BS-RIDP-3) was used to evaluate the stability of the nasopharyngeal, oropharyngeal, nasal, and oral swab samples stored in the *v*NAT® Transfer Tubes. Negative clinical samples were collected using the *v*NAT® Transfer Tubes. Subsequently, each sample was subjected to 5 tests using the Bio-Speedy® Respiratory ID-3 Panel to confirm the absence of any positive results. All tests yielded negative results for the analyte and positive results for the internal control (IC). Then, reference materials of Group A *Streptococcus* (Zeptometrix, #0801512), *Streptococcus pneumoniae* (Zeptometrix, 0801439), *Mycoplasma pneumoniae* (Zeptometrix, 0801579), *Chlamydophila pneumoniae* (ATCC, VR-2282), *Haemophilus influenzae* (Zeptometrix, 0801679), SARS-CoV-2 (Zeptometrix, 0810589CFHI), Influenza A (Zeptometrix, 0810036CF), RSV A (Zeptometrix, 0810040ACF), Adenovirus (Zeptometrix, 0810050CF), Rhinovirus (Zeptometrix, 0810012CFN), and Parainfluenza virus 3 (Zeptometrix, 0810016CF) were diluted in the negative samples to reach an analyte concentration at the LoD of the Bio-Speedy® Respiratory ID-3 Panel, which is 250 copies/mL.

The spiked tubes were stored at 4 °C and 30 °C for four months at 85% relative humidity in the stability chamber. Daily testing was conducted on the five contrived samples for each condition using the Bio-Speedy® Respiratory ID-3 Panel. A baseline was established by defining a 5% deterioration from the initial Cq value. The stability of the sample was determined by selecting the time point prior to the last time point at which it met the acceptance criteria.

Table 8-15 displays the results of the specimen stability tests. The analysis reveals that the nasopharyngeal, oropharyngeal, nasal, and oral swab samples stored in the *v*NAT® Transfer Tubes remained stable for a period of 4 days at 30 °C. Therefore, it is recommended to store these samples at 30 °C for a maximum duration of 3 days.

Furthermore, all sample types in the *v*NAT® Transfer Tubes demonstrated stability even after 4 months of storage at 4 °C. As a result, it is advised to store these samples at 4 °C for up to 3 months.

Table 8. Stability results of nasopharyngeal swab samples at 30 °C

Analyte	t = 0					t = Day 4					t = Day 5				
	Analyte		IC		Hit Rate	Analyte		IC		Hit Rate	Analyte		IC		Hit Rate
	Cq	± SD	Cq	± SD		Cq	± SD	Cq	± SD		Cq	± SD	Cq	± SD	
Group A *Streptococcus*	25.72	0.6	17.81	0.53	5/5	26.61	0.54	18.12	0.58	5/5	28.19	1.85	19.49	0.63	3/5
Streptococcus pneumoniae	25.63	0.45	14.72	0.74	5/5	26.28	0.46	15.02	0.64	5/5	27.54	1.37	16	0.81	4/5
Mycoplasma pneumoniae	25.38	0.47	19.76	0.54	5/5	26.01	0.85	20.18	0.46	5/5	26.85	1.78	20.81	0.63	5/5
Chlamydophila pneumoniae	25.33	0.73	15.81	0.78	5/5	26.21	0.49	16.02	0.47	5/5	27.39	1.31	17.28	0.82	4/5
Haemophilus influenzae	24.29	0.79	17.3	0.48	5/5	24.93	0.68	17.81	0.76	5/5	25.95	1.32	18.45	0.59	5/5
SARS-CoV-2	24.75	0.51	12.3	0.87	5/5	25.24	0.81	12.58	0.73	5/5	26.2	1.28	13.27	0.7	5/5
Influenza A	24.27	0.42	14.33	0.81	5/5	25.07	0.57	14.85	0.57	5/5	26.11	1.75	15.65	0.56	5/5
RSV A	24.81	0.73	14.12	0.42	5/5	25.66	0.49	14.57	0.44	5/5	26.56	1.83	15.42	0.66	5/5
Adenovirus	25.59	0.72	18.23	0.56	5/5	26.09	0.64	18.66	0.89	5/5	26.95	1.43	19.16	0.63	5/5
Rhinovirus	24.90	0.66	13.27	0.64	5/5	25.53	0.49	13.86	0.41	5/5	27.31	1.33	14.79	0.6	4/5
Parainfluenza virus 3	25.82	0.43	14.38	0.57	5/5	26.64	0.72	14.96	0.7	5/5	27.8	1.61	15.78	0.81	2/5

Table 9. Stability results of nasopharyngeal swab samples at 4 °C

Analyte	t = 0					t = Day 120				
	Analyte		IC		Hit Rate	Analyte		IC		Hit Rate
	Cq	± SD	Cq	± SD		Cq	± SD	Cq	± SD	
Group A *Streptococcus*	25.72	0.6	17.81	0.53	5/5	26.38	0.4	18.09	0.24	5/5
Streptococcus pneumoniae	25.63	0.45	14.72	0.74	5/5	26.24	0.38	15.12	0.23	5/5
Mycoplasma pneumoniae	25.38	0.47	19.76	0.54	5/5	26.19	0.29	20.14	0.3	5/5
Chlamydophila pneumoniae	25.33	0.73	15.81	0.78	5/5	26.06	0.34	16.13	0.25	5/5
Haemophilus influenzae	24.29	0.79	17.3	0.48	5/5	24.81	0.29	17.57	0.31	5/5
SARS-CoV-2	24.75	0.51	12.3	0.87	5/5	25.31	0.23	12.64	0.3	5/5
Influenza A	24.27	0.42	14.33	0.81	5/5	24.91	0.32	14.72	0.26	5/5
RSV A	24.81	0.73	14.12	0.42	5/5	25.40	0.28	14.44	0.27	5/5
Adenovirus	25.59	0.72	18.23	0.56	5/5	26.44	0.35	18.49	0.37	5/5
Rhinovirus	24.90	0.66	13.27	0.64	5/5	25.66	0.39	13.56	0.22	5/5
Parainfluenza virus 3	25.82	0.43	14.38	0.57	5/5	26.29	0.39	14.72	0.4	5/5

Table 10. Stability results of oropharyngeal swab samples at 30 °C

Analyte	t = 0					t = Day 4					t = Day 5				
	Analyte		IC		Hit Rate	Analyte		IC		Hit Rate	Analyte		IC		Hit Rate
	Cq	± SD	Cq	± SD		Cq	± SD	Cq	± SD		Cq	± SD	Cq	± SD	
Group A *Streptococcus*	25.95	0.28	19.48	0.21	5/5	26.17	0.42	19.92	0.43	5/5	27.49	0.31	22.12	0.28	3/5
Streptococcus pneumoniae	24.64	0.67	14.85	0.25	5/5	25.09	0.37	15.13	0.4	5/5	27.79	0.44	16.53	0.42	4/5
Mycoplasma pneumoniae	25.85	0.64	13.45	0.34	5/5	26.12	0.34	13.88	0.43	5/5	27.74	0.43	16.03	0.22	3/5
Chlamydophila pneumoniae	24.47	0.47	16.18	0.23	5/5	24.86	0.45	16.64	0.36	5/5	27.20	0.42	18.94	0.39	4/5
Haemophilus influenzae	25.25	0.32	13.39	0.32	5/5	25.72	0.45	13.62	0.36	5/5	28.54	0.46	14.77	0.43	2/5
SARS-CoV-2	25.94	0.55	18.31	0.4	5/5	26.27	0.43	18.74	0.37	5/5	28.25	0.38	20.89	0.36	2/5
Influenza A	24.26	0.5	19.94	0.39	5/5	24.60	0.46	20.3	0.47	5/5	26.64	0.29	22.1	0.26	5/5
RSV A	25.13	0.33	19.15	0.27	5/5	25.56	0.31	19.58	0.33	5/5	28.14	0.25	21.73	0.21	3/5
Adenovirus	24.64	0.21	19.63	0.28	5/5	25.05	0.32	19.88	0.21	5/5	27.51	0.25	21.13	0.37	4/5
Rhinovirus	25.43	0.57	19.61	0.3	5/5	25.69	0.32	20.07	0.21	5/5	27.25	0.44	22.37	0.36	4/5
Parainfluenza virus 3	25.47	0.36	16.26	0.31	5/5	25.77	0.35	16.59	0.34	5/5	27.57	0.35	18.24	0.29	4/5

Table 11. Stability results of oropharyngeal swab samples at 4 °C

Analyte	t = 0					t = Day 120				
	Analyte		IC		Hit Rate	Analyte		IC		Hit Rate
	Cq	± SD	Cq	± SD		Cq	± SD	Cq	± SD	
Group A *Streptococcus*	25.95	0.28	19.48	0.21	5/5	26.64	0.24	19.75	0.42	5/5
Streptococcus pneumoniae	24.64	0.67	14.85	0.25	5/5	25.05	0.45	15.45	0.4	5/5
Mycoplasma pneumoniae	25.85	0.64	13.45	0.34	5/5	26.53	0.35	14.11	0.45	5/5
Chlamydophila pneumoniae	24.47	0.47	16.18	0.23	5/5	24.81	0.45	16.46	0.37	5/5
Haemophilus influenzae	25.25	0.32	13.39	0.32	5/5	25.86	0.26	13.79	0.43	5/5
SARS-CoV-2	25.94	0.55	18.31	0.4	5/5	26.52	0.3	18.56	0.36	5/5
Influenza A	24.26	0.5	19.94	0.39	5/5	24.61	0.23	20.29	0.32	5/5
RSV A	25.13	0.33	19.15	0.27	5/5	25.41	0.46	19.57	0.28	5/5
Adenovirus	24.64	0.21	19.63	0.28	5/5	25.08	0.34	20.26	0.24	5/5
Rhinovirus	25.43	0.57	19.61	0.3	5/5	26.08	0.42	20.08	0.33	5/5
Parainfluenza virus 3	25.47	0.36	16.26	0.31	5/5	25.91	0.28	16.83	0.25	5/5

Table 12. Stability results of nasal swab samples at 30 °C

Analyte	t = 0					t = Day 4					t = Day 5				
	Analyte		IC		Hit Rate	Analyte		IC		Hit Rate	Analyte		IC		Hit Rate
	Cq	± SD	Cq	± SD		Cq	± SD	Cq	± SD		Cq	± SD	Cq	± SD	
Group A *Streptococcus*	24.21	0.4	14.93	0.27	5/5	24.42	0.34	15.17	0.36	5/5	25.68	0.3	16.37	0.35	5/5
Streptococcus pneumoniae	24.74	0.39	15.49	0.28	5/5	25.17	0.38	15.76	0.42	5/5	27.75	0.29	17.11	0.31	4/5
Mycoplasma pneumoniae	24.30	0.28	14.23	0.36	5/5	24.69	0.41	14.64	0.33	5/5	27.03	0.27	16.69	0.29	4/5
Chlamydophila pneumoniae	25.92	0.34	13.42	0.26	5/5	26.28	0.31	13.76	0.4	5/5	28.44	0.22	15.46	0.31	3/5
Haemophilus influenzae	25.84	0.31	15.71	0.37	5/5	26.28	0.25	15.99	0.45	5/5	28.92	0.38	17.39	0.34	2/5
SARS-CoV-2	25.78	0.42	12.25	0.47	5/5	26.13	0.26	12.71	0.44	5/5	28.23	0.26	15.01	0.25	3/5
Influenza A	25.39	0.23	13.27	0.35	5/5	25.80	0.43	13.66	0.45	5/5	28.26	0.25	15.61	0.33	3/5
RSV A	25.85	0.41	18.69	0.46	5/5	26.20	0.44	19.07	0.38	5/5	28.30	0.38	20.97	0.22	3/5
Adenovirus	24.68	0.3	12.56	0.39	5/5	25.00	0.42	12.88	0.38	5/5	26.92	0.29	14.48	0.31	4/5
Rhinovirus	24.55	0.38	14.78	0.36	5/5	24.85	0.26	15.1	0.41	5/5	26.65	0.26	16.7	0.29	5/5
Parainfluenza virus 3	25.26	0.4	12.97	0.45	5/5	25.48	0.35	13.33	0.4	5/5	26.80	0.23	15.13	0.22	5/5

Table 13. Stability results of nasal swab samples at 4 °C

Analyte	t = 0					t = Day 120				
	Analyte		IC		Hit Rate	Analyte		IC		Hit Rate
	Cq	± SD	Cq	± SD		Cq	± SD	Cq	± SD	
Group A *Streptococcus*	24.21	0.4	14.93	0.27	5/5	24.67	0.24	15.27	0.31	5/5
Streptococcus pneumoniae	24.74	0.39	15.49	0.28	5/5	25.14	0.36	15.95	0.23	5/5
Mycoplasma pneumoniae	24.30	0.28	14.23	0.36	5/5	24.58	0.36	14.6	0.28	5/5
Chlamydophila pneumoniae	25.92	0.34	13.42	0.26	5/5	26.24	0.31	13.65	0.28	5/5
Haemophilus influenzae	25.84	0.31	15.71	0.37	5/5	26.28	0.4	16.16	0.28	5/5
SARS-CoV-2	25.78	0.42	12.25	0.47	5/5	26.23	0.31	12.52	0.31	5/5
Influenza A	25.39	0.23	13.27	0.35	5/5	25.60	0.34	13.59	0.38	5/5
RSV A	25.85	0.41	18.69	0.46	5/5	26.29	0.27	19.14	0.36	5/5
Adenovirus	24.68	0.3	12.56	0.39	5/5	24.95	0.4	13.02	0.3	5/5
Rhinovirus	24.55	0.38	14.78	0.36	5/5	24.77	0.29	15.24	0.4	5/5
Parainfluenza virus 3	25.26	0.4	12.97	0.45	5/5	25.65	0.28	13.29	0.43	5/5

Table 14. Stability results of oral swab samples at 30 °C

Analyte	t = 0					t = Day 4					t = Day 5				
	Analyte		IC		Hit Rate	Analyte		IC		Hit Rate	Analyte		IC		Hit Rate
	Cq	± SD	Cq	± SD		Cq	± SD	Cq	± SD		Cq	± SD	Cq	± SD	
Group A *Streptococcus*	24.56	0.4	15.28	0.4	5/5	24.86	0.46	15.59	0.43	5/5	26.66	0.24	17.14	0.26	5/5
Streptococcus pneumoniae	24.72	0.21	18.33	0.37	5/5	24.99	0.36	18.78	0.32	5/5	26.61	0.3	21.03	0.21	5/5
Mycoplasma pneumoniae	25.36	0.46	14.94	0.29	5/5	25.68	0.43	15.15	0.47	5/5	27.60	0.37	16.2	0.21	4/5
Chlamydophila pneumoniae	24.22	0.33	19.88	0.31	5/5	24.69	0.44	20.18	0.27	5/5	27.51	0.27	21.68	0.24	4/5
Haemophilus influenzae	25.57	0.45	17.96	0.21	5/5	25.95	0.42	18.35	0.46	5/5	28.23	0.26	20.3	0.3	3/5
SARS-CoV-2	25.88	0.33	12.76	0.4	5/5	26.26	0.4	13.13	0.35	5/5	28.54	0.38	14.98	0.44	2/5
Influenza A	24.13	0.33	16.41	0.45	5/5	24.55	0.21	16.66	0.42	5/5	27.07	0.22	17.91	0.47	4/5
RSV A	24.94	0.21	14.16	0.3	5/5	25.17	0.45	14.43	0.43	5/5	26.55	0.4	15.78	0.36	5/5
Adenovirus	24.63	0.28	18.82	0.35	5/5	24.85	0.4	19.22	0.44	5/5	26.17	0.43	21.22	0.24	5/5
Rhinovirus	25.35	0.43	13.9	0.29	5/5	25.72	0.33	14.13	0.34	5/5	27.94	0.34	15.28	0.26	4/5
Parainfluenza virus 3	24.73	0.26	16.71	0.34	5/5	24.97	0.38	16.93	0.27	5/5	26.41	0.21	18.03	0.45	5/5

Table 15. Stability results of oral swab samples at 4 °C

Analyte	t = 0					t = Day 120				
	Analyte		IC		Hit Rate	Analyte		IC		Hit Rate
	Cq	± SD	Cq	± SD		Cq	± SD	Cq	± SD	
Group A *Streptococcus*	24.56	0.4	15.28	0.4	5/5	24.78	0.43	15.72	0.37	5/5
Streptococcus pneumoniae	24.72	0.21	18.33	0.37	5/5	25.17	0.41	18.61	0.34	5/5
Mycoplasma pneumoniae	25.36	0.46	14.94	0.29	5/5	25.63	0.4	15.37	0.22	5/5
Chlamydophila pneumoniae	24.22	0.33	19.88	0.31	5/5	24.61	0.29	20.34	0.36	5/5
Haemophilus influenzae	25.57	0.45	17.96	0.21	5/5	26.04	0.24	18.19	0.27	5/5
SARS-CoV-2	25.88	0.33	12.76	0.4	5/5	26.21	0.44	13.19	0.21	5/5
Influenza A	24.13	0.33	16.41	0.45	5/5	24.47	0.24	16.77	0.21	5/5
RSV A	24.94	0.21	14.16	0.3	5/5	25.37	0.38	14.59	0.38	5/5
Adenovirus	24.63	0.28	18.82	0.35	5/5	25.04	0.27	19.07	0.35	5/5
Rhinovirus	25.35	0.43	13.9	0.29	5/5	25.61	0.38	14.36	0.3	5/5
Parainfluenza virus 3	24.73	0.26	16.71	0.34	5/5	25.03	0.3	17.04	0.34	5/5

3.3 Inactivation performance

Archived clinical respiratory tract samples that were collected in Copan Universal Transport Medium (UTM) were used in the inactivation performance studies. The samples were tested using the Bio-Speedy® Respiratory Tract RT-qPCR MX-24L Panel (Cat No: BS-SY-MX24L) or Bio-Speedy® Lower Respiratory Bacteria qPCR Panel (Cat No: BS-LRB-L), which detected the following pathogens: Group A *Streptococcus, Streptococcus pneumoniae, Mycoplasma pneumoniae, Chlamydophila pneumoniae, Haemophilus influenzae*, SARS-CoV-2, Influenza A, RSV A/B, Adenovirus, Rhinovirus, and Parainfluenza virus 3. For the subsequent viability studies, three levels of positivity were chosen. These levels include:

1. High positive samples: These samples exhibit a Cq value ranging from 6 to 10.
2. Positive samples: These samples have a Cq value ranging from 15 to 19.
3. Low positive samples: These samples possess a Cq value ranging from 23 to 26.

Pathogen viability in the samples was assessed using specific growth media. Group A *Streptococcus* and *Streptococcus pneumoniae* were cultured on Blood Agar. *Chlamydophila pneumoniae*, RSV A/B, and Parainfluenza virus 3 were assessed using HEp-2 cell culture media. *Mycoplasma pneumoniae* was cultured on SP4 agar. *Haemophilus influenzae* was cultured on Chocolate Agar. SARS-CoV-2 was propagated in Vero E6 cell culture media. Influenza A was cultured in Madin-Darby Canine Kidney (MDCK) cell culture media. Adenovirus was cultured in HEK293 cell culture media. Rhinovirus was cultured in nasal epithelial cell culture media.

The positive samples were added to both the *v*NAT® Transfer Tube and the Copan Universal Transport Medium (UTM) in a manner that resulted in a five-fold dilution of the sample within the media. After a one-minute incubation at room temperature, the tubes were immediately subjected to cultivation. The unused UTM and *v*NAT® tubes were also included in the cultivation as negative controls. Plaque-forming units (PFU)/mL, tissue culture infectious dose 50 (TCID50), or colony-forming units (CFU)/mL were subsequently calculated for each condition.

The results were presented in Table 16. The concentrations were between 10^2-10^6 units/mL when cultivated from the samples in the UTM. All the concentrations resulted in negative results for the samples in the *v*NAT® Transfer Tubes indicating successful inactivation by the *v*NAT® reagent.

Table 16-18 displays the results of the viability study. The concentrations of the cultivated samples from the Universal Transport Medium (UTM) ranged between 10^2-10^6 units/mL. However, all the concentrations derived from the samples in the *v*NAT® Transfer Tubes showed negative results, indicating successful inactivation of the analytes by the *v*NAT® reagent.

Table 16. Results of the viable pathogen count in the high positive samples

Analyte	Unit	Spiked Media		Clean Media	
		UTM	*v*NAT®	UTM	*v*NAT®
Group A *Streptococcus*	cfu/mL	$2.1x10^5$	Not detected	Not detected	Not detected
Streptococcus pneumoniae	cfu/mL	$8.6x10^5$	Not detected	Not detected	Not detected
Mycoplasma pneumoniae	cfu/mL	$8x10^4$	Not detected	Not detected	Not detected
Chlamydophila pneumoniae	cfu/mL	$1.2x10^5$	Not detected	Not detected	Not detected
Haemophilus influenzae	cfu/mL	$2.4x10^5$	Not detected	Not detected	Not detected
SARS-CoV-2	TCID50/mL	$3.2x10^4$	Not detected	Not detected	Not detected
Influenza A	PFU/mL	$8.9x10^5$	Not detected	Not detected	Not detected
RSV A	TCID50/mL	$8.6x10^4$	Not detected	Not detected	Not detected
Adenovirus	PFU/mL	$9.5x10^5$	Not detected	Not detected	Not detected
Rhinovirus	TCID50/mL	$9.1x10^4$	Not detected	Not detected	Not detected
Parainfluenza virus 3	PFU/mL	$8.3x10^5$	Not detected	Not detected	Not detected

Table 17. Results of the viable pathogen count in the positive samples

Analyte	Unit	Spiked Media		Clean Media	
		UTM	vNAT®	UTM	vNAT®
Group A *Streptococcus*	cfu/mL	$8.1x10^3$	Not detected	Not detected	Not detected
Streptococcus pneumoniae	cfu/mL	$9.2x10^3$	Not detected	Not detected	Not detected
Mycoplasma pneumoniae	cfu/mL	$9.7x10^2$	Not detected	Not detected	Not detected
Chlamydophila pneumoniae	cfu/mL	$3.3x10^3$	Not detected	Not detected	Not detected
Haemophilus influenzae	cfu/mL	$1.7x10^3$	Not detected	Not detected	Not detected
SARS-CoV-2	TCID50/mL	$8.6x10^2$	Not detected	Not detected	Not detected
Influenza A	PFU/mL	$9.1x10^3$	Not detected	Not detected	Not detected
RSV A	TCID50/mL	$8.6x10^2$	Not detected	Not detected	Not detected
Adenovirus	PFU/mL	$9.7x10^3$	Not detected	Not detected	Not detected
Rhinovirus	TCID50/mL	$3.8x10^2$	Not detected	Not detected	Not detected
Parainfluenza virus 3	PFU/mL	$7.5x10^3$	Not detected	Not detected	Not detected

Table 18. Results of the viable pathogen count in the low positive samples

Analyte	Unit	Spiked Media		Clean Media	
		UTM	vNAT®	UTM	vNAT®
Group A *Streptococcus*	cfu/mL	136	Not detected	Not detected	Not detected
Streptococcus pneumoniae	cfu/mL	255	Not detected	Not detected	Not detected
Mycoplasma pneumoniae	cfu/mL	331	Not detected	Not detected	Not detected
Chlamydophila pneumoniae	cfu/mL	214	Not detected	Not detected	Not detected
Haemophilus influenzae	cfu/mL	451	Not detected	Not detected	Not detected
SARS-CoV-2	TCID50/mL	102	Not detected	Not detected	Not detected
Influenza A	PFU/mL	394	Not detected	Not detected	Not detected
RSV A	TCID50/mL	155	Not detected	Not detected	Not detected
Adenovirus	PFU/mL	619	Not detected	Not detected	Not detected
Rhinovirus	TCID50/mL	113	Not detected	Not detected	Not detected
Parainfluenza virus 3	PFU/mL	652	Not detected	Not detected	Not detected

4 WARNINGS AND PRECAUTIONS

4.1 Use Statements

For In Vitro Diagnostic (IVD) Use Only.

For Professional Use Only.

4.2 Safety and Hazards

4.2.1 General Safety

Using this product in a manner not specified in the user documentation may result in personal injury or damage to the instrument or device. Ensure that anyone using this product has received instructions in general safety practices for laboratories and the safety information provided in this document.

4.2.2 Chemical Safety

To minimize hazards, ensure laboratory personnel read and practice the general safety guidelines for chemical usage, storage, and waste provided below, and consult the relevant SDS for specific precautions and instructions.

4.2.2.1 Biohazard

Follow all applicable local, state/provincial, and/or national regulations and standard precautions. All patient specimens should be considered potentially infectious and handled accordingly.

4.3 Waste Management

4.3.1 Medical Waste

Appropriate waste management and decontamination procedures should be used. Biological samples such as tissues, body fluids, infectious agents, and blood of humans and other animals have the potential to transmit infectious diseases. All medical wastes including the IVD, and its consumables used with it should be collected

in transportable and sealed biohazard bags/containers that are resistant to tear, puncture, breakage in accordance with the regulations on medical wastes. The contents of medical waste bags/containers should be never compressed, removed from the bag/container, emptied, and transferred to another container. Dispose of waste in a designated matter in accordance with local, regional, and federal regulations.

4.3.2. Molecular Waste

Nucleic acid contamination from molecular waste can be caused by dust and spreading aerosols. PCR products can be destroyed using a 3 % (mass fraction) hypochlorite solution (refer to ISO 22174:2005).

4.3.3. Chemical Waste

Characterize (by analysis if necessary) the waste generated by the applications, reagents, and substrates used in your laboratory.

Ensure use of primary and secondary waste containers (a primary waste container holds the immediate waste. A secondary container contains spills or leaks from the primary container. Both containers must be compatible with the waste material and meet federal, state, and local requirements for container storage).

After emptying a waste container, seal it with the cap provided.

Ensure that the waste is stored, transferred, transported, and disposed of according to all local, state/provincial, and/or national regulations.

IMPORTANT! Radioactive or biohazardous materials may require special handling, and disposal limitations may apply.

5 EXPLANATION OF SYMBOL

Symbol	Title of Symbol	Symbol	Title of Symbol	Symbol	Title of Symbol
CE	European Conformity CE Mark	IVD	*In vitro* diagnostic *medical device*		Keep away from sunlight
	Manufacturer	LOT	Batch code		Protect from heat and radioactive sources
	Use-by date	REF	Catalogue number		Do not use if package is damaged and consult *instructions for use*
	Temperature limit	NON STERILE	Non-*sterile*		Keep dry
	Caution		Consult *instructions for use* or consult electronic *instructions for use*		
	Keep it upright	2	Do not re-use		

6 MANUFACTURER AND TECHNICAL SUPPORT

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Notice to User: Please inform us about product-related incidents at "**vigilance@bioeksen.com.tr**" within 24 hours.

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For professional use only.
Cat No: BS-DTC-103-25/BS-DTC-103-100
Ordering Ref No: BORD-T-25/BORD-T-100

Bordetella pertussis, B.parapertussis, B.bronchiseptica and B.holmesii Real-Time PCR Detection Kit

Package Insert

Table 1. Kit Content

Component	Intended Use	25 Reactions	100 Reactions
2X qPCR Mix	Optimized ready-to-use mix for qPCR assay	1 x 500 µL	2 x 1000 µL
Bor 1 Oligo Mix	Specific nucleic acid amplification and detection: **FAM**: *IS481* gene **HEX:** Human (IC-Internal Control)	1 x 125 µL	1 x 500 µL
Bor 2 Oligo Mix	**FAM:** h*IS1001* gene **ROX:** *IS1001* gene **CY5:** *ptxP* gene	1 x 125 µL	1 x 500 µL
NTC	Negative Control	1 x 1000 µL	1 x 1000 µL
PC-Bor 1 / PC-Bor 2	Positive Control (PC)	1 x 100 µL	1 x 100 µL

Table 2. Transport Condition, Storage Condition, and Shelf Life of the Components

Component	Transport Condition	Storage Condition*	Shelf Life
2X qPCR Mix	(-22) °C – (+8) °C	(-22) °C – (-18) °C	12 Months
Oligo Mix		(-22) °C – (-18) °C	
NTC		(-22) °C – (-18) °C before opening, (+2) °C – (+8) °C after first thaw	
PC		(-22) °C – (-18) °C before opening, (+2) °C – (+8) °C after first thaw	

* Following the first opening, each reagent stored at storage temperature can be used until the expiration date indicated on the tube. The kit's expiration date is determined by the expiration date of the reagents.

Table 3. Required Components Not Included in the Package

Required Components Not Included in the Package
1. Real-Time PCR Instrument
2. ***v*NAT® Transfer Tube** (Cat. No: BS-NA-513m-100) or nucleic acid preparation instruments and nucleic acid preparation consumables
3. Micropipettes and compatible filtered pipette tips (nuclease-free) suitable for transferring 1-10 µL, 10-100 µL, and 100-1000 µL of liquid
4. A centrifuge or Mini-spin
5. Vortex
6. Reaction tubes,PCR strips, PCR plates and caps/films specific to qPCR instruments and compatible with the reaction volume

Table 4. Intended Use, Test Principle, and Analytical Specifications

Function	Aid to diagnosis	**Sample Type(s)**	**Table 5**
Analyte(s)	**Table 1**	**Nucleic Acid Extraction Method(s)**	***v*NAT® Transfer Tube** Zybio EXM3000 Nucleic Acid Isolation System Adaltis EXTRAlab and MDXlab
Qualitative/Quantitative	Qualitative	**Validated qPCR Instrument(s)**	Bio Molecular Systems: Magnetic Induction Cycler (Mic)/Mic IVD Bio-Rad: CFX96 Touch/Dx, CFX Opus 96/Dx, CFX384 Touch, CFX Opus 384 Qiagen: Rotor-Gene Q 5-Plex/MDx Roche: LightCycler 96 Thermo Fisher Scientific: QuantStudio 5/5 Dx/6/7/12k Flex/Pro, StepOne Plus, Applied Biosystems 7500/7500 Fast Adaltis: AmpliLab, MDXlab HiMedia: InstaQ 96 Bioer: Linegene 9600 Plus Atila Biosystems: Fujirebio Co-Dx: Co-Dx Box Tianlong: Gentier 96E Sansure: SLAN-96P Azure: Cielo
Test Principle	Real-Time PCR (qPCR)	**Inclusivity and Exclusivity**	Validated on the reference strains and the field isolates
Automated/Manual	Manual		
Intended Users	Laboratory professionals trained in the techniques of qPCR and in vitro diagnostic procedures	**Limit of Detection (LoD)**	**Table 5**
Target Population	Individuals with the suspected infection	**Sensitivity and Specificity**	98.8% and 100.00%

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Table 5. Collection, Storage, and Transfer of Clinical Specimens / Nucleic Acid Preparation Methods

Sample Type**	Sample Transfer	Sample Storage	Nucleic Acid Preparation Method	LoD (cp/mL)
Combined nasopharyngeal and oropharyngeal swabs***	**vNAT® Transfer Tube** (Cat. No: BS-NA-513m-100)	3 months at (+2) °C – (+8) °C 1 year at (-20) °C	Nucleic acid preparation is not needed, samples can be used directly in qPCR	250
	Viral Transport Medium (VTM) (CDC SOP#: DSR-052-05 without antibiotics)	3 days at (+2) °C – (+8) °C 1 year at (-20) °C	**Nucleic acid preparation instruments:** 1) Zybio EXM3000, 2) Adaltis EXTRAlab, 3) Adaltis MDXlab **Nucleic acid preparation consumables:** Bio-Speedy® Rapid Nucleic Acid Extraction Kit (Cat. No: ZFNAE01)	125
Bronchoalveolar lavage, nasopharyngeal aspirate, and sputum	Preservative-free sterile containers	3 days at (+2) °C – (+8) °C 1 year at (-20) °C		500

** Clinical specimens should be collected by a healthcare provider in accordance with national/international clinical specimen collection regulations.
*** If dry swab samples are received, put them into the **vNAT® Transfer Tube** for nucleic acid isolation.

1. APPLICATION PROTOCOL

1. Program the qPCR device using the QR Code/Link as indicated in **Table 6**.
2. Take the PCR kit out of the -20°C freezer.
3. Pipette (Sample Count + 3) *5 µL of Bor Oligo Mix 1 into an empty eppendorf tube. (i.e Sample Count = 3, pipette 5*(3+3) = 30 µL of Bor Oligo Mix 1)
4. Add (Sample Count + 3) *10 µL of 2X qPCR Mix into the tube prepared in Step 3. (i.e Sample Count = 3, pipette 10*(3+3) = 60 µL of 2X qPCR Mix)
5. Vortex the master mix to homogenize.
6. Repeat steps 3,4 and 5 for all master mixes. (Total 2 master mixes).
7. Pipette 15 µL of master mix into all PCR tubes, or wells to be used (including all samples, NTC and PC).
8. Pipette 5 µL of each isolated/ extracted sample into the relative PCR tube, or well.
9. Pipette 5 µL of NTC into the Negative Control PCR tube, or well.
10. Pipette 5 µL of PC-Bor 1 into the Positive Control tubes, or wells. Repeat for all PC.
11. Close the cap of the strips, or PCR tubes or seal PCR plate. Label to avoid confusion during spin -centrifuge.
12. Spin-centrifuge the strips, or PCR tubes or PCR plate.
13. Open the lid of the instrument. Place the strips, or PCR tubes or PCR plate.
14. Close the lid and start the instrument.

Table 6. Real Time qPCR Program Details

Reaction Setup		RT-qPCR Program							
		Protocol 1: Bio Molecular Systems: Magnetic Induction Cycler (Mic)/Mic IVD, Bio-Rad: CFX96 Touch/Dx, CFX Opus 96/Dx, CFX384 Touch, CFX Opus 384, Roche: LightCycler 96, Co-Dx: Co-Dx Box, Azure: Cielo				**Protocol 2:** Qiagen: Rotor-Gene Q 5-Plex/MDx, Thermo Fisher Scientific: QuantStudio 5/5 Dx/6/7/12k Flex/Pro, StepOne Plus, Applied Biosystems 7500/7500 Fast, Adaltis: AmpliLab, MDXlab, HiMedia: InstaQ 96, Bioer: Linegene 9600 Plus, Atila Biosystems: Fujirebio, Tianlong: Gentier 96E, Sansure: SLAN-96P			
Reagent	**Volume/ Rxn**	**Step**	**Cycle No.**	**Temperature**	**Duration**	**Step**	**Cycle No.**	**Temperature**	**Duration**
2X qPCR Mix	10 µL	**Enzyme Activation**	1 Cycle	52 °C	3 min	**Enzyme Activation**	1 Cycle	52 °C	3 min
		Pre-Incubation	1 Cycle	95 °C	10 sec	**Pre-Incubation**	1 Cycle	95 °C	10 sec
Oligo Mix	5 µL	**Denaturation**	12 Touchdown Cycles: 1 °C decrement in annealing temperature per cycle	95 °C	1 sec	**Denaturation**	40 Cycles	95 °C	1 sec
		Annealing and Extension		67 °C to 56 °C	15 sec	**Annealing and Extension**		55 °C	15 sec
Template Nucleic Acid/NTC/PC	5 µL	**Denaturation**	30 Cycles	95 °C	1 sec	**Detection (Reading)**		FAM/HEX/ROX/CY5	
		Annealing and Extension		55 °C	15 sec				
Total Reaction Volume	**20 µL**	**Detection (Reading)**		FAM/HEX/ROX/CY5					

WARNING: The qPCR program file should be downloaded from the QR code on the left or from the link below.

https://www.bioeksen.com.tr/files/L_TD_43B

2. INTERPRETATION OF THE ASSAY RESULTS

Cq values of the results obtained from PCR instruments indicated in **Table 7** are calculated referring to the relative RFU threshold levels and Cq cut-offs. Auto-threshold and default options are used for devices not included in **Table 7**. For all targets that do not exceed the Cq cut-off, the shape of the amplification curve must be analyzed, and Cq values of the sigmoidal curves must be determined. Non-sigmoidal curves must be reported as "negative". The PCR results can be reported manually, as indicated in **Table 8**, or using the "**Sigmoida**" software for BMS Magnetic Induction Cycler (Mic)/Mic IVD and Bio-Rad CFX instruments. Sigmoida software sorts each target as positive or negative. To obtain the "**Sigmoida**" software installer, please send an e-mail to support@bioeksen.com.tr.

Table 7. Threshold Levels for Calculating Cq Values

Analyte	Real Time PCR Instrument											
	Bio-Rad CFX		Cielo		LightCycler 96		Mic/Mic IVD and Co-Dx Box		Rotor-Gene Q****		QuantStudio 5/5 Dx/6/7/12k Flex/Pro	
	RFU	Cq Cut-off	RFU	Cq Cut-off	RFU	Cq Cut-off	RFU	Cq Cut-off	RFU	Cq Cut-off	RFU	Cq Cut-off
***IS481* gene**	200	30	20000	30	0.05	30	0.2	30	0.02	40	20000	30

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Human (IC-Internal Control)	200	30	20000	30	0.05	30	0.2	30	0.02	40	20000	30
***hIS1001* gene**	200	30	20000	30	0.05	30	0.2	30	0.02	40	20000	30
***IS1001* gene**	200	30	20000	30	0.05	30	0.2	30	0.02	40	20000	30
***ptxP* gene**	200	30	20000	30	0.05	30	0.2	30	0.02	40	20000	30

**** Defined threshold with specific settings of "Outlier Removal = 0", "Dynamic Tube = On", and "Slope Correct = Off"

Table 8. Interpretation of Patient Results

Target	**Internal Control (IC)**	**Result Interpretation**		
Positive (+)	**Positive (+)** or **Negative (-)**	Results are valid Target is detected	**Protocol 1**	If 26<Cq ≤30 "Low Positive" If 16<Cq≤26 "Positive" If Cq≤16 "High Positive"
			Protocol 2	If 34<Cq ≤40 "Low Positive" If 22<Cq≤34 "Positive" If Cq≤22 "High Positive"
Negative (-)	**Positive (+)**	Results are valid Target is not detected		
Target	**Results Interpretation**	**Action**		
Bordetella pertussis	*IS481* and *ptxP* should be positive	Report as *Bordetella pertussis* **POSITIVE**		
Bordetella parapertussis	*IS1001* should be positive	Report as *Bordetella parapertussis* **POSITIVE**		
Bordetella holmesii	*IS481* and h*IS1001* should be positive	Report as *Bordetella pholmesi* **POSITIVE**		
Bordetella branchiseptica	*IS1001* and *IS481* should be positive*	Report *as Bordetella bronchiseptica* **POSITIVE**		

Cq values should be examined. If the condition for the Cq values "IS481<IS1001" is met, the result should be reported as Bordetella bronchiseptica. Otherwise, it should be reported as Bordetella parapertussis.

Table 9. Expected Performance of Kit Controls

Control Type	**Purpose**	**Expected Results and Cq Values**			
		Protocol 1		**Protocol 2**	
		IC (HEX)	**Target**	**IC (HEX)**	**Target**
Negative Control	Contamination control during qPCR	**Not Detected**	**Not Detected**	**Not Detected**	**Not Detected**
Positive Control	Reagent stability control	**Detected** (Cq≤30)	**Detected** (Cq≤30)	**Detected** (Cq≤40)	**Detected** (Cq≤40)
Internal Control	Nucleic acid extraction and sampling control	**Detected**	Detection insignificant	**Detected**	Detection insignificant
		If "**Not Detected**" check the target Cq	If "**Detected"** IC is valid	If "**Not Detected**" check the target Cq	If "**Detected"** IC is valid

If a control does not work as expected (**Table 9**), apply the procedures described below.

1. **Contamination Problem:** If a target in the Negative Control reaction is "**Detected**".
   Recommended action: Repeat the run, paying attention to the "Warnings and Limitations" section.

2. **Invalid Internal Control Problem:** If the Internal Control (IC) and all other targets of a sample are "**Not Detected**".
   Recommended action: Sampling was not successfully done, or there was a problem during the sample transportation or extraction. Re-test the sample. If the problem repeats, a new sample from the same patient should be collected and tested again.

3. **Reagent Problem**: If all Internal Controls, Positive Controls and targets in the run are "**Not Detected**".
   Recommended action: The run is considered invalid. Re-test the PC. If the problem repeats, please reach out to the manufacturer for further assistance.

3. WARNINGS AND LIMITATIONS

1. False-negative results may occur if inadequate number (below the LoD) of organisms are present in the specimen.
2. Mutations within the target regions could affect primer and/or probe binding, resulting in failure to detect the presence of agents.
3. The use of swabs with wooden sticks, cotton or calcium alginate swabs can lead to false negative results since they may contain substances that inactivate some pathogens and inhibit PCR.
4. False-negative results may occur if a specimen is improperly collected, transported, or handled.
5. The clinical specimens shall be collected by a healthcare provider in accordance with the national/international specimen collection guidelines.
6. Test procedures should be performed by personnel trained in the use of the kit.
7. Sample tubes should always be kept closed except for liquid transfers.
8. Filtered and nuclease-free pipette tips should be used for sample transfer.
9. The components in the kit should not be used together with different LOT numbers or chemicals of the same name but from different manufacturers.
10. ***The caps of the reaction tubes must not be opened after the PCR run.*** The PCR tubes should be placed in a bag and thrown away after the bag is tightly closed.
11. The surfaces of the workbenches should be wiped with freshly diluted 10% bleach (0.5% NaClO) at the beginning and end of each day.
12. Waste disposal must be carried out in accordance with local, state, and federal regulations.
13. Proper personal protective equipment including lab coats, gowns, gloves, eye protection, and a biological safety cabinet are recommended for manipulation of clinical specimens.
14. Immediately clean up any spill containing potentially infectious material with 0.5-1% (w/v) sodium hypochlorite (10-20% v/v bleach). Dispose of cleaning materials in a biohazard waste stockpot.
15. The micropipettes used for pipetting PCR mixes and template nucleic acids should be separate. Filtered and nuclease-free pipette tips should be used.
16. Maintenance/ calibration interval should be determined for all instruments and equipment used with the kit.

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For professional use only.

4. EXPLANATION OF SYMBOL

Symbol	Title of Symbol	Symbol	Title of Symbol	Symbol	Title of Symbol
CE	European Conformity CE Mark	LOT	Batch code		Keep away from sunlight
IVD	*In vitro* diagnostic *medical device*	REF	Catalogue number		Protect from heat and radioactive sources
	Manufacturer	NON STERILE	Non-sterile		Do not use if package is damaged and consult *Instructions for Use*
	Expiration Date YYYY-MM		Consult *Instructions for Use* or consult electronic *Instructions for Use*		Keep dry
CONTROL -	Negative Control		Caution		Keep upright
CONTROL +	Positive Control		Temperature limit	Σ	Contains sufficient for <*n*> tests
CONTROL	Control				

5. MANUFACTURER AND TECHNICAL SUPPORT

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Notice to User: Please inform us about product-related incidents at "**vigilance@bioeksen.com.tr**" within 24 hours.

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Cat No: BS-HEV-DTC-304-25/BS-HEV-DTC-304-100
Ordering Ref No: ENT-T-25/ENT-T-100

Human Enterovirus (HEV) qPCR Detection Kit

Package Insert

Table 1. Kit Content

Component	Intended Use	25 Reactions	100 Reactions
2X Prime Script Mix	Optimized ready-to-use mix for RT-qPCR assay	1 x 125 µL	1 x 500 µL
HEV Oligo Mix	Specific nucleic acid amplification and detection: **FAM**: Human Enterovirus **HEX:** Human (IC-Internal Control)	1 x 62,5 µL	1 x 250 µL
NTC	Negative Control	1 x 1000 µL	1 x 1000 µL
PC-HEV	Positive Control (PC)	1 x 100 µL	1 x 100 µL

Table 2. Transport Condition, Storage Condition, and Shelf Life of the Components

Component	Transport Condition	Storage Condition*	Shelf Life
2X Prime Script Mix	(-22) °C – (+8) °C	(-22) °C – (-18) °C	12 Months
Oligo Mix		(-22) °C – (-18) °C	
NTC		(-22) °C – (-18) °C before opening, (+2) °C – (+8) °C after first thaw	
PC		(-22) °C – (-18) °C before opening, (+2) °C – (+8) °C after first thaw	

* Following the first opening, each reagent stored at storage temperature can be used until the expiration date indicated on the tube. The kit's expiration date is determined by the expiration date of the reagents.

Table 3. Required Components Not Included in the Package

Required Components Not Included in the Package
1. Real-Time PCR Instrument
2. Bioeksen **vNAT® Transfer Tube** (Cat. No: BS-NA-513m) or nucleic acid preparation instruments and nucleic acid preparation consumables
3. Micropipettes and compatible filtered pipette tips (nuclease-free) suitable for transferring 1-10 µL, 10-100 µL, and 100-1000 µL of liquid
4. A centrifuge or Mini-spin
5. Vortex
6. Reaction tubes,PCR strips, PCR plates and caps/films specific to qPCR instruments and compatible with the reaction volume

Table 4. Intended Use, Test Principle, and Analytical Specifications

Function	Aid to diagnosis	**Sample Type(s)**	**Table 5**
Analyte(s)	**Table 1**	**Nucleic Acid Extraction Method(s)**	Bioeksen **vNAT® Transfer Tube** Zybio EXM3000 Nucleic Acid Isolation System Adaltis EXTRAlab and MDXlab
Qualitative/Quantitative	Qualitative	**Validated qPCR Instrument(s)**	Bio Molecular Systems: Magnetic Induction Cycler (Mic)/Mic IVD Bio-Rad: CFX96 Touch/Dx, CFX Opus 96/Dx, CFX384 Touch, CFX Opus 384 Qiagen: Rotor-Gene Q 5-Plex/MDx Roche: LightCycler 96 Thermo Fisher Scientific: QuantStudio 5/5 Dx/6/7/12k Flex/Pro, StepOne Plus, Applied Biosystems 7500/7500 Fast Adaltis: AmpliLab, MDXlab HiMedia: InstaQ 96 Bioer: Linegene 9600 Plus Atila Biosystems: Fujirebio Co-Dx: Co-Dx Box Tianlong: Gentier 96E Sansure: SLAN-96P Azure: Cielo
Test Principle	Reverse Transcription and Real-Time PCR (RT-qPCR)	**Inclusivity and Exclusivity**	Validated on the reference strains and the field isolates
Automated/Manual	Manual		
Intended Users	Laboratory professionals trained in the techniques of qPCR and in vitro diagnostic procedures.	**Limit of Detection (LoD)**	**Table 5**
Target Population	Individuals with the suspected infection	**Sensitivity and Specificity**	100.00% and 100.00%

Table 5. Collection, Storage, and Transfer of Clinical Specimens / Nucleic Acid Preparation Methods

Sample Type**	Sample Transfer	Sample Storage	Nucleic Acid Preparation Method	LoD (cp/mL)
Combined nasopharyngeal and oropharyngeal swab***	**vNAT® Transfer Tube** (Cat. No: BS-NA-513m)	3 months at (+2) °C – (+8) °C 1 year at (-20) °C	Nucleic acid extraction is not needed. The samples can be used directly in RT-qPCR.	250
	Viral Transport Medium (VTM) (CDC SOP#: DSR-052-05)	3 days at (+2) °C – (+8) °C 1 year at (-20) °C	**Nucleic acid preparation instruments:** 1) Zybio EXM3000, 2) Adaltis EXTRAlab, 3) Adaltis MDXlab	125

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Bronchoalveolar lavage, nasopharyngeal aspirate, and sputum	Preservative-free sterile containers/tubes	3 days at (+2) – (+8) °C 1 year at (-20) °C	**Nucleic acid preparation consumables:** Bioeksen Bio-Speedy® Rapid Nucleic Acid Extraction Kit (Cat. No: ZFNAE01)	500

**Clinical specimens should be collected by a healthcare provider in accordance with national/international clinical specimen collection regulations.
*** If dry swab samples are received, put them into the ***v*NAT® Transfer Tube** for nucleic acid isolation

1. APPLICATION PROTOCOL

1. Program the qPCR device using the QR Code/Link as indicated in **Table 6.**
2. Take the PCR kit out of the -20°C freezer.
3. Pipette (Sample Count + 3) *2,5 µL of HEV Oligo Mix into an empty eppendorf tube. (i.e Sample Count = 3, pipette 2,5*(3+3) = 15 µL of HEV Oligo Mix)
4. Add (Sample Count + 3) *5 µL of 2X Prime Script Mix into the tube prepared in Step 3. (i.e Sample Count = 3, pipette 5*(3+3) = 30 µL of 2X Prime Script Mix)
5. Vortex the master mix to homogenize.
6. Pipette 7,5 µL of master mix into all PCR tubes, or wells to be used (including all samples, NTC and PC).
7. Pipette 2,5 µL of each isolated/ extracted sample into the relative PCR tube, or well.
8. Pipette 2,5 µL of NTC into the Negative Control PCR tube, or well.
9. Pipette 2,5 µL of PC-HEV into the Positive Control tubes, or wells.
10. Close the cap of the strips, or PCR tubes or seal PCR plate. Label to avoid confusion during spin -centrifuge.
11. Spin-centrifuge the strips, or PCR tubes or PCR plate.
12. Open the lid of the instrument. Place the strips, PCR tubes or PCR plate.
13. Close the lid and start the instrument.

Table 6. Real-Time qPCR Program Details

Reaction Setup		RT-qPCR Program							
		Protocol 1: Bio Molecular Systems: Magnetic Induction Cycler (Mic)/Mic IVD, Bio-Rad: CFX96 Touch/Dx, CFX Opus 96/Dx, CFX384 Touch, CFX Opus 384, Roche: LightCycler 96, Co-Dx: Co-Dx Box, Azure: Cielo				**Protocol 2:** Qiagen: Rotor-Gene Q 5-Plex/MDx, Thermo Fisher Scientific: QuantStudio 5/5 Dx/6/7/12k Flex/Pro, StepOne Plus, Applied Biosystems 7500/7500 Fast, Adaltis: AmpliLab, MDXlab, HiMedia: InstaQ 96, Bioer: Linegene 9600 Plus, Atila Biosystems: FujirebioTianlong: Gentier 96E, Sansure: SLAN-96P			
Reagent	**Volume/ Rxn**	**Step**	**Cycle No.**	**Temperature**	**Duration**	**Step**	**Cycle No.**	**Temperature**	**Duration**
2X Prime Script Mix	5 µL	**Reverse Transcription**	1 Cycle	52 °C	3 min	**Reverse Transcription**	1 Cycle	52 °C	3 min
		Pre-Incubation	1 Cycle	95 °C	10 sec	**Pre-Incubation**	1 Cycle	95 °C	10 sec
Oligo Mix	2,5 µL	**Denaturation**	12 Touchdown Cycles: 1 °C decrement in annealing temperature per cycle	95 °C	1 sec	**Denaturation**	40 Cycles	95 °C	1 sec
		Annealing and Extension		67 °C to 56 °C	15 sec	**Annealing and Extension**		55 °C	15 sec
Template Nucleic Acid/NTC/PC	2,5 µL	**Denaturation**	30 Cycles	95 °C	1 sec	**Detection (Reading)**		FAM/HEX	
		Annealing and Extension		55 °C	15 sec				
Total Reaction Volume	**10 µL**	**Detection (Reading)**		FAM/HEX					

WARNING: The qPCR program file should be downloaded from the QR code on the left or from the link below.

https://www.bioeksen.com.tr/files/L_TD_43B

2. INTERPRETATION OF THE ASSAY RESULTS

Cq values of the results obtained from PCR instruments indicated in **Table 7** are calculated referring to the relative RFU threshold levels and Cq cut-offs. Auto-threshold and default options are used for devices not included in **Table 7**. For all targets that do not exceed the Cq cut-off, the shape of the amplification curve must be analyzed, and Cq values of the sigmoidal curves must be determined. Non-sigmoidal curves must be reported as "negative". The PCR results can be reported manually, as indicated in **Table 8**, or using the "**Sigmoida**" software for BMS Magnetic Induction Cycler (Mic)/Mic IVD and Bio-Rad CFX instruments. Sigmoida software sorts each target as positive or negative. To obtain the "**Sigmoida**" software installer, please send an e-mail to support@bioeksen.com.tr.

Table 7. Threshold Levels and Cq Cut-offs for Calculating Cq Values

Analyte	Real Time PCR Instrument											
	Bio-Rad CFX		Cielo		LightCycler 96		Mic/Mic IVD and Co-Dx Box		Rotor-Gene Q****		QuantStudio 5/5 Dx/6/7/12k Flex/Pro	
	RFU	Cq Cut-off	RFU	Cq Cut-off	RFU	Cq Cut-off	RFU	Cq Cut-off	RFU	Cq Cut-off	RFU	Cq Cut-off
Human (IC-Internal Control)	200	30	20000	30	0.05	30	0.2	30	0.02	40	20000	30
Human Enterovirus	200	30	20000	30	0.05	30	0.2	30	0.02	40	20000	30

**** Defined threshold with specific settings of "Outlier Removal = 0", "Dynamic Tube = On", and "Slope Correct = Off"

Table 8. Interpretation of Patient Results

Target	Internal Control (IC)	Result Interpretation		
Positive (+)	**Positive (+)** or **Negative (-)**	Results are valid Target is detected	**Protocol 1**	If 26<Cq ≤30 "Low Positive" If 16<Cq≤26 "Positive" If Cq≤16 "High Positive"

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			Protocol 2	If 34<Cq ≤40 "Low Positive" If 22<Cq≤34 "Positive" If Cq≤22 "High Positive"
Negative (-)	**Positive (+)**	Results are valid Target is not detected		

Table 9. Expected Performance of Kit Controls

Control Type	Purpose	Expected Results and Cq Values			
		Protocol 1		Protocol 2	
		IC (HEX)	Target	IC (HEX)	Target
Negative Control	Contamination control during RT-qPCR	**Not Detected**	**Not Detected**	**Not Detected**	**Not Detected**
Positive Control	Reagent stability control	**Detected** (Cq≤30)	**Detected** (Cq≤30)	**Detected** (Cq≤40)	**Detected** (Cq≤40)
Internal Control	Nucleic acid extraction and sampling control	**Detected**	Detection insignificant	**Detected**	Detection insignificant
		If "**Not Detected**" check the target Cq	If "**Detected"** IC is valid	If "**Not Detected**" check the target Cq	If "**Detected"** IC is valid

If a control does not work as expected (**Table 9**), apply the procedures described below.

1. **Contamination Problem:** If a target in the Negative Control reaction is "**Detected**".
   Recommended action: Repeat the run, paying attention to the "Warnings and Limitations" section.

2. **Invalid Internal Control Problem:** If the Internal Control (IC) and all other targets of a sample are "**Not Detected**".
   Recommended action: Sampling was not successfully done, or there was a problem during the sample transportation or extraction. Re-test the sample. If the problem repeats, a new sample from the same patient should be collected and tested again.

3. **Reagent Problem**: If all Internal Controls, Positive Controls and targets in the run are "**Not Detected**".
   Recommended action: The run is considered invalid. Re-test the PC. If the problem repeats, please reach out to the manufacturer for further assistance.

3. WARNINGS AND LIMITATIONS

1. False-negative results may occur if inadequate number (below the LoD) of organisms are present in the specimen.
2. Mutations within the target regions could affect primer and/or probe binding, resulting in failure to detect the presence of agents.
3. The use of cotton or calcium alginate swabs or swabs with wooden sticks can lead to false negative results since they may contain substances that inactivate some pathogens and inhibit PCR.
4. False-negative results may occur if a specimen is improperly collected, transported, or handled.
5. The clinical specimens shall be collected by a healthcare provider in accordance with the national/international specimen collection guidelines.
6. Test procedures should be performed by personnel trained in the use of the kit.
7. Sample tubes should always be kept closed except for liquid transfers.
8. Filtered and nuclease-free pipette tips should be used for sample transfer.
9. The components in the kit should not be used together with different LOT numbers or chemicals of the same name but from different manufacturers.
10. ***The caps of the reaction tubes must not be opened after the PCR run.*** The PCR tubes should be placed in a bag and thrown away after the bag is tightly closed.
11. The surfaces of the workbenches should be wiped with freshly diluted 10% bleach (0.5% NaClO) at the beginning and end of each day.
12. Waste disposal must be carried out in accordance with local, state, and federal regulations.
13. Proper personal protective equipment including lab coats, gowns, gloves, eye protection, and a biological safety cabinet are recommended for manipulation of clinical specimens.
14. Immediately clean up any spill containing potentially infectious material with 0.5-1% (w/v) sodium hypochlorite (10-20% v/v bleach). Dispose of cleaning materials in a biohazard waste stockpot.
15. The micropipettes used for pipetting PCR mixes and template nucleic acids should be separated. Filtered and nuclease-free pipette tips should be used.
16. Maintenance/ calibration interval should be determined for all instruments and equipment used with the kit.

4. EXPLANATION OF SYMBOL

Symbol	Title of Symbol	Symbol	Title of Symbol	Symbol	Title of Symbol
CE	European Conformity CE Mark	LOT	Batch code		Keep away from sunlight
IVD	*In vitro* diagnostic *medical device*	REF	Catalogue number		Protect from heat and radioactive sources
	Manufacturer	NON STERILE	Non-*sterile*		Do not use if package is damaged and consult I*nstructions for Use*
	Expiration Date YYYY-MM		Consult I*nstructions for Use* or consult electronic I*nstructions for Use*		Keep dry
CONTROL -	Negative Control		Caution		Keep upright
CONTROL +	Positive Control		Temperature limit	Σ	Contains sufficient for *<n>* tests
CONTROL	Control				

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5. MANUFACTURER AND TECHNICAL SUPPORT

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Cat No: BS-DTC-V-224-25/BS-DTC-V-224-100
Ordering Ref No: ANTX-T-25/ANTX-T-100

Bacillus anthracis Real-Time PCR Detection Kit

Package Insert

Table 1. Kit Content

Component	Intended Use	25 Reactions	100 Reactions
2X qPCR Mix	Optimized ready-to-use mix for qPCR assay	1 x 125 µL	1 x 500 µL
BA Oligo Mix	Specific nucleic acid amplification and detection: **FAM:** *Bacillus anthracis* **HEX:** Human (IC-Internal Control)	1 x 62,5 µL	1 x 250 µL
PC-BA	Positive Control (PC)	1 x 100 µL	1 x 100 µL
NTC	Negative (No Template) Control	1 x 1000 µL	1 x 1000 µL

Table 2. Transport Condition, Storage Condition, and Shelf Life of the Components

Component	Transport Condition	Storage Condition*	Shelf Life
2X qPCR Mix	(-22) °C – (+8) °C	(-22) °C – (-18) °C	12 Months
Oligo Mix		(-22) °C – (-18) °C	
NTC		(-22) °C – (-18) °C before opening, (+2) °C – (+8) °C after first thaw	
PC		(-22) °C – (-18) °C before opening, (+2) °C – (+8) °C after first thaw	

* Following the first opening, each reagent stored at storage temperature can be used until the expiration date indicated on the tube. The kit's expiration date is determined by the expiration date of the reagents.

Table 3. Required Components Not Included in the Package

Required Components Not Included in the Package
1. Real-Time PCR Instrument
2. Nucleic acid preparation instruments and nucleic acid preparation consumables
3. Micropipettes and compatible filtered pipette tips (nuclease-free) suitable for transferring 1-10 µL, 10-100 µL, and 100-1000 µL of liquid
4. A centrifuge or Mini-spin
5. Vortex
6. Reaction tubes,PCR strips, PCR plates and caps/films specific to qPCR instruments and compatible with the reaction volume

Table 4. Intended Use, Test Principle, and Analytical Specifications

Function	Aid to diagnosis	**Sample Type(s)**	**Table 5**
Analyte(s)	**Table 1**	**Nucleic Acid Extraction Method(s)**	Zybio EXM3000 Nucleic Acid Isolation System Adaltis EXTRAlab and MDXlab
Qualitative/Quantitative	Qualitative	**Validated qPCR Instrument(s)**	Bio Molecular Systems: Magnetic Induction Cycler (Mic)/Mic IVD Bio-Rad: CFX96 Touch/Dx, CFX Opus 96/Dx, CFX384 Touch, CFX Opus 384 Qiagen: Rotor-Gene Q 5-Plex/MDx Roche: LightCycler 96 Thermo Fisher Scientific: QuantStudio 5/5 Dx/6/7/12k Flex/Pro, StepOne Plus, Applied Biosystems 7500/7500 Fast Adaltis: AmpliLab, MDXlab HiMedia: InstaQ 96 Bioer: Linegene 9600 Plus Atila Biosystems: Fujirebio Co-Dx: Co-Dx Box Tianlong: Gentier 96E Sansure: SLAN-96P Azure: Cielo
Test Principle	Real-Time PCR (qPCR)	**Inclusivity and Exclusivity**	Validated on the reference strains and the field isolates
Automated/Manual	Manual		
Intended Users	Professional use	**Limit of Detection (LoD)**	**Table 5**
Target Population	Individuals with the suspected infection	**Sensitivity and Specificity**	100.00% and 100.00%

Table 5. Collection, Storage, and Transfer of Clinical Specimens / Nucleic Acid Preparation Methods

Sample Type**	Sample Transfer	Sample Storage	Nucleic Acid Preparation Method	LoD (cp/mL)
Whole blood and serum	EDTA-treated tube	3 days at (+2) °C – (+8) °C 1 year at (-20) °C	**Nucleic acid preparation instruments:** 1) Zybio EXM3000, 2) Adaltis EXTRAlab **Nucleic acid preparation consumables:** Bioeksen Bio-Speedy® Rapid Nucleic Acid Extraction Kit (Cat. No: ZFNAE01)	150
Cerebrospinal Fluid (CSF) samples	Preservative-free sterile containers			

**Clinical specimens should be collected by a healthcare provider in accordance with national/international clinical specimen collection regulations.

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1. APPLICATION PROTOCOL

1. Program the qPCR device using the QR Code/Link as indicated in **Table 6.**
2. Take the PCR kit out of the -20°C freezer.
3. Pipette (Sample Count + 3) *2,5 µL of BA Oligo Mix into an empty eppendorf tube. (i.e Sample Count = 3, pipette 2,5*(3+3) = 15 µL of BA Oligo Mix)
4. Add (Sample Count + 3) *5 µL of 2X qPCR Mix into the tube prepared in Step 3. (i.e Sample Count = 3, pipette 5*(3+3) = 30 µL of 2X qPCR Mix)
5. Vortex the master mix to homogenize.
6. Pipette 7,5 µL of master mix into all PCR tubes, or wells to be used (including all samples, NTC and PC).
7. Pipette 2,5 µL of each extracted/isolated sample into the relative PCR tube, or well.
8. Pipette 2,5 µL of NTC into the Negative Control PCR tube, or well.
9. Pipette 2,5 µL of PC-BA into the Positive Control tube, or well.
10. Close the cap of the strips or PCR tubes or seal the PCR plate. Label to avoid confusion during spin-centrifuge.
11. Spin-centrifuge the strips, or PCR tubes or PCR plates.
12. Open the lid of the instrument. Place the strips, PCR tubes or PCR plate.
13. Close the lid and start the instrument.

Table 6. Real-Time qPCR Program Details

Reaction Setup		qPCR Program							
		Protocol 1: Bio Molecular Systems: Magnetic Induction Cycler (Mic)/Mic IVD, Bio-Rad: CFX96 Touch/Dx, CFX Opus 96/Dx, CFX384 Touch, CFX Opus 384, Roche: LightCycler 96, Co-Dx: Co-Dx Box, Azure: Cielo				**Protocol 2:** Qiagen: Rotor-Gene Q 5-Plex/MDx, Thermo Fisher Scientific: QuantStudio 5/5 Dx/6/7/12k Flex/Pro, StepOne Plus, Applied Biosystems 7500/7500 Fast, Adaltis: AmpliLab, MDXlab, HiMedia: InstaQ 96, Bioer: Linegene 9600 Plus, Atila Biosystems: FujirebioTianlong: Gentier 96E, Sansure: SLAN-96P			
Reagent	**Volume/ Rxn**	**Step**	**Cycle No.**	**Temperature**	**Duration**	**Step**	**Cycle No.**	**Temperature**	**Duration**
2X qPCR Mix	5 µL	**Enzyme Activation**	1 Cycle	52 °C	3 min	**Enzyme Activation**	1 Cycle	52 °C	3 min
		Pre-Incubation	1 Cycle	95 °C	10 sec	**Pre-Incubation**	1 Cycle	95 °C	10 sec
Oligo Mix	2,5 µL	**Denaturation**	12 Touchdown Cycles: 1 °C decrement in annealing temperature per cycle	95 °C	1 sec	**Denaturation**	40 Cycles	95 °C	1 sec
		Annealing and Extension		67 °C to 56 °C	15 sec	**Annealing and Extension**		55 °C	15 sec
Template Nucleic Acid/NTC/PC	2,5 µL	**Denaturation**	30 Cycles	95 °C	1 sec	**Detection (Reading)**		FAM/HEX	
		Annealing and Extension		55 °C	15 sec				
Total Reaction Volume	**10 µL**	**Detection (Reading)**		FAM/HEX					

WARNING: The qPCR program file should be downloaded from the QR code on the left or from the link below.

https://www.bioeksen.com.tr/files/L_TD_43B

2. INTERPRETATION OF THE ASSAY RESULTS

Cq values of the results obtained from PCR instruments indicated in **Table 7** are calculated referring to the relative RFU threshold levels and Cq cut-offs. Auto-threshold and default options are used for devices not included in **Table 7**. For all targets that do not exceed the Cq cut-off, the shape of the amplification curve must be analyzed, and Cq values of the sigmoidal curves must be determined. Non-sigmoidal curves must be reported as "negative". The PCR results can be reported manually, as indicated in **Table 8**, or using the "**Sigmoida**" software for BMS Magnetic Induction Cycler (Mic)/Mic IVD and Bio-Rad CFX instruments. Sigmoida software sorts each target as positive or negative. To obtain the "**Sigmoida**" software installer, please send an e-mail to support@bioeksen.com.tr.

Table 7. Threshold Levels and Cq Cut-offs for Calculating Cq Values

Analyte	Real Time PCR Instrument											
	Bio-Rad CFX		Cielo		LightCycler 96		Mic/Mic IVD and Co-Dx Box		Rotor-Gene Q***		QuantStudio 5/5 Dx/6/7/12k Flex/Pro	
	RFU	Cq Cut-off	RFU	Cq Cut-off	RFU	Cq Cut-off	RFU	Cq Cut-off	RFU	Cq Cut-off	RFU	Cq Cut-off
Human (IC-Internal Control)	200	30	20000	30	0.05	30	0.2	30	0.02	40	20000	30
Bacillus anthracis	200	30	20000	30	0.05	30	0.2	30	0.02	40	20000	30

*** Defined threshold with specific settings of "Outlier Removal = 0", "Dynamic Tube = On", and "Slope Correct = Off"

Table 8. Interpretation of Patient Results

Target	Internal Control (IC)	Result Interpretation		
Positive (+)	**Positive (+)** or **Negative (-)**	Results are valid Target is detected	**Protocol 1**	If 26<Cq ≤30 "Low Positive" If 16<Cq≤26 "Positive" If Cq≤16 "High Positive"
			Protocol 2	If 34<Cq ≤40 "Low Positive" If 22<Cq≤34 "Positive" If Cq≤22 "High Positive"
Negative (-)	**Positive (+)**	Results are valid Target is not detected		

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Table 9. Expected Performance of Kit Controls

Control Type	Purpose	Expected Results and Cq Values			
		Protocol 1		Protocol 2	
		IC (HEX)	Target	IC (HEX)	Target
Negative Control	Contamination control during qPCR	**Not Detected**	**Not Detected**	**Not Detected**	**Not Detected**
Positive Control	Reagent stability control	**Detected** (Cq≤30)	**Detected** (Cq≤30)	**Detected** (Cq≤40)	**Detected** (Cq≤40)
Internal Control	Nucleic acid extraction and sampling control	**Detected**	Detection insignificant	**Detected**	Detection insignificant
		If "**Not Detected**" check the target Cq	If "**Detected"** IC is valid	If "**Not Detected**" check the target Cq	If "**Detected"** IC is valid

If a control does not work as expected (**Table 9**), apply the procedures described below.

1. **Contamination Problem:** If a target in the Negative Control reaction is "**Detected**".
   Recommended action: Repeat the run, paying attention to the "Warnings and Limitations" section.

2. **Invalid Internal Control Problem:** If the Internal Control (IC) and all other targets of a sample are "**Not Detected**".
   Recommended action: Sampling was not successfully done, or there was a problem during the sample transportation or extraction. Re-test the sample. If the problem repeats, a new sample from the same patient should be collected and tested again.

3. **Reagent Problem**: If all Internal Controls, Positive Controls and targets in the run are "**Not Detected**".
   Recommended action: The run is considered invalid. Re-test the PC. If the problem repeats, please reach out to the manufacturer for further assistance.

3. WARNINGS AND LIMITATIONS

1. False-negative results may occur if inadequate number (below the LoD) of organisms are present in the specimen.
2. Mutations within the target regions could affect primer and/or probe binding, resulting in failure to detect the presence of agents.
3. False-negative results may occur if a specimen is improperly collected, transported, or handled.
4. The clinical specimens shall be collected by a healthcare provider in accordance with the national/international specimen collection guidelines.
5. Test procedures should be performed by personnel trained in the use of the kit.
6. Sample tubes should always be kept closed except for liquid transfers.
7. Filtered and nuclease-free pipette tips should be used for sample transfer.
8. The components in the kit should not be used together with different LOT numbers or chemicals of the same name but from different manufacturers.
9. ***The caps of the reaction tubes must not be opened after the PCR run.*** The PCR tubes should be placed in a bag and thrown away after the bag is tightly closed.
10. The surfaces of the workbenches should be wiped with freshly diluted 10% bleach (0.5% NaClO) at the beginning and end of each day.
11. Waste disposal must be carried out in accordance with local, state, and federal regulations.
12. Proper personal protective equipment including lab coats, gowns, gloves, eye protection, and a biological safety cabinet are recommended for manipulation of clinical specimens.
13. Immediately clean up any spill containing potentially infectious material with 0.5-1% (w/v) sodium hypochlorite (10-20% v/v bleach). Dispose of cleaning materials in a biohazard waste stockpot.
14. The micropipettes used for pipetting PCR mixes and template nucleic acids should be separate. Filtered and nuclease-free pipette tips should be used.
15. Maintenance/ calibration interval should be determined for all instruments and equipment used with the kit.

4. EXPLANATION OF SYMBOL

Symbol	Title of Symbol	Symbol	Title of Symbol	Symbol	Title of Symbol
CE	European Conformity CE Mark	LOT	Batch code		Keep away from sunlight
IVD	*In vitro* diagnostic *medical device*	REF	Catalogue number		Protect from heat and radioactive sources
	Manufacturer	NON STERILE	Non-*sterile*		Do not use if package is damaged and consult I*nstructions for Use*
	Expiration Date YYYY-MM		Consult I*nstructions for Use* or consult electronic I*nstructions for Use*		Keep dry
CONTROL -	Negative Control		Caution		Keep upright
CONTROL +	Positive Control		Temperature limit	Σ	Contains sufficient for *<n>* tests
CONTROL	Control				

5. MANUFACTURER AND TECHNICAL SUPPORT

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Notice to User: Please inform us about product-related incidents at " **vigilance@bioeksen.com.tr** " within 24 hours.

For in vitro diagnostic use only.
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Cat No: BS-SY-SI-100/BS-SY-SI-250/BS-SY-SI-500/BS-SY-SI-1000
Ordering Ref No: COV-FLU-T-100/COV-FLU-T-250/COV-FLU-T-500/COV-FLU-T-1000

COVID-19/Flu RT-qPCR

Package Insert

Table 1. Kit Content

Component	Intended Use	100 Reactions	250 Reactions	500 Reactions	1000 Reactions
2X Prime Script Mix	Optimized ready-to-use mix for RT-qPCR assay	1 x 1000 µL	1 x 1000 µL	2 x 1250 µL	4 x 1250 µL
CVD19/FLU Oligo Mix	**FAM**: SARS-CoV-2 **HEX:** Human (IC-Internal Control) **ROX:** Influenza B **CY5:** Influenza A	1 x 500 µL	1 x 500 µL	2 x 1250 µL	4 x 1250 µL
NTC	Negative Control	1 x 1000 µL	1 x 1000 µL	1 x 1000 µL	1 x 1000 µL
PC-CVD19/FLU	Positive Control (PC)	1 x 100 µL	1 x 250 µL	1 x 250 µL	1 x 500 µL

Table 2. Transport Condition, Storage Condition, and Shelf Life of the Components

Component	Transport Condition	Storage Condition*	Shelf Life
2X Prime Script Mix	(-22) °C – (+8) °C	(-22) °C – (-18) °C	12 Months
Oligo Mix		(-22) °C – (-18) °C	
NTC		(-22) °C – (-18) °C before opening, (+2) °C – (+8) °C after first thaw	
PC		(-22) °C – (-18) °C before opening, (+2) °C – (+8) °C after first thaw	

* Following the first opening, each reagent stored at storage temperature can be used until the expiration date indicated on the tube. The kit's expiration date is determined by the expiration date of the reagents.

Table 3. Required Components Not Included in the Package

Required Components Not Included in the Package
1. Real-Time PCR Instrument
2. Bioeksen ***v*NAT® Transfer Tube** (Cat. No: BS-NA-513m) or nucleic acid preparation instruments and nucleic acid preparation consumables
3. Micropipettes and compatible filtered pipette tips (nuclease-free) suitable for transferring 1-10 µL, 10-100 µL, and 100-1000 µL of liquid
4. A centrifuge or Mini-spin
5. Vortex
6. Reaction tubes,PCR strips, PCR plates and caps/films specific to qPCR instruments and compatible with the reaction volume

Table 4. Intended Use, Test Principle, and Analytical Specifications

Function	Aid to diagnosis	**Sample Type(s)**	**Table 5**
Analyte	**Table 1**	**Nucleic Acid Extraction Method(s)**	Bioeksen ***v*NAT® Transfer Tube** Zybio EXM3000 Nucleic Acid Isolation System Adaltis EXTRAlab and MDXlab
Qualitative/Quantitative	Qualitative	**Validated qPCR Instrument(s)**	Bio Molecular Systems: Magnetic Induction Cycler (Mic)/Mic IVD Bio-Rad: CFX96 Touch/Dx, CFX Opus 96/Dx, CFX384 Touch, CFX Opus 384 Qiagen: Rotor-Gene Q 5-Plex/MDx Roche: LightCycler 96 Thermo Fisher Scientific: QuantStudio 5/5 Dx/6/7/12k Flex/Pro, StepOne Plus, Applied Biosystems 7500/7500 Fast Adaltis: AmpliLab, MDXlab HiMedia: InstaQ 96 Bioer: Linegene 9600 Plus Atila Biosystems: Fujirebio Co-Dx: Co-Dx Box Tianlong: Gentier 96E Sansure: SLAN-96P Azure: Cielo
Test Principle	Reverse Transcription and Real-Time PCR (RT-qPCR)	**Inclusivity and Exclusivity**	Validated on the reference strains and the field isolates
Automated/Manual	Manual		
Intended Users	Laboratory professionals trained in the techniques of qPCR and in vitro diagnostic procedures.	**Limit of Detection (LoD)**	**Table 5**
Target Population	Individuals with the suspected infection	**Sensitivity and Specificity**	%100.00 ve %100.00

Table 5. Collection, Storage, and Transfer of Clinical Specimens / Nucleic Acid Preparation Methods

Sample Type**	Sample Transfer	Sample Storage	Nucleic Acid Preparation Method	LoD (cp/mL)
Combined nasopharyngeal, and oropharyngeal swabs***	***v*NAT® Transfer Tube** (Cat. No: BS-NA-513m)	3 months at (+2) °C – (+8) °C 1 year at (-20) °C	Nucleic acid preparation is not required. The sample can be used directly in qPCR.	250
	Viral Transport Medium (VTM) (CDC SOP#: DSR-052-05)	3 days at (+2) °C – (+8) °C 1 year at (-20) °C	**Nucleic acid preparation instruments:** 1) Zybio EXM3000, 2) Adaltis EXTRAlab, 3) Adaltis MDXlab	125
Bronchoalveolar lavage (BAL) and nasopharyngeal aspirate	Preservative-free sterile containers/tubes	3 days at (+2) °C – (+8) °C 1 year at (-20) °C	**Nucleic acid preparation consumables:** Bioeksen Bio-Speedy® Rapid Nucleic Acid Extraction Kit (Cat. No: ZFNAE01)	500

**Clinical specimens should be collected by a healthcare provider in accordance with national/international clinical specimen collection regulations.
*** If dry swab samples are received, put them into the ***v*NAT® Transfer Tube** for nucleic acid isolation.

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1. APPLICATION PROTOCOL

1. Program the qPCR device using the QR Code/Link as indicated in **Table 6.**
2. Take the PCR kit out of the -20°C freezer.
3. Pipette (Sample Count + 3) *5 µL of CVD19/FLU Oligo Mix into an empty eppendorf tube. (i.e Sample Count = 3, pipette 5*(3+3) = 30 µL of CVD19/FLU Oligo Mix)
4. Add (Sample Count + 3) *10 µL of 2X Prime Script Mix into the tube prepared in Step 3. (i.e Sample Count = 3, pipette 10*(3+3) = 60 µL of 2X Prime Script Mix)
5. Vortex the master mix to homogenize.
6. Pipette 15 µL of master mix into all PCR tubes, or wells to be used (including all samples, NTC and PC).
7. Pipette 5 µL of each extracted/isolated sample into the relative PCR tube, or well.
8. Pipette 5 µL of NTC into the Negative Control PCR tube, or well.
9. Pipette 5 µL of PC-CVD19/FLU into the Positive Control tube, or well.
10. Close the cap of the strips or PCR tubes or seal the PCR plate. Label to avoid confusion during spin-centrifuge.
11. Spin-centrifuge the strips, or PCR tubes or PCR plate.
12. Open the lid of the instrument. Place the strips, or PCR tubes or PCR plate.
13. Close the lid and start the instrument.

Table 6. Real-Time qPCR Program Details

Reaction Setup		RT-qPCR Program							
		Protocol 1: Bio Molecular Systems: Magnetic Induction Cycler (Mic)/Mic IVD, Bio-Rad: CFX96 Touch/Dx, CFX Opus 96/Dx, CFX384 Touch, CFX Opus 384, Roche: LightCycler 96, Co-Dx: Co-Dx Box, Azure: Cielo				**Protocol 2:** Qiagen: Rotor-Gene Q 5-Plex/MDx, Thermo Fisher Scientific: QuantStudio 5/5 Dx/6/7/12k Flex/Pro, StepOne Plus, Applied Biosystems 7500/7500 Fast, Adaltis: AmpliLab, MDXlab, HiMedia: InstaQ 96, Bioer: Linegene 9600 Plus, Atila Biosystems: FujirebioTianlong: Gentier 96E, Sansure: SLAN-96P			
Reagent	**Volume/ Rxn**	**Step**	**Cycle No.**	**Temperature**	**Duration**	**Step**	**Cycle No.**	**Temperature**	**Duration**
2X Prime Script Mix	10 µL	**Reverse Transcription**	1 Cycle	52 °C	3 min	**Reverse Transcription**	1 Cycle	52 °C	3 min
		Pre-Incubation	1 Cycle	95 °C	10 sec	**Pre-Incubation**	1 Cycle	95 °C	10 sec
Oligo Mix	5 µL	**Denaturation**	12 Touchdown Cycles: 1 °C decrement in annealing temperature per cycle	95 °C	1 sec	**Denaturation**	40 Cycles	95 °C	1 sec
		Annealing and Extension		67 °C to 56 °C	15 sec	**Annealing and Extension**		55 °C	15 sec
Template Nucleic Acid/NTC/PC	5 µL	**Denaturation**	30 Cycles	95 °C	1 sec	**Detection (Reading)**		FAM/HEX/ROX/CY5	
		Annealing and Extension		55 °C	15 sec				
Total Reaction Volume	**20 µL**	**Detection (Reading)**		FAM/HEX/ROX/CY5					

WARNING: The qPCR program file should be downloaded from the QR code on the left or from the link below.

https://www.bioeksen.com.tr/files/L_TD_43B

2. INTERPRETATION OF THE ASSAY RESULTS

Cq values of the results obtained from PCR instruments indicated in **Table 7** are calculated referring to the relative RFU threshold levels and Cq cut-offs. Auto-threshold and default options are used for devices not included in **Table 7**. For all targets that do not exceed the Cq cut-off, the shape of the amplification curve must be analyzed, and Cq values of the sigmoidal curves must be determined. Non-sigmoidal curves must be reported as "negative". The PCR results can be reported manually, as indicated in **Table 8**, or using the "**Sigmoida**" software for BMS Magnetic Induction Cycler (Mic)/Mic IVD and Bio-Rad CFX instruments. Sigmoida software sorts each target as positive or negative. To obtain the "**Sigmoida**" software installer, please send an e-mail to support@bioeksen.com.tr.

Table 7. Threshold Levels and Cq Cut-offs for Calculating Cq Values

Analyte	Real Time PCR Instrument											
	Bio-Rad CFX		Cielo		LightCycler 96		Mic/Mic IVD and Co-Dx Box		Rotor-Gene Q****		QuantStudio 5/5 Dx/6/7/12k Flex/Pro	
	RFU	Cq Cut-off	RFU	Cq Cut-off	RFU	Cq Cut-off	RFU	Cq Cut-off	RFU	Cq Cut-off	RFU	Cq Cut-off
Human (IC-Internal Control)	200	30	20000	30	0.05	30	0.2	30	0.02	30	20000	30
SARS-CoV2	200	30	20000	30	0.05	30	0.5	30	0.02	30	20000	30
Influenza A	200	30	20000	30	0.05	30	0.5	30	0.02	30	20000	30
Influenza B	750	30	75000	30	0.1	30	0.5	30	0.05	30	20000	30

**** Defined threshold with specific settings of "Outlier Removal = 0", "Dynamic Tube = On", and "Slope Correct = Off"

Table 8. Interpretation of Patient Results

Target	Internal Control (IC)	Result Interpretation		
Positive (+)	**Positive (+)** or **Negative (-)**	Results are valid Target is detected	**Protocol 1**	If 26<Cq ≤30 "Low Positive" If 16<Cq≤26 "Positive" If Cq≤16 "High Positive"
			Protocol 2	If 34<Cq ≤40 "Low Positive" If 22<Cq≤34 "Positive" If Cq≤22 "High Positive"
Negative (-)	**Positive (+)**	Results are valid		

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		Target is not detected

Table 9. Expected Performance of Kit Controls

Control Type	Purpose	Expected Results and Cq Values			
		Protocol 1		Protocol 2	
		IC (HEX)	Target	IC (HEX)	Target
Negative Control	Contamination control during RT-qPCR	**Not Detected**	**Not Detected**	**Not Detected**	**Not Detected**
Positive Control	Reagent stability control	**Detected** (Cq≤30)	**Detected** (Cq≤30)	**Detected** (Cq≤40)	**Detected** (Cq≤40)
Internal Control	Nucleic acid extraction and sampling control	**Detected**	Detection insignificant	**Detected**	Detection insignificant
		If "**Not Detected**" check the target Cq	If "**Detected"** IC is valid	If "**Not Detected**" check the target Cq	If "**Detected"** IC is valid

If a control does not work as expected (**Table 9**), apply the procedures described below.

1. **Contamination Problem:** If a target in the Negative Control reaction is "**Detected**".
   Recommended action: Repeat the run, paying attention to the "Warnings and Limitations" section.

2. **Invalid Internal Control Problem:** If the Internal Control (IC) and all other targets of a sample are "**Not Detected**".
   Recommended action: Sampling was not successfully done, or there was a problem during the sample transportation or extraction. Re-test the sample. If the problem repeats, a new sample from the same patient should be collected and tested again.

3. **Reagent Problem**: If all Internal Controls, Positive Controls and targets in the run are "**Not Detected**".
   Recommended action: The run is considered invalid. Re-test the PC. If the problem repeats, please reach out to the manufacturer for further assistance.

3. WARNINGS AND LIMITATIONS

1. False-negative results may occur if inadequate number (below the LoD) of organisms are present in the specimen.
2. Mutations within the target regions could affect primer and/or probe binding, resulting in failure to detect the presence of agents.
3. The use of cotton or calcium alginate swabs or swabs with wooden sticks can lead to false negative results since they may contain substances that inactivate some pathogens and inhibit PCR.
4. False-negative results may occur if a specimen is improperly collected, transported, or handled.
5. The clinical specimens shall be collected by a healthcare provider in accordance with the national/international specimen collection guidelines.
6. Test procedures should be performed by personnel trained in the use of the kit.
7. Sample tubes should always be kept closed except for liquid transfers.
8. Filtered and nuclease-free pipette tips should be used for sample transfer.
9. The components in the kit should not be used together with different LOT numbers or chemicals of the same name but from different manufacturers.
10. ***The caps of the reaction tubes must not be opened after the PCR run.*** The PCR tubes should be placed in a bag and thrown away after the bag is tightly closed.
11. The surfaces of the workbenches should be wiped with freshly diluted 10% bleach (0.5% NaClO) at the beginning and end of each day.
12. Waste disposal must be carried out in accordance with local, state, and federal regulations.
13. Proper personal protective equipment including lab coats, gowns, gloves, eye protection, and a biological safety cabinet are recommended for manipulation of clinical specimens.
14. Immediately clean up any spill containing potentially infectious material with 0.5-1% (w/v) sodium hypochlorite (10-20% v/v bleach). Dispose of cleaning materials in a biohazard waste stockpot.
15. The micropipettes used for pipetting PCR mixes and template nucleic acids should be separate. Filtered and nuclease-free pipette tips should be used.
16. Maintenance/ calibration interval should be determined for all instruments and equipment used with the kit.

4. EXPLANATION OF SYMBOL

Symbol	Title of Symbol	Symbol	Title of Symbol	Symbol	Title of Symbol
CE	European Conformity CE Mark	LOT	Batch code		Keep away from sunlight
IVD	*In vitro* diagnostic *medical device*	REF	Catalogue number		Protect from heat and radioactive sources
	Manufacturer	NON STERILE	Non-*sterile*		Do not use if package is damaged and consult I*nstructions for Use*
	Expiration Date YYYY-MM		Consult I*nstructions for Use* or consult electronic I*nstructions for Use*		Keep dry
CONTROL -	Negative Control		Caution		Keep upright
CONTROL +	Positive Control		Temperature limit	Σ	Contains sufficient for *<n>* tests
CONTROL	Control				

5. MANUFACTURER AND TECHNICAL SUPPORT

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Cat No: BS-SE-MX30T-25/BS-SE-MX30T-100
Ordering Ref No: Sepsis-P1-T-25/Sepsis-P1-T-100

Sepsis qPCR MX-30T Panel

Package Insert

Table 1. Kit Content

Component	Target	25 Reactions	100 Reactions
2X qPCR Mix	Optimized ready-to-use mix for qPCR assay	2 x 1000 µL	7 x 1250 µL
SPVC Oligo Mix	**FAM :** *Staphylococcus aureus* **HEX :** *Pseudomonas* spp. **ROX:** *VanA*-Vancomycin resistance **CY5:** *Candida krusei*	1 x 125 µL	1 x 500 µL
CRVS Oligo Mix	**FAM:** *Candida glabrata* **HEX:** Human (IC-Internal Control) **ROX:** *VanB*-Vancomycin resistance **CY5:** *Staphylococcus* spp.	1 x 125 µL	1 x 500 µL
KPAC Oligo Mix	**FAM:** *Pseudomonas aeruginosa* **HEX:** *Candida albicans* **ROX:** *Klebsiella pneumoniae* **CY5:** *Acinetobacter baumannii*	1 x 125 µL	1 x 500 µL
HKOC Oligo Mix	**FAM:** *Haemophilus influenzae* **HEX:** *Klebsiella oxytoca* **ROX:** *Candida parapsilosis* **CY5:** *OXA-48*-Carbapenem resistance	1 x 125 µL	1 x 500 µL
CRE Oligo Mix	**FAM:** *KPC*-Carbapenem resistance **HEX:** *NDM*-Carbapenem resistance **ROX:** *VIM*-Carbapenem resistance **CY5:** *IMP*-Carbapenem resistance	1 x 125 µL	1 x 500 µL
LEMC Oligo Mix	**FAM:** *Listeria monocytogenes* **HEX:** *Enterococcus faecalis* **ROX:** *mecA/mecC*-Methicillin resistance **CY5:** *Candida tropicalis*	1 x 125 µL	1 x 500 µL
SES Oligo Mix	**FAM:** *Stenotrophomonas maltophilia* **ROX:** *Enterobacteriaceae* spp. **CY5:** *Streptococcus* spp.	1 x 125 µL	1 x 500 µL
ENES Oligo Mix	**FAM:** *Enterococcus faecium* **HEX:** *Escherichia coli* **ROX:** *Neisseria meningitidis* **CY5:** *Streptococcus pneumoniae*	1 x 125 µL	1 x 500 µL
NTC	Negative Control	1 x 1000 µL	1 x 1000 µL
PC-SPVC / PC-CRVS / PC-KPAC / PC-HKOC / PC-CRE / PC-LEMC / PC-SES / PC-ENES	Positive Control (PC)	1 x 100 µL	1 x 100 µL

Table 2. Transport Condition, Storage Condition and Shelf Life of The Components

Component	Transport Condition	Storage Condition*	Shelf Life
2X qPCR Mix	(-22) °C – (+8) °C	(-22) °C – (-18) °C	12 Months
Oligo Mix		(-22) °C – (-18) °C	
NTC		(-22) °C – (-18) °C before opening, (+2) °C – (+8) °C after first thaw	
PC		(-22) °C – (-18) °C before opening, (+2) °C – (+8) °C after first thaw	

* Following the first opening, each reagent stored at storage temperature can be used until the expiration date indicated on the tube. The kit's expiration date is determined by the expiration date of the reagents.

Table 3. Required Components Not Included in the Package

Required Components Not Included in the Package
1. Real-Time PCR Instrument
2. Nucleic acid preparation instruments and nucleic acid preparation consumables
3. Micropipettes and compatible filtered pipette tips (nuclease-free) suitable for transferring 1-10 µL, 10-100 µL, and 100-1000 µL of liquid
4. A centrifuge or Mini-spin
5. Vortex
6. Reaction tubes,PCR strips, PCR plates and caps/films specific to qPCR instruments and compatible with the reaction volume

Table 4. Intended Use, Test Principle, and Analytical Specifications

Function	Aid to diagnosis	**Sample Type(s)**	**Table 5**
Analyte	**Table 1**	**Nucleic Acid Extraction Method(s)**	Zybio EXM3000 Nucleic Acid Isolation System Adaltis EXTRAlab and MDXlab
Qualitative/Quantitative	Qualitative	**Validated qPCR Instrument(s)**	Bio Molecular Systems: Magnetic Induction Cycler (Mic)/Mic IVD Bio-Rad: CFX96 Touch/Dx, CFX Opus 96/Dx, CFX384 Touch, CFX Opus 384 Qiagen: Rotor-Gene Q 5-Plex/MDx Roche: LightCycler 96

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			Thermo Fisher Scientific: QuantStudio 5/5 Dx/6/7/12k Flex/Pro, StepOne Plus, Applied Biosystems 7500/7500 Fast Adaltis: AmpliLab, MDXlab HiMedia: InstaQ 96 Bioer: Linegene 9600 Plus Atila Biosystems: Fujirebio Co-Dx: Co-Dx Box Tianlong: Gentier 96E Sansure: SLAN-96P Azure: Cielo
Test Principle	Real-Time PCR (qPCR)	**Inclusivity and Exclusivity**	Validated on the reference strains and the field isolates
Automated/Manual	Manual		
Intended Users	Laboratory professionals trained in the techniques of qPCR and in vitro diagnostic procedures.	**Limit of Detection (LoD)**	**Table 5**
Target Population	Individuals with the suspected infection	**Sensitivity and Specificity**	91.69% and 98.76%

Table 5. Collection, Storage, Transfer of Clinical Specimens/ Nucleic Acid Preparation Method

Sample Type**	Sample Transfer	Sample Storage	Nucleic Acid Preparation Method	LoD (cp/mL)
Whole blood	EDTA-treated tube	3 days at (+2) °C – (+8) °C 1 year at (-20) °C	**Nucleic acid preparation instruments:** 1) Zybio EXM3000, 2) Adaltis EXTRAlab, 3) Adaltis MDXlab **Nucleic acid preparation consumables:** Bio-Speedy® Rapid Nucleic Acid Extraction Kit (Cat. No: ZFNAE01)	500-1000
Positive blood culture	Blood culture bottle	Room temperature		100-500

** Clinical specimens should be collected by a healthcare provider in accordance with national/international clinical specimen collection regulations.

1. APPLICATION PROTOCOL

1. Program the qPCR device using the QR Code/Link as indicated in **Table 6.**
2. Take the PCR kit out of the -20°C freezer.
3. Pipette (Sample Count + 3) *5 µL of SPVC Oligo Mix into an empty eppendorf tube. (i.e Sample Count = 3, pipette 5*(3+3) = 30 µL of SPVC Oligo Mix)
4. Add (Sample Count + 3) *10 µL of 2X qPCR Mix into SPVC Oligo Mix. (i.e Sample Count = 3, pipette 10*(3+3) = 60 µL of 2X qPCR Mix)
5. Vortex the master mix to homogenize.
6. Repeat Steps 3, 4 and 5 for all master mixes (8 master mixes in total).
7. Pipette 15 µL of each master mix into relative PCR tube, or wells to be used (including all samples, NTC and PC).
8. Pipette 5 µL of extracted/isolated sample into relative PCR tube, or wells.
9. Pipette 5 µL of NTC into the Negative Control PCR tube, or wells.
10. Pipette 5 µL of PC-SPVC into the PC tube, or wells. Repeat for all PC.
11. Close the cap of the strips, or PCR tubes or seal PCR plate. Label to avoid confusion during spin-centrifuge.
12. Spin-centrifuge the strips, or PCR tubes and PCR plate.
13. Open the lid of the instrument. Place the strips, or PCR tubes and PCR plate.
14. Close the lid and start the instrument.

Table 6. Real Time qPCR Program Details

Reaction Setup		qPCR Program							
		Protocol 1: Bio Molecular Systems: Magnetic Induction Cycler (Mic)/Mic IVD, Bio-Rad: CFX96 Touch/Dx, CFX Opus 96/Dx, CFX384 Touch, CFX Opus 384, Roche: LightCycler 96, Co-Dx: Co-Dx Box, Azure: Cielo				**Protocol 2:** Qiagen: Rotor-Gene Q 5-Plex/MDx, Thermo Fisher Scientific: QuantStudio 5/5 Dx/6/7/12k Flex/Pro, StepOne Plus, Applied Biosystems 7500/7500 Fast, Adaltis: AmpliLab, MDXlab, HiMedia: InstaQ 96, Bioer: Linegene 9600 Plus, Atila Biosystems: Fujirebio, Tianlong: Gentier 96E, Sansure: SLAN-96P			
Reagent	**Volume/Rxn**	**Step**	**Cycle No**	**Temperature**	**Duration**	**Step**	**Cycle No**	**Temperature**	**Duration**
2X qPCR Mix	10 µL	**Enzyme Activation**	1 Cycle	52 °C	3 min	**Enzyme Activation**	1 Cycle	52 °C	3 min
		Pre-Incubation	1 Cycle	95 °C	10 sec	**Pre-Incubation**	1 Cycle	95 °C	10 sec
Oligo Mix	5 µL	**Denaturation**	12 Touchdown Cycles: 1 °C decrement in annealing temperature per cycle	95 °C	1 sec	**Denaturation**	40 Cycles	95 °C	1 sec
		Annealing and Extension		67 °C to 56 °C	15 sec	**Annealing and Extension**		55 °C	15 sec
Template Nucleic Acid/NTC/PC	5 µL	**Denaturation**	30 Cycles	95 °C	1 sec	**Detection (Reading)**		FAM/HEX/ROX/CY5	
		Annealing and Extension		55 °C	15 sec				
Total Reaction Volume	**20 µL**	**Detection (Reading)**		FAM/HEX/ROX/CY5					

WARNING: The qPCR program file should be downloaded from the QR code on the left or from the link below.

https://www.bioeksen.com.tr/files/L_TD_43B

2. INTERPRETATION OF THE ASSAY RESULTS

Cq values of the results obtained from PCR instruments indicated in **Table 7** are calculated referring to the relative RFU threshold levels and Cq cut-offs. Auto-threshold and default options are used for devices not included in **Table 7**. For all targets that do not exceed the Cq cut-off, the shape of the amplification curve must be analyzed, and Cq values of the sigmoidal curves must be determined. Non-sigmoidal curves must be reported as "negative". The PCR results can be reported manually, as indicated in **Table 8**, or using the

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"**Sigmoida**" software for BMS Magnetic Induction Cycler (Mic)/Mic IVD and Bio-Rad CFX instruments. Sigmoida software sorts each target as positive or negative. To obtain the "**Sigmoida**" software installer, please send an e-mail to support@bioeksen.com.tr.

Table 7. Threshold Levels and Cq Cut-offs for Calculating Cq Values

Analyte	Real Time PCR Instrument											
	Bio-Rad CFX		Cielo		LightCycler 96		Mic/Mic IVD and Co-Dx Box		Rotor-Gene Q***		QuantStudio 5/5 Dx/6/7/12k Flex/Pro	
	RFU	Cq Cut-off	RFU	Cq Cut-off	RFU	Cq Cut-off	RFU	Cq Cut-off	RFU	Cq Cut-off	RFU	Cq Cut-off
Staphylococcus aureus	750	30	75000	30	0.1	30	0.5	30	0.05	40	20000	30
Pseudomonas spp.	1000	26	100000	26	0.12	26	0.75	26	0.08	34	75000	26
VanA-Vancomycin resistance	750	30	75000	30	0.1	30	0.5	30	0.05	40	20000	30
Candida krusei	1000	26	100000	26	0.12	26	0.75	26	0.08	34	75000	26
Candida glabrata	750	30	75000	30	0.1	30	0.5	30	0.05	40	20000	30
Human (IC-Internal Control)	200	30	20000	30	0.05	30	0.2	30	0.02	40	20000	30
VanB-Vancomycin resistance	750	30	75000	30	0.1	30	0.5	30	0.05	40	20000	30
Staphylococcus spp.	1000	26	100000	26	0.12	26	0.75	26	0.08	34	75000	26
Pseudomonas aeruginosa	1000	26	100000	26	0.12	26	0.75	26	0.08	34	75000	26
Candida albicans	750	30	75000	30	0.1	30	0.5	30	0.05	40	20000	30
Klebsiella pneumoniae	1000	26	100000	26	0.12	26	0.75	26	0.08	34	75000	26
Acinetobacter baumannii	1000	26	100000	26	0.12	26	0.75	26	0.08	34	75000	26
Haemophilus influenzae	750	30	75000	30	0.1	30	0.5	30	0.05	40	20000	30
Klebsiella oxytoca	750	30	75000	30	0.1	30	0.5	30	0.05	40	20000	30
Candida parapsilosis	750	30	75000	30	0.1	30	0.5	30	0.05	40	20000	30
OXA-48-Carbapenem resistance	750	30	75000	30	0.1	30	0.5	30	0.05	40	20000	30
KPC-Carbapenem resistance	750	30	75000	30	0.1	30	0.5	30	0.05	40	20000	30
NDM-Carbapenem resistance	1000	26	100000	26	0.12	26	0.75	26	0.08	34	75000	26
VIM-Carbapenem resistance	750	30	75000	30	0.1	30	0.5	30	0.05	40	20000	30
IMP-Carbapenem resistance	750	30	75000	30	0.1	30	0.5	30	0.05	40	20000	30
Listeria monocytogenes	750	30	75000	30	0.1	30	0.5	30	0.05	40	20000	30
Enterococcus faecalis	750	30	75000	30	0.1	30	0.5	30	0.05	40	20000	30
mecA/mecC-Methicillin resistance	1000	26	100000	26	0.12	26	0.75	26	0.08	34	75000	26
Candida tropicalis	750	30	75000	30	0.1	30	0.5	30	0.05	40	20000	30
Stenotrophomonas maltophilia	1000	26	100000	26	0.12	26	0.75	26	0.08	34	75000	26
Enterobacteriaceae spp.	1000	26	100000	26	0.12	26	0.75	26	0.08	34	75000	26
Streptococcus spp.	1000	26	100000	26	0.12	26	0.75	26	0.08	34	75000	26
Enterococcus faecium	750	30	75000	30	0.1	30	0.5	30	0.05	40	20000	30
Escherichia coli	750	30	75000	30	0.1	30	0.5	30	0.05	40	20000	30
Neisseria meningitidis	750	30	75000	30	0.1	30	0.5	30	0.05	40	20000	30
Streptococcus pneumoniae	1000	26	100000	26	0.12	26	0.75	26	0.08	34	75000	26

*** Defined threshold with specific settings of "Outlier Removal = 0", "Dynamic Tube = On", and "Slope Correct = Off"

Table 8. Interpretation of Patient Results

Target	Internal Control (IC)	Result Interpretation		
Positive (+)	**Positive (+)** or **Negative (-)**	Results are valid Target is detected	**Protocol 1**	If 26<Cq ≤30 "Low Positive" If 16<Cq≤26 "Positive" If Cq≤16 "High Positive"
			Protocol 2	If 34<Cq ≤40 "Low Positive" If 22<Cq≤34 "Positive" If Cq≤22 "High Positive"
Negative (-)	**Positive (+)**	Results are valid Target is not detected		

Table 9. Expected Performance of Kit Controls

Control Type	Purpose	Expected Results and Cq Values			
		Protocol 1		Protocol 2	
		IC (HEX)	Target	IC (HEX)	Target
Negative Control	Contamination control during qPCR	**Not Detected**	**Not Detected**	**Not Detected**	**Not Detected**
Positive Control	Reagent stability control	**Detected** (Cq≤30)	**Detected** (Cq≤30)	**Detected** (Cq≤40)	**Detected** (Cq≤40)
Internal Control	Nucleic acid extraction and sampling control	**Detected**	Detection insignificant	**Detected**	Detection insignificant
		If "**Not Detected**" check the target Cq	If "**Detected"** IC is valid	If "**Not Detected**" check the target Cq	If "**Detected"** IC is valid

If a control does not work as expected (**Table 9**), apply the procedures described below.

1. **Contamination Problem:** If a target in the Negative Control reaction is "**Detected**".
   Recommended action: Repeat the run, paying attention to the "Warnings and Limitations" section.

2. **Invalid Internal Control Problem:** If the Internal Control (IC) and all other targets of a sample are "**Not Detected**".
   Recommended action: Sampling was not successfully done, or there was a problem during the sample transportation or extraction. Re-test the sample. If the problem repeats, a new sample from the same patient should be collected and tested again.

3. **Reagent Problem**: If all Internal Controls, Positive Controls and targets in the run are "**Not Detected**".
   Recommended action: The run is considered invalid. Re-test the PC. If the problem repeats, please reach out to the manufacturer for further assistance.

For positive blood culture samples:

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If **more than one parameter (except drug resistance genes)** gives positive results in positive blood culture sample, the final reporting is performed after the following evaluation process:

1. The parameter giving the lowest Cq is determined = Min Cq
2. (Cq value of other parameter) – (Min Cq) If <7, a **positive** result is given for other parameter
3. (Cq value of other parameter) – (Min Cq) If ≥7, a **negative** result is given for other parameter

For drug resistance gene targets (VanA, and VanB-Vancomycin resistance, OXA-48, KPC, NDM, VIM, IMP-Carbapenem resistance, mecA/mecC-Methicillin resistance) and *Candida krusei*, *Candida glabrata, Candida albicans, Candida parapsilosis, Candida tropicalis* gene targets:

1. **Protocol 1:**
   - If the Cq value is **≤27**, it is reported as **positive.**
   - If the Cq value is **>27**, it is reported as **negative**.
2. **Protocol 2:**
   - If the Cq value is **≤35**, it is reported as **positive.**
   - If the Cq value is **>35**, it is reported as **negative**.

For all other gene targets:

1. **Protocol 1:**
   - If the Cq value is **≤23**, it is reported as **positive.**
   - If the Cq value is **>23**, it is reported as **negative.**
2. **Protocol 2:**
   - If the Cq value is **≤31**, it is reported as **positive.**
   - If the Cq value is **>31**, it is reported as **negative.**

3. WARNINGS AND LIMITATIONS

1. False-negative results may occur if inadequate number (below the LoD) of organisms are present in the specimen.
2. Mutations within the target regions could affect primer and/or probe binding, resulting in failure to detect the presence of agents.
3. False-negative results may occur if a specimen is improperly collected, transported, or handled.
4. The clinical specimens shall be collected by a healthcare provider in accordance with the national/international specimen collection guidelines.
5. Test procedures should be performed by personnel trained in the use of the kit.
6. Sample tubes should always be kept closed except for liquid transfers.
7. Filtered and nuclease-free pipette tips should be used for sample transfer.
8. The components in the kit should not be used together with different LOT numbers or chemicals of the same name but from different manufacturers.
9. The caps of the reaction tubes must not be opened after the PCR run. The PCR tubes should be placed in a bag and thrown away after the bag is tightly closed.
10. The surfaces of the workbenches should be wiped with freshly diluted 10% bleach (0.5% NaClO) at the beginning and end of each day.
11. Waste disposal must be carried out in accordance with local, state, and federal regulations.
12. Proper personal protective equipment including lab coats, gowns, gloves, eye protection, and a biological safety cabinet are recommended for manipulation of clinical specimens.
13. Immediately clean up any spill containing potentially infectious material with 0.5-1% (w/v) sodium hypochlorite (10-20% v/v bleach). Dispose of cleaning materials in a biohazard waste stockpot.
14. The micropipettes used for pipetting PCR mixes and template nucleic acids should be separate. Filtered and nuclease-free pipette tips should be used.
15. Maintenance/ calibration interval should be determined for all instruments and equipment used with the kit.

4. EXPLANATIONS OF SYMBOLS

Symbol	Title of Symbol	Symbol	Title of Symbol	Symbol	Title of Symbol
CE	European Conformity CE Mark	LOT	Batch code		Keep away from sunlight
IVD	*In vitro* diagnostic medical device	REF	Catalog number		Protect from heat and radioactive sources
	Manufacturer	NON STERILE	Non-sterile		Do not use if package is damaged and consult *Instructions for Use*
	Expiration Date YYYY-MM		Consult *Instructions for Use* or consult electronic *Instructions for Use*		Keep dry
CONTROL -	Negative Control		Caution		Keep upright
CONTROL +	Positive Control		Temperature limit	Σ	Contains sufficient for *<n>* tests
CONTROL	Control				

5. MANUFACTURER AND TECHNICAL SUPPORT

Bioeksen AR GE Teknolojileri A.Ş
Address: Huzur Mah. Metin Oktay Cad. Nurol Life Sitesi D Blok No:3/31, 34396 Sarıyer/İstanbul-TÜRKİYE
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Web: www.bioeksen.com.tr, **e-mail:** info@bioeksen.com.tr,
Technical Support: support@bioeksen.com.tr

Notice to User: Please send an e-mail to **vigilance@bioeksen.com.tr** about product-related incidents, within 24 hours.

For in vitro diagnostic use only.
For laboratory professional use only.

Cat No: BS-NA-513m-100

*v*NAT® Transfer Tube

Package Insert

1. KIT CONTENT

Table 1. Kit Content

Component	Description	Amount
*v*NAT® Transfer Tube	Microbial nucleic acid storage and stabilization device	100 Tubes

Table 2. Storage Requirements and Shelf Life

Component	Transport Conditions	Storage Conditions	Shelf Life
*v*NAT® Transfer Tube	(+2) °C to (+50) °C	(+15) °C to (+30) °C	60 months

2. INTENDED USE

***v*NAT ® Transfer Tube**, 2 mL of nucleic acid extraction and preservation liquid. The ***v*NAT® Transfer Tube** is intended for single use. When clinical specimens suspected of infections are transferred in the ***v*NAT ® Transfer Tube**, the liquid inside the tube can be used directly in Real-Time PCR (qPCR) reactions. The nucleic acid extraction and preservation liquid inactivates all viral, bacterial, or eukaryotic pathogens in the sample 1 minute after contact with the clinical specimen. The ***v*NAT® Transfer Tube** allows from sample to RT-qPCR in a minute.

3. ANALYTICAL SPECIFICATIONS

***v*NAT® Transfer Tube** is validated for RT-qPCR based test kits produced by Bioeksen AR GE Teknolojileri A.Ş.

4. SAMPLING PROTOCOL

Nasopharyngeal, oropharyngeal, throat, rectal, vaginal, cervical, urethral, urogenital, endocervical, penile, and conjunctival swab samples shall be collected by a healthcare provider in accordance with the specimen collection guidelines. The swab samples should be placed immediately into the ***v*NAT ® Transfer Tube**.

5. COLLECTION, STORAGE AND SHIPMENT OF CLINICAL SPECIMENS

The specimen should be stored at +2 °C to +8 °C and be shipped to the laboratory with the ice pack. If a specimen is frozen at -20 °C or lower temperature, it should be shipped to the laboratory with dry ice.

Specimens in the ***v*NAT® Transfer Tube** can be stored at +2 °C to +30 °C for up to 72 hours and +2 °C to +8 °C for up to 3 months after collection. If a delay in the RT-qPCR test is expected, the specimen should be stored at -20 °C or lower in accordance with national/international clinical specimen collection regulations.

- One minute after the sampling, the samples in the ***v*NAT® Transfer Tube** can be used directly in RT-qPCR.
- Vortex the tube at the highest speed for 3 seconds before adding the sample into the RT-qPCR.

6. EXPLANATION OF SYMBOL

Symbol	Title of Symbol	Symbol	Title of Symbol	Symbol	Title of Symbol
CE	European Conformity CE Mark	IVD	*In vitro* diagnostic *medical device*		Keep away from sunlight
	Manufacturer	LOT	Batch code		Protect from heat and radioactive sources
	Use-by date	REF	Catalogue number		Do not use if package is damaged and consult *instructions for use*
	Temperature limit	NON STERILE	Non-*sterile*		Keep dry
	Caution		Consult *instructions for use* or consult electronic *instructions for use*		
	Keep it upright	2	Do not re-use		

7. MANUFACTURER AND TECHNICAL SUPPORT

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Web: www.bioeksen.com.tr, **E-mail:** info@bioeksen.com.tr,
Technical Support: support@bioeksen.com.tr

Notice to User: Please inform us about product-related incidents at "**vigilance@bioeksen.com.tr**" within 24 hours.

For in vitro diagnostic use only.
For professional use only.
Cat No: BS-GE-MX5T-25/BS-GE-MX5T-100
Ordering Ref No: GTI-VIR-T-25/GTI-VIR-T-100

Gastroenteritis RT-qPCR MX-5T Viral Panel

Package Insert

Table 1. Kit Content

Component	Intended Use	25 Reactions	100 Reactions
2X Prime Script Mix	Optimized ready-to-use mix for RT-qPCR assay	1 x 500 µL	2 x 1000 µL
SA Oligo Mix	Specific nucleic acid amplification and detection: **FAM:** Sapovirus (GI/GII/GIV/GV) **HEX:** Human (IC-Internal Control) **CY5:** Adenovirus Type F	1 x 125 µL	1 x 500 µL
ANR Oligo Mix	**FAM:** Astrovirus **HEX:** Norovirus (GI/GII) **ROX:** Rotavirus (A)	1 x 125 µL	1 x 500 µL
NTC	Negative Control	1 x 1000 µL	1 x 1000 µL
PC-SA/PC-ANR	Positive Control (PC)	1 x 100 µL	1 x 100 µL

Table 2. Storage Requirements and Shelf Life

Component	Transport Condition	Storage Condition*	Shelf Life
2X Prime Script Mix	(-22) °C – (+8) °C	(-22) °C – (+8) °C	12 Months
Oligo Mix		(-22) °C – (+8) °C	
NTC		(-22) °C – (-18) °C before opening, (+2) °C – (+8) °C after first thaw	
PC		(-22) °C – (-18) °C before opening, (+2) °C – (+8) °C after first thaw	

* Following the first opening, each reagent stored at storage temperature can be used until the expiration date indicated on the tube. The kit's expiration date is determined by the expiration date of the reagents.

Table 3. Required Components Not Included in the Package

Required Components Not Included in the Package
1. Real-Time PCR Instrument
2. ***v*NAT® Transfer Tube** (Cat. No: BS-NA-513m-100) or nucleic acid preparation instruments and nucleic acid preparation consumables
3. Micropipettes and compatible filtered pipette tips (nuclease-free) suitable for transferring 1-10 µL, 10-100 µL, and 100-1000 µL of liquid
4. A centrifuge or Mini-spin
5. Vortex
6. Reaction tubes,PCR strips, PCR plates and caps/films specific to qPCR instruments and compatible with the reaction volume

Table 4. Intended Use, Test Principle and Analytical Specifications

Function	Aid to diagnosis	**Sample Type(s)**	**Table 5**
Analyte(s)	**Table 1**	**Nucleic Acid Extraction Methods**	***v*NAT® Transfer Tube** Zybio EXM3000 Nucleic Acid Extraction System Adaltis EXTRAlab and MDXlab
Qualitative/Quantitative	Qualitative	**Validated qPCR Instrument(s)**	Bio Molecular Systems: Magnetic Induction Cycler (Mic)/Mic IVD Bio-Rad: CFX96 Touch/Dx, CFX Opus 96/Dx, CFX384 Touch, CFX Opus 384 Qiagen: Rotor-Gene Q 5-Plex/MDx Roche: LightCycler 96 Thermo Fisher Scientific: QuantStudio 5/5 Dx/6/7/12k Flex/Pro, StepOne Plus, Applied Biosystems 7500/7500 Fast Adaltis: AmpliLab, MDXlab HiMedia: InstaQ 96 Bioer: Linegene 9600 Plus Atila Biosystems: Fujirebio Co-Dx: Co-Dx Box Tianlong: Gentier 96E Sansure: SLAN-96P Azure: Cielo
Test Principle	Reverse Transcription and Real-Time PCR (RT-qPCR)	**Inclusivity and Exclusivity**	Validated on the reference strains and the field isolates
Automatic/Manual	Manual		
Intended Users	Laboratory professionals trained in the techniques of qPCR and in vitro diagnostic procedures.	**Limit of Detection**	**Table 5**
Target Population	Individuals with the suspected infection	**Sensitivity and Specificity**	98.93% and 99.14%

Table 5. Collection, Storage, Transfer of Clinical Specimens/ Nucleic Acid Preparation Method

Sample Type**	Sample Transfer	Sample Storage	Nucleic Acid Preparation Method	LoD (cp/mL)
Stool	Preservative-free sterile containers	1 day at (+2) °C - (+8) °C 1 year at (-20) °C	**Nucleic acid preparation instruments:** 1) Zybio EXM3000, 2) Adaltis EXTRAlab, 3) Adaltis MDXlab **Nucleic acid preparation consumables:** Bio-Speedy® Rapid Nucleic Acid Extraction Kit (Cat. No: ZFNAE01)	25-100

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Rectal Swab***	**vNAT® Transfer Tube** (Cat. No: BS-NA-513m-100)	3 months at (+2) °C – (+8) °C 1 year at (-20) °C	Nucleic acid preparation is not needed, samples can be used directly in qPCR	500

** Clinical specimens should be collected by a healthcare provider in accordance with national/international clinical specimen collection regulations.
*** If dry swab samples are received, put them into the **vNAT® Transfer Tube** for nucleic acid preparation.

1. APPLICATION PROTOCOL

1. Program the qPCR device using the QR Code/Link as indicated in **Table 6**.
2. Take the PCR kit out of the -20°C freezer.
3. Pipette (Sample Count + 3)*5 µL of SA Oligo Mix into an empty eppendorf tube. (i.e Sample Count = 3, pipette 5*(3+3) = 30 µL of SA Oligo Mix)
4. Add (Sample Count + 3)*10 µL of 2X Prime Script Mix into the tube prepared in Step 3. (i.e Sample Count = 3, pipette 10*(3+3) = 60 µL of 2X Prime Script Mix)
5. Vortex the master mix to homogenize.
6. Repeat steps 3,4,5 for all master mixes (Total 2 master mixes in total).
7. Pipette 15 µL of master mix into all PCR tubes, or wells to be used (including all samples, NTC and PC).
8. Pipette 5 µL of each isolated/ extracted sample into the relative PCR tube, or well.
9. Pipette 5 µL of NTC into the Negative Control PCR tube, or well.
10. Pipette 5 µL of PC-SA into the Positive Control tubes, or wells. Repeat for all PC.
11. Close the cap of the strips, or PCR tubes or seal PCR plate. Label to avoid confusion during spin-centrifuge.
12. Spin-centrifuge the strips, or PCR tubes or PCR plate.
13. Open the lid of the instrument. Place the strips, or PCR tubes or PCR plate.
14. Close the lid and start the instrument.

Table 6. Real-Time qPCR Program

Reaction Setup		**RT-qPCR Program**							
		Protocol 1: Bio Molecular Systems: Magnetic Induction Cycler (Mic)/Mic IVD, Bio-Rad: CFX96 Touch/Dx, CFX Opus 96/Dx, CFX384 Touch, CFX Opus 384, Roche: LightCycler 96, Co-Dx: Co-Dx Box, Azure: Cielo				**Protocol 2:** Qiagen: Rotor-Gene Q 5-Plex/MDx, Thermo Fisher Scientific: QuantStudio 5/5 Dx/6/7/12k Flex/Pro, StepOne Plus, Applied Biosystems 7500/7500 Fast, Adaltis: AmpliLab, MDXlab, HiMedia: InstaQ 96, Bioer: Linegene 9600 Plus, Atila Biosystems: Fujirebio, Tianlong: Gentier 96E, Sansure: SLAN-96P			
Reagent	**Volume/ Rxn**	**Step**	**Cycle No.**	**Temperature**	**Duration**	**Step**	**Cycle No.**	**Temperature**	**Duration**
2X Prime Script Mix	10 µL	**Reverse Transcription**	1 Cycle	52 °C	3 min	**Reverse Transcription**	1 Cycle	52 °C	3 min
		Pre-Incubation	1 Cycle	95 °C	10 sec	**Pre-Incubation**	1 Cycle	95 °C	10 sec
Oligo Mix	5 µL	**Denaturation**	12 Touchdown Cycles: 1 °C decrement in annealing temperature per cycle	95 °C	1 sec	**Denaturation**	40 Cycles	95 °C	1 sec
		Annealing and Extension		67 °C to 56 °C	15 sec	**Annealing and Extension**		55 °C	15 sec
Template Nucleic Acid/NTC/PC	5 µL	**Denaturation**	30 Cycles	95 °C	1 sec	**Detection (Reading)**		FAM/HEX/ROX/CY5	
		Annealing and Extension		55 °C	15 sec				
Total Reaction Volume	**20 µL**	**Detection (Reading)**		FAM/HEX/ROX/CY5					

WARNING: The qPCR program file should be downloaded from the QR code on the left or from the link below.

https://www.bioeksen.com.tr/files/L_TD_43B

2. INTERPRETATION OF THE ASSAY RESULTS

Cq values of the results obtained from PCR instruments indicated in **Table 7** are calculated referring to the relative RFU threshold levels and Cq cut-offs. Auto-threshold and default options are used for devices not included in **Table 7**. For all targets that do not exceed the Cq cut-off, the shape of the amplification curve must be analyzed, and Cq values of the sigmoidal curves must be determined. Non-sigmoidal curves must be reported as "negative". The PCR results can be reported manually, as indicated in **Table 8**, or using the "**Sigmoida**" software for BMS Magnetic Induction Cycler (Mic)/Mic IVD and Bio-Rad CFX instruments. Sigmoida software sorts each target as positive or negative. To obtain the "**Sigmoida**" software installer, please send an e-mail to support@bioeksen.com.tr.

Table 7. Threshold Levels and Cq Cut-offs for Calculating Cq Values

Analyte	**Real Time PCR Instrument**											
	Bio-Rad CFX		**Cielo**		**LightCycler 96**		**Mic/Mic IVD and Co-Dx Box**		**Rotor-Gene Q****		**QuantStudio 5/5 Dx/6/7/12k Flex/Pro**	
	RFU	**Cq Cut-off**	**RFU**	**Cq Cut-off**	**RFU**	**Cq Cut-off**	**RFU**	**Cq Cut-off**	**RFU**	**Cq Cut-off**	**RFU**	**Cq Cut-off**
Sapovirus (GI/GII/GIV/GV)	750	30	75000	30	0.1	30	0.5	30	0.05	40	20000	30
Human (IC-Internal Control)	200	30	20000	30	0.05	30	0.2	30	0.02	40	20000	30
Adenovirus Type F	750	30	75000	30	0.1	30	0.5	30	0.05	40	20000	30
Astrovirus	750	30	75000	30	0.1	30	0.5	30	0.05	40	20000	30
Norovirus (GI/GII)	750	30	75000	30	0.1	30	0.5	30	0.05	40	20000	30
Rotavirus (A)	750	30	75000	30	0.1	30	0.5	30	0.05	40	20000	30

**** Defined threshold with specific settings of "Outlier Removal = 0", "Dynamic Tube = On", and "Slope Correct = Off"

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Table 8. Interpretation of Patient Results

Target	Internal Control (IC)	Result Interpretation		
Positive (+)	**Positive (+)** or **Negative (-)**	Results are valid Target is detected	**Protocol 1**	If 26<Cq ≤30 "Low Positive" If 16<Cq≤26 "Positive" If Cq≤16 "High Positive"
			Protocol 2	If 34<Cq ≤40 "Low Positive" If 22<Cq≤34 "Positive" If Cq≤22 "High Positive"
Negative (-)	**Positive (+)**	Results are valid Target is not detected		

Table 9. Expected Performance of Kit Controls

Control Type	Purpose	Expected Results and Cq Values			
		Protocol 1		Protocol 2	
		IC (HEX)	Target	IC (HEX)	Target
Negative Control	Contamination control during RT-qPCR	**Not Detected**	**Not Detected**	**Not Detected**	**Not Detected**
Positive Control	Reagent stability control	**Detected** (Cq≤30)	**Detected** (Cq≤30)	**Detected** (Cq≤40)	**Detected** (Cq≤40)
Internal Control	Nucleic acid extraction and sampling control	**Detected**	Detection insignificant	**Detected**	Detection insignificant
		If "**Not Detected**" check the target Cq	If "**Detected"** IC is valid	If "**Not Detected**" check the target Cq	If "**Detected"** IC is valid

If a control does not work as expected (**Table 9**), apply the procedures described below.

1. **Contamination Problem:** If a target in the Negative Control reaction is "**Detected**".
   Recommended action: Repeat the run, paying attention to the "Warnings and Limitations" section.

2. **Invalid Internal Control Problem:** If the Internal Control (IC) and all other targets of a sample are "**Not Detected**".
   Recommended action: Sampling was not successfully done, or there was a problem during the sample transportation or extraction. Re-test the sample. If the problem repeats, a new sample from the same patient should be collected and tested again.

3. **Reagent Problem**: If all Internal Controls, Positive Controls and targets in the run are "**Not Detected**".
   Recommended action: The run is considered invalid. Re-test the PC. If the problem repeats, please reach out to the manufacturer for further assistance.

3. WARNINGS AND LIMITATIONS

1. False-negative results may occur if inadequate number (below the LoD) of organisms are present in the specimen.
2. Mutations within the target regions could affect primer and/or probe binding, resulting in failure to detect the presence of agents.
3. False-negative results may occur if a specimen is improperly collected, transported, or handled.
4. The clinical specimens shall be collected by a healthcare provider in accordance with the national/international specimen collection guidelines.
5. Test procedures should be performed by personnel trained in the use of the kit.
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7. Filtered and nuclease-free pipette tips should be used for sample transfer.
8. The components in the kit should not be used together with different LOT numbers or chemicals of the same name but from different manufacturers.
9. ***The caps of the reaction tubes must not be opened after the PCR run.*** The PCR tubes should be placed in a bag and thrown away after the bag is tightly closed.
10. The surfaces of the workbenches should be wiped with freshly diluted 10% bleach (0.5% NaClO) at the beginning and end of each day.
11. Waste disposal must be carried out in accordance with local, state, and federal regulations.
12. Proper personal protective equipment including lab coats, gowns, gloves, eye protection, and a biological safety cabinet are recommended for manipulation of clinical specimens.
13. Immediately clean up any spill containing potentially infectious material with 0.5-1% (w/v) sodium hypochlorite (10-20% v/v bleach). Dispose of cleaning materials in a biohazard waste stockpot.
14. The micropipettes used for pipetting PCR mixes and template nucleic acids should be separate. Filtered and nuclease-free pipette tips should be used.
15. Maintenance/ calibration interval should be determined for all instruments and equipment used with the kit.

4. EXPLANATION OF SYMBOLS

Symbol	Title of Symbol	Symbol	Title of Symbol	Symbol	Title of Symbol
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IVD	*In vitro* diagnostic *medical device*	REF	Catalogue number		Protect from heat and radioactive sources
	Manufacturer	NON STERILE	Non-sterile		Do not use if package is damaged and consult *Instructions for Use*
	Expiration Date YYYY-MM		Consult *Instructions for Use* or consult electronic *Instructions for Use*		Keep dry
CONTROL -	Negative Control		Caution		Keep upright
CONTROL +	Positive Control		Temperature limit	Σ	Contains sufficient for *<n>* tests

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CONTROL	Control				

5. MANUFACTURER AND TECHNICAL SUPPORT

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Technical Support: support@bioeksen.com.tr.

Notice to User: Please inform us about product-related incidents at "**vigilance@bioeksen.com.tr**" within 24 hours.

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For professional use only.
Cat No: BS-ME-MX6T-25/BS-ME-MX6T-100
Ordering Ref No: CNS-BAC-T-25/CNS-BAC-T-100

Meningitis/Encephalitis RT-qPCR MX-6T Panel

Package Insert

Table 1. Kit Content

Component	Intended Use	25 Reactions	100 Reactions
2X qPCR Mix	Optimized ready-to-use mix for qPCR assay	1 x 500 µL	2 x 1000 µL
LNS Oligo Mix	**FAM**: *Listeria monocytogenes* **HEX:** Human (IC-Internal Control) **ROX:** *Neisseria meningitidis* **CY5:** *Streptococcus pneumoniae*	1 x 125 µL	1 x 500 µL
HES Oligo Mix	**FAM:** *Haemophilus influenzae* **ROX:** *Streptococcus agalactiae* **CY5:** *Escherichia coli* K1	1 x 125 µL	1 x 500 µL
PC-LNS / PC-HES	Positive Control (PC)	1 x 100 µL	1 x 100 µL
NTC	Negative Control	1 x 1000 µL	1 x 1000 µL

Table 2. Transport Condition, Storage Condition, and Shelf Life of the Components

Component	Transport Condition	Storage Condition*	Shelf Life
2X qPCR Mix	(-22) °C – (+8) °C	(-22) °C – (-18) °C	12 Months
Oligo Mix		(-22) °C – (-18) °C	
NTC		(-22) °C – (-18) °C before opening, (+2) °C – (+8) °C after first thaw	
PC		(-22) °C – (-18) °C before opening, (+2) °C – (+8) °C after first thaw	

* Following the first opening, each reagent stored at storage temperature can be used until the expiration date indicated on the tube. The kit's expiration date is determined by the expiration date of the reagents.

Table 3. Required Components Not Included in the Package

Required Components Not Included in the Package
1. Real-Time PCR Instrument
2. Nucleic acid preparation instruments and nucleic acid preparation consumables
3. Micropipettes and compatible filtered pipette tips (nuclease-free) suitable for transferring 1-10 µL, 10-100 µL, and 100-1000 µL of liquid
4. A centrifuge or Mini-spin
5. Vortex
6. Reaction tubes,PCR strips, PCR plates and caps/films specific to qPCR instruments and compatible with the reaction volume

Table 4. Intended Use, Test Principle and Analytical Specifications

Function	Aid to diagnosis	**Sample Type(s)**	**Table 5**
Analyte	**Table 1**	**Nucleic Acid Extraction Method(s)**	Zybio EXM3000 Nucleic Acid Extraction System Adaltis EXTRAlab and MDXlab
Qualitative/Quantitative	Qualitative	**Validated qPCR Instrument(s)**	Bio Molecular Systems: Magnetic Induction Cycler (Mic)/Mic IVD Bio-Rad: CFX96 Touch/Dx, CFX Opus 96/Dx, CFX384 Touch, CFX Opus 384 Qiagen: Rotor-Gene Q 5-Plex/MDx Roche: LightCycler 96 Thermo Fisher Scientific: QuantStudio 5/5 Dx/6/7/12k Flex/Pro, StepOne Plus, Applied Biosystems 7500/7500 Fast Adaltis: AmpliLab, MDXlab HiMedia: InstaQ 96 Bioer: Linegene 9600 Plus Atila Biosystems: Fujirebio Co-Dx: Co-Dx Box Tianlong: Gentier 96E Sansure: SLAN-96P Azure: Cielo
Test Principle	Real-Time PCR (qPCR)	**Inclusivity and Exclusivity**	Validated on the reference strains and the field isolates
Automated/Manual	Manual		
Intended Users	Laboratory professionals trained in the techniques of qPCR and in vitro diagnostic procedures	**Limit of Detection (LoD)**	**Table 5**
Target Population	Individuals with the suspected infection	**Sensitivity and Specificity**	100.00% and 98.04%

Table 5. Collection, Storage, and Transfer of Clinical Specimens / Nucleic Acid Preparation Methods

Sample Type**	Sample Transfer	Sample Storage	Nucleic Acid Preparation Method	LoD (cp/mL)
Cerebrospinal Fluid (CSF) samples	Preservative-free sterile containers	3 days at (+2) °C - (+8) °C 1 year at (-20) °C	**Nucleic acid preparation instruments:** 1) Zybio EXM3000, 2) Adaltis EXTRAlab, 3) Adaltis MDXlab	50-100

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			Nucleic acid preparation consumables: Bioeksen Bio-Speedy® Rapid Nucleic Acid Extraction Kit (Cat. No: ZFNAE01)	

** Clinical specimens should be collected by a healthcare provider in accordance with national/international clinical specimen collection regulations.

1. APPLICATION PROTOCOL

1. Program the qPCR device using the QR Code/Link as indicated in **Table 6.**
2. Take the PCR kit out of the -20°C freezer.
3. Pipette (Sample Count + 3) *5 µL of LNS Oligo Mix into an empty eppendorf tube. (i.e Sample Count = 3, pipette 5*(3+3) = 30 µL of LNS Oligo Mix)
4. Add (Sample Count + 3) *10 µL of 2X qPCR Mix into the tube prepared in Step 3. (i.e Sample Count = 3, pipette 10*(3+3) = 60 µL of 2X qPCR Mix)
5. Vortex the master mix to homogenize.
6. Repeat Steps 3, 4 and 5 for all master mixes (2 master mixes in total).
7. Pipette 15 µL of each master mix into relative PCR tube, or wells to be used (including all samples, NTC and PC).
8. Pipette 5 µL of extracted/isolated sample into relative PCR tube, or wells.
9. Pipette 5 µL of NTC into the Negative Control PCR tube, or wells.
10. Pipette 5 µL of PC-LNS into the PC tube or wells. Repeat for all PC.
11. Close the cap of the strips, or PCR tubes or seal PCR plate. Label to avoid confusion during spin-centrifuge.
12. Spin-centrifuge the strips, or PCR tubes and PCR plate.
13. Open the lid of the instrument. Place the strips, or PCR tubes and PCR plate.
14. Close the lid and start the instrument.

Table 6. Real-Time qPCR Program

<table>
<tr><th rowspan="2">Reaction Setup</th><th colspan="10">RT-qPCR Program</th></tr>
<tr><th colspan="5"><u>Protocol 1:</u>
Bio Molecular Systems: Magnetic Induction Cycler (Mic)/Mic IVD, Bio-Rad: CFX96 Touch/Dx, CFX Opus 96/Dx, CFX384 Touch, CFX Opus 384, Roche: LightCycler 96, Co-Dx: Co-Dx Box, Azure: Cielo</th><th colspan="5"><u>Protocol 2:</u>
Qiagen: Rotor-Gene Q 5-Plex/MDx, Thermo Fisher Scientific: QuantStudio 5/5 Dx/6/7/12k Flex/Pro, StepOne Plus, Applied Biosystems 7500/7500 Fast, Adaltis: AmpliLab, MDXlab, HiMedia: InstaQ 96, Bioer: Linegene 9600 Plus, Atila Biosystems: FujirebioTianlong: Gentier 96E, Sansure: SLAN-96P</th></tr>
<tr><th>Reagent</th><th>Volume/ Rxn</th><th>Step</th><th>Cycle No.</th><th>Temperature</th><th>Duration</th><th>Step</th><th>Cycle No.</th><th>Temperature</th><th>Duration</th></tr>
<tr><td rowspan="2">2X qPCR Mix</td><td rowspan="2">10 µL</td><td>Enzyme Activation</td><td>1 Cycle</td><td>52 °C</td><td>3 min</td><td>Enzyme Activation</td><td>1 Cycle</td><td>52 °C</td><td>3 min</td></tr>
<tr><td>Pre-Incubation</td><td>1 Cycle</td><td>95 °C</td><td>10 sec</td><td>Pre-Incubation</td><td>1 Cycle</td><td>95 °C</td><td>10 sec</td></tr>
<tr><td rowspan="2">Oligo Mix</td><td rowspan="2">5 µL</td><td>Denaturation</td><td rowspan="2">12 Touchdown Cycles:
1 °C decrement in annealing temperature per cycle</td><td>95 °C</td><td>1 sec</td><td>Denaturation</td><td rowspan="3">40 Cycles</td><td>95 °C</td><td>1 sec</td></tr>
<tr><td>Annealing and Extension</td><td>67 °C to 56 °C</td><td>15 sec</td><td>Annealing and Extension</td><td>55 °C</td><td>15 sec</td></tr>
<tr><td rowspan="2">Template Nucleic Acid/NTC/PC</td><td rowspan="2">5 µL</td><td>Denaturation</td><td rowspan="3">30 Cycles</td><td>95 °C</td><td>1 sec</td><td rowspan="3">Detection (Reading)</td><td rowspan="3">FAM/HEX/ROX/CY5</td></tr>
<tr><td>Annealing and Extension</td><td>55 °C</td><td>15 sec</td></tr>
<tr><td>Total Reaction Volume</td><td>20 µL</td><td>Detection (Reading)</td><td colspan="2">FAM/HEX/ROX/CY5</td></tr>
</table>

WARNING: The qPCR program file should be downloaded from the QR code on the left or from the link below.

https://www.bioeksen.com.tr/files/L_TD_43B

2. INTERPRETATION OF THE ASSAY RESULTS

Cq values of the results obtained from PCR instruments indicated in **Table 7** are calculated referring to the relative RFU threshold levels and Cq cut-offs. Auto-threshold and default options are used for devices not included in **Table 7**. For all targets that do not exceed the Cq cut-off, the shape of the amplification curve must be analyzed, and Cq values of the sigmoidal curves must be determined. Non-sigmoidal curves must be reported as "negative". The PCR results can be reported manually, as indicated in **Table 8**, or using the "**Sigmoida**" software for BMS Magnetic Induction Cycler (Mic)/Mic IVD and Bio-Rad CFX instruments. Sigmoida software sorts each target as positive or negative. To obtain the "**Sigmoida**" software installer, please send an e-mail to support@bioeksen.com.tr.

Table 7. Threshold Levels and Cq Cut-offs for Calculating Cq Values

Analyte	Real Time PCR Instrument											
	Bio-Rad CFX		Cielo		LightCycler 96		Mic/Mic IVD and Co-Dx Box		Rotor-Gene Q***		QuantStudio 5/5 Dx/6/7/12k Flex/Pro	
	RFU	Cq Cut-off	RFU	Cq Cut-off	RFU	Cq Cut-off	RFU	Cq Cut-off	RFU	Cq Cut-off	RFU	Cq Cut-off
Listeria monocytogenes	750	30	75000	30	0.1	30	0.5	30	0.05	40	20000	30
Human (IC-Internal Control)	200	30	20000	30	0.05	30	0.2	30	0.02	40	20000	30
Neisseria meningitidis	750	30	75000	30	0.1	30	0.5	30	0.05	40	20000	30
Streptococcus pneumoniae	1000	26	100000	26	0.12	26	0.75	26	0.08	34	75000	26
Haemophilus influenzae	750	30	75000	30	0.1	30	0.5	30	0.05	40	20000	30
Streptococcus agalactiae	750	30	75000	30	0.1	30	0.5	30	0.05	40	20000	30
***Escherichia coli* K1**	750	30	75000	30	0.1	30	0.5	30	0.02	40	20000	30

*** Defined threshold with specific settings of "Outlier Removal = 0", "Dynamic Tube = On", and "Slope Correct = Off"

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Table 8. Interpretation of Patient Results

Target	Internal Control (IC)	Result Interpretation		
Positive (+)	**Positive (+)** or **Negative (-)**	Results are valid Target is detected	**Protocol 1**	If 26<Cq ≤30 "Low Positive" If 16<Cq≤26 "Positive" If Cq≤16 "High Positive"
			Protocol 2	If 34<Cq ≤40 "Low Positive" If 22<Cq≤34 "Positive" If Cq≤22 "High Positive"
Negative (-)	**Positive (+)**	Results are valid Target is not detected		

Table 9. Expected Performance of Kit Controls

Control Type	Purpose	Expected Results and Cq Values			
		Protocol 1		Protocol 2	
		IC (HEX)	Target	IC (HEX)	Target
Negative Control	Contamination control during qPCR	**Not Detected**	**Not Detected**	**Not Detected**	**Not Detected**
Positive Control	Reagent stability control	**Detected** (Cq≤30)	**Detected** (Cq≤30)	**Detected** (Cq≤40)	**Detected** (Cq≤40)
Internal Control	Nucleic acid extraction and sampling control	**Detected**	Detection insignificant	**Detected**	Detection insignificant
		If "**Not Detected**" check the target Cq	If "**Detected"** IC is valid	If "**Not Detected**" check the target Cq	If "**Detected"** IC is valid

If a control does not work as expected (**Table 9**), apply the procedures described below.

1. **Contamination Problem:** If a target in the Negative Control reaction is "**Detected**".
   Recommended action: Repeat the run, paying attention to the "Warnings and Limitations" section.

2. **Invalid Internal Control Problem:** If the Internal Control (IC) and all other targets of a sample are "**Not Detected**".
   Recommended action: Sampling was not successfully done, or there was a problem during the sample transportation or extraction. Re-test the sample. If the problem repeats, a new sample from the same patient should be collected and tested again.

3. **Reagent Problem**: If all Internal Controls, Positive Controls and targets in the run are "**Not Detected**".
   Recommended action: The run is considered invalid. Re-test the PC. If the problem repeats, please reach out to the manufacturer for further assistance.

3. WARNINGS AND LIMITATIONS

1. False-negative results may occur if inadequate number (below the LoD) of organisms are present in the specimen.
2. Mutations within the target regions could affect primer and/or probe binding, resulting in failure to detect the presence of agents.
3. False-negative results may occur if a specimen is improperly collected, transported, or handled.
4. The clinical specimens shall be collected by a healthcare provider in accordance with the national/international specimen collection guidelines.
5. Test procedures should be performed by personnel trained in the use of the kit.
6. Sample tubes should always be kept closed except for liquid transfers.
7. Filtered and nuclease-free pipette tips should be used for sample transfer.
8. The components in the kit should not be used together with different LOT numbers or chemicals of the same name but from different manufacturers.
9. ***The caps of the reaction tubes must not be opened after the PCR run.*** The PCR tubes should be placed in a bag and thrown away after the bag is tightly closed.
10. The surfaces of the workbenches should be wiped with freshly diluted 10% bleach (0.5% NaClO) at the beginning and end of each day.
11. Waste disposal must be carried out in accordance with local, state, and federal regulations.
12. Proper personal protective equipment including lab coats, gowns, gloves, eye protection, and a biological safety cabinet are recommended for manipulation of clinical specimens.
13. Immediately clean up any spill containing potentially infectious material with 0.5-1% (w/v) sodium hypochlorite (10-20% v/v bleach). Dispose of cleaning materials in a biohazard waste stockpot.
14. The micropipettes used for pipetting PCR mixes and template nucleic acids should be separate. Filtered and nuclease-free pipette tips should be used.
15. Maintenance/ calibration interval should be determined for all instruments and equipment used with the kit.

4. EXPLANATION OF SYMBOLS

Symbol	Title of Symbol	Symbol	Title of Symbol	Symbol	Title of Symbol
CE	European Conformity CE Mark	LOT	Batch code		Keep away from sunlight
IVD	*In vitro* diagnostic *medical device*	REF	Catalogue number		Protect from heat and radioactive sources
	Manufacturer	NON STERILE	Non-sterile		Do not use if package is damaged and consult *Instructions for Use*
	Expiration Date YYYY-MM		Consult *Instructions for Use* or consult electronic *Instructions for Use*		Keep dry
CONTROL -	Negative Control		Caution		Keep upright
CONTROL +	Positive Control		Temperature limit	Σ	Contains sufficient for <*n*> tests
CONTROL	Control				

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5. MANUFACTURER AND TECHNICAL SUPPORT

Bioeksen AR GE Teknolojileri A.Ş
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Web: www.bioeksen.com.tr, **e-mail:** info@bioeksen.com.tr,
Technical Support: support@bioeksen.com.tr.

Notice to User: Please inform us about product-related incidents at "**vigilance@bioeksen.com.tr**" within 24 hours.

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Cat No: BS-SP-B-12-50

Brucella spp. qPCR Kit

Package Insert

Table 1. Kit Content

Component	Intended Use	50 Reactions
2X qPCR Mix	Optimized ready-to-use mix for qPCR assay	1 x 250 µL
Brucella spp. Oligo Mix	Specific nucleic acid amplification and detection: **FAM:** *Brucella* spp. **HEX:** Human (IC-Internal Control)	1 x 125 µL
NTC	Negative Control	1 x 1000 µL
PC-Brucella spp.	Positive Control (PC)	1 x 100 µL

Table 2. Transport Condition, Storage Condition, and Shelf Life of the Components

Component	Transport Condition	Storage Condition*	Shelf Life
2X qPCR Mix	(-22) °C – (+8) °C	(-22) °C – (-18) °C	12 Months
Oligo Mix		(-22) °C – (-18) °C	
PC		(-22) °C – (-18) °C before opening, (+2) °C – (+8) °C after first thaw	
NTC		(-22) °C – (-18) °C before opening, (+2) °C – (+8) °C after first thaw	

* Following the first opening, each reagent stored at storage temperature can be used until the expiration date indicated on the tube. The kit's expiration date is determined by the expiration date of the reagents.

Table 3. Required Components Not Included in the Package

Required Components Not Included in the Package
1. Real-Time PCR Instrument
2. Nucleic acid preparation instruments and nucleic acid preparation consumables
3. Micropipettes and compatible filtered pipette tips (nuclease-free) suitable for transferring 1-10 µL, 10-100 µL, and 100-1000 µL of liquid
4. A centrifuge or Mini-spin
5. Vortex
6. Reaction tubes,PCR strips, PCR plates and caps/films specific to qPCR instruments and compatible with the reaction volume

Table 4. Intended Use, Test Principle, and Analytical Specifications

Function	Aid to diagnosis	**Sample Type(s)**	**Table 5**
Analyte(s)	**Table 1**	**Nucleic Acid Extraction Method(s)**	Zybio EXM3000 Nucleic Acid Isolation System Adaltis EXTRAlab and MDXlab
Qualitative/Quantitative	Qualitative	**Validated qPCR Instrument(s)**	Bio Molecular Systems: Magnetic Induction Cycler (Mic)/Mic IVD Bio-Rad: CFX96 Touch/Dx, CFX Opus 96/Dx, CFX384 Touch, CFX Opus 384 Qiagen: Rotor-Gene Q 5-Plex/MDx Roche: LightCycler 96 Thermo Fisher Scientific: QuantStudio 5/5 Dx/6/7/12k Flex/Pro, StepOne Plus, Applied Biosystems 7500/7500 Fast Adaltis: AmpliLab, MDXlab HiMedia: InstaQ 96 Bioer: Linegene 9600 Plus Atila Biosystems: Fujirebio Co-Dx: Co-Dx Box Tianlong: Gentier 96E Sansure: SLAN-96P Azure: Cielo
Test Principle	Real-Time PCR (qPCR)	**Inclusivity and Exclusivity**	Validated on the reference strains and the field isolates
Automated/Manual	Manual		
Intended Users	Laboratory professionals trained in the techniques of qPCR and in vitro diagnostic procedures.	**Limit of Detection (LoD)**	**Table 5**
Target Population	Individuals with the suspected infection	**Sensitivity and Specificity**	96.06% and 100.00%

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Table 5. Collection, Storage, Transfer of Clinical Specimens / Nucleic Acid Preparation Method

Sample Type**	Sample Transfer	Sample Storage	Nucleic Acid Preparation Method	LoD (cp/mL)
Positive blood culture	Blood culture bottle	Room temperature	**Nucleic acid preparation instruments:** 1) Zybio EXM3000, 2) Adaltis EXTRAlab, 3) Adaltis MDXlab **Nucleic acid preparation consumables:** Bio-Speedy® Rapid Nucleic Acid Extraction Kit (Cat. No: ZFNAE01)	100
Whole blood	EDTA-treated blood tube	3 days at (+2) °C – (+8) °C 1 year at (-20) °C		250
Synovial fluid	Preservative-free sterile tubes/containers	3 days at (+2) °C – (+8) °C 1 year at (-20) °C		250

**Clinical specimens should be collected by a healthcare provider in accordance with national/international clinical specimen collection regulations.

1. APPLICATION PROTOCOL

1. Program the qPCR device using the QR Code/Link as indicated in **Table 6.**
2. Take the PCR kit out of the -20°C freezer.
3. Pipette (Sample Count + 3) *2,5 µL of Brucella spp. Oligo Mix into an empty eppendorf tube. (i.e Sample Count = 3, pipette 2,5*(3+3) = 15 µL of Brucella spp. Oligo Mix)
4. Add (Sample Count + 3) *5 µL of 2X qPCR Mix into the tube prepared in Step 3. (i.e Sample Count = 3, pipette 5*(3+3) = 30 µL of 2X qPCR Mix)
5. Vortex the master mix to homogenize.
6. Pipette 7,5 µL of master mix into all PCR tubes, or wells to be used (including all samples, NTC and PC).
7. Pipette 2,5 µL of each extracted/isolated sample into the relative PCR tube, or well.
8. Pipette 2,5 µL of NTC into the Negative Control PCR tube, or well.
9. Pipette 2,5 µL of PC-Brucella spp into the Positive Control tube, or well.
10. Close the cap of the strips or PCR tubes or seal the PCR plate. Label to avoid confusion during spin-centrifuge.
11. Spin-centrifuge the strips, or PCR tubes or PCR plate.
12. Open the lid of the instrument. Place the strips, or PCR tubes or PCR plate.
13. Close the lid and start the instrument.

Table 6. Real-Time qPCR Program Details

Reaction Setup		qPCR Program							
		Protocol 1: Bio Molecular Systems: Magnetic Induction Cycler (Mic)/Mic IVD, Bio-Rad: CFX96 Touch/Dx, CFX Opus 96/Dx, CFX384 Touch, CFX Opus 384, Roche: LightCycler 96, Co-Dx: Co-Dx Box, Azure: Cielo				**Protocol 2:** Qiagen: Rotor-Gene Q 5-Plex/MDx, Thermo Fisher Scientific: QuantStudio 5/5 Dx/6/7/12k Flex/Pro, StepOne Plus, Applied Biosystems 7500/7500 Fast, Adaltis: AmpliLab, MDXlab, HiMedia: InstaQ 96, Bioer: Linegene 9600 Plus, Atila Biosystems: Fujirebio, Tianlong: Gentier 96E, Sansure: SLAN-96P			
Reagent	**Volume/ Rxn**	**Step**	**Cycle No.**	**Temperature**	**Duration**	**Step**	**Cycle No.**	**Temperature**	**Duration**
2X qPCR Mix	5 µL	**Enzyme Activation**	1 Cycle	52 °C	3 min	**Enzyme Activation**	1 Cycle	52 °C	3 min
		Pre-Incubation	1 Cycle	95 °C	10 sec	**Pre-Incubation**	1 Cycle	95 °C	10 sec
Oligo Mix	2,5 µL	**Denaturation**	12 Touchdown Cycles: 1 °C decrement in annealing temperature per cycle	95 °C	1 sec	**Denaturation**	40 Cycles	95 °C	1 sec
		Annealing and Extension		67 °C to 56 °C	15 sec	**Annealing and Extension**		55 °C	15 sec
Template Nucleic Acid/NTC/PC	2,5 µL	**Denaturation**	30 Cycles	95 °C	1 sec	**Detection (Reading)**		FAM/HEX	
		Annealing and Extension		55 °C	15 sec				
Total Reaction Volume	**10 µL**	**Detection (Reading)**		FAM/HEX					

WARNING: The qPCR program file should be downloaded from the QR code on the left or from the link below.

https://www.bioeksen.com.tr/files/L_TD_43B

2. INTERPRETATION OF THE ASSAY RESULTS

Cq values of the results obtained from PCR instruments indicated in **Table 7** are calculated referring to the relative RFU threshold levels and Cq cut-offs. Auto-threshold and default options are used for devices not included in **Table 7**. For all targets that do not exceed the Cq cut-off, the shape of the amplification curve must be analyzed, and Cq values of the sigmoidal curves must be determined. Non-sigmoidal curves must be reported as "negative". The PCR results can be reported manually, as indicated in **Table 8**, or using the "**Sigmoida**" software for BMS Magnetic Induction Cycler (Mic)/Mic IVD and Bio-Rad CFX instruments. Sigmoida software sorts each target as positive or negative. To obtain the "**Sigmoida**" software installer, please send an e-mail to support@bioeksen.com.tr.

Table 7. Threshold Levels and Cq Cut-offs for Calculating Cq Values

Analyte	Real Time PCR Instrument											
	Bio-Rad CFX		Cielo		LightCycler 96		Mic/Mic IVD and Co-Dx Box		Rotor-Gene Q***		QuantStudio 5/5 Dx/6/7/12k Flex/Pro	
	RFU	Cq Cut-off	RFU	Cq Cut-off	RFU	Cq Cut-off	RFU	Cq Cut-off	RFU	Cq Cut-off	RFU	Cq Cut-off
Human (IC-Internal Control)	200	30	20000	30	0.05	30	0.2	30	0.02	40	20000	30
Brucella spp.	200	30	20000	30	0.05	30	0.2	30	0.02	40	20000	30

*** Defined threshold with specific settings of "Outlier Removal = 0", "Dynamic Tube = On", and "Slope Correct = Off"

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Table 8. Interpretation of Patient Results

Target	Internal Control (IC)	Result Interpretation		
Positive (+)	**Positive (+)** or **Negative (-)**	Results are valid Target is detected	**Protocol 1**	If 26<Cq ≤30 "Low Positive" If 16<Cq≤26 "Positive" If Cq≤16 "High Positive"
			Protocol 2	If 34<Cq ≤40 "Low Positive" If 22<Cq≤34 "Positive" If Cq≤22 "High Positive"
Negative (-)	**Positive (+)**	Results are valid Target is not detected		

Table 9. Expected Performance of Kit Controls

Control Type	Purpose	Expected Results and Cq Values			
		Protocol 1		Protocol 2	
		IC (HEX)	Target	IC (HEX)	Target
Negative Control	Contamination control during qPCR	**Not Detected**	**Not Detected**	**Not Detected**	**Not Detected**
Positive Control	Reagent stability control	**Detected** (Cq≤30)	**Detected** (Cq≤30)	**Detected** (Cq≤40)	**Detected** (Cq≤40)
Internal Control	Nucleic acid extraction and sampling control	**Detected**	Detection insignificant	**Detected**	Detection insignificant
		If "**Not Detected**" check the target Cq	If "**Detected"** IC is valid	If "**Not Detected**" check the target Cq	If "**Detected"** IC is valid

If a control does not work as expected (**Table 9**), apply the procedures described below.

1. **Contamination Problem:** If a target in the Negative Control reaction is "**Detected**".
   Recommended action: Repeat the run, paying attention to the "Warnings and Limitations" section.

2. **Invalid Internal Control Problem:** If the Internal Control (IC) and all other targets of a sample are "**Not Detected**".
   Recommended action: Sampling was not successfully done, or there was a problem during the sample transportation or extraction. Re-test the sample. If the problem repeats, a new sample from the same patient should be collected and tested again.

3. **Reagent Problem**: If all Internal Controls, Positive Controls and targets in the run are "**Not Detected**".
   Recommended action: The run is considered invalid. Re-test the PC. If the problem repeats, please reach out to the manufacturer for further assistance.

For positive blood culture samples:

All default analysis options (e.g., auto-calculated threshold) in the **Magnetic Induction Cycler (Mic)/Mic IVD (Bio Molecular System - BMS)** software should not be changed to calculate Cq values.
If the Cq value is **≤23**, it is reported as **positive.**

If the Cq value is **>23**, it is reported as **negative.**

The results produced by the qPCR instrument can manually be reported as described above or can automatically be reported using the "**Sigmoida**" software.

3. WARNINGS AND LIMITATIONS

1. False-negative results may occur if inadequate number (below the LoD) of organisms are present in the specimen.
2. Mutations within the target regions could affect primer and/or probe binding, resulting in failure to detect the presence of agents.
3. False-negative results may occur if a specimen is improperly collected, transported, or handled.
4. The clinical specimens shall be collected by a healthcare provider in accordance with the national/international specimen collection guidelines.
5. Test procedures should be performed by personnel trained in the use of the kit.
6. Sample tubes should always be kept closed except for liquid transfers.
7. Filtered and nuclease-free pipette tips should be used for sample transfer.
8. The components in the kit should not be used together with different LOT numbers or chemicals of the same name but from different manufacturers.
9. ***The caps of the reaction tubes must not be opened after the PCR run.*** The PCR tubes should be placed in a bag and thrown away after the bag is tightly closed.
10. The surfaces of the workbenches should be wiped with freshly diluted 10% bleach (0.5% NaClO) at the beginning and end of each day.
11. Waste disposal must be carried out in accordance with local, state, and federal regulations.
12. Proper personal protective equipment including lab coats, gowns, gloves, eye protection, and a biological safety cabinet are recommended for manipulation of clinical specimens.
13. Immediately clean up any spill containing potentially infectious material with 0.5-1% (w/v) sodium hypochlorite (10-20% v/v bleach). Dispose of cleaning materials in a biohazard waste stockpot.
14. The micropipettes used for pipetting PCR mixes and template nucleic acids should be separate. Filtered and nuclease-free pipette tips should be used.
15. Maintenance/ calibration interval should be determined for all instruments and equipment used with the kit.

4. EXPLANATION OF SYMBOL

Symbol	Title of Symbol	Symbol	Title of Symbol	Symbol	Title of Symbol
CE	European Conformity CE Mark	LOT	Batch code		Keep away from sunlight
IVD	*In vitro* diagnostic *medical device*	REF	Catalogue number		Protect from heat and radioactive sources
	Manufacturer	NON STERILE	Non-*sterile*		Do not use if package is damaged and consult I*nstructions for Use*
	Expiration Date YYYY-MM		Consult I*nstructions for Use* or consult electronic I*nstructions for Use*		Keep dry

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For professional use only.

CONTROL −	Negative Control	⚠	Caution		Keep upright
CONTROL +	Positive Control		Temperature limit	Σ	Contains sufficient for <*n*> tests
CONTROL	Control				

5. MANUFACTURER AND TECHNICAL SUPPORT

Bioeksen AR GE Teknolojileri A.Ş
Address: Huzur Mah. Metin Oktay Cad. Nurol Life Sitesi D Blok No:3/31, 34396 Sarıyer/İstanbul-TÜRKİYE
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Web: www.bioeksen.com.tr, **E-mail:** info@bioeksen.com.tr,
Technical Support: support@bioeksen.com.tr

Notice to User: Please inform us about product-related incidents at " **vigilance@bioeksen.com.tr** " within 24 hours.

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For professional use only.
Cat No: BS-RTV-T-25/ BS-RTV-T-100
Ordering Ref No: RTI-P3-T-25/ RTI-P3-T-100

Respiratory Tract Virus RT-qPCR Panel

Package Insert

Table 1. Kit Content

Component	Intended Use	25 Reactions	100 Reactions
2X Prime Script Mix	Optimized ready-to-use mix for RT-qPCR assay	1 x 1000 µL	4 x 1000 µL
RTV Oligo Mix 1	Specific nucleic acid amplification and detection: **FAM:** SARS-CoV-2 **HEX:** Human (IC-Internal Control) **ROX:** Influenza B **CY5:** Influenza A	1 x 125 µL	1 x 500 µL
RTV Oligo Mix 2	**FAM**: Human Coronavirus 229E/ OC43 **HEX:** Human Parainfluenza 1/2 **ROX:** Human Coronavirus NL63/ HKU1 **CY5:** Human Parainfluenza 3/4	1 x 125 µL	1 x 500 µL
RTV Oligo Mix 3	**FAM**: Respiratory Syncytial Virus A/B **HEX:** Human Metapneumovirus **ROX:** Human Enterovirus **CY5:** Human Adenovirus	1 x 125 µL	1 x 500 µL
RTV Oligo Mix 4	**FAM**: Human Bocavirus **CY5:** Human Rhinovirus	1 x 125 µL	1 x 500 µL
NTC	Negative Control	1 x 1000 µL	1 x 1000 µL
PC-RTV 1 / PC-RTV 2 PC-RTV 3 / PC-RTV 4	Positive Control (PC)	1 x 100 µL	1 x 100 µL

Table 2. Transport Condition, Storage Condition, and Shelf Life of the Components

Component	Transport Condition	Storage Condition*	Shelf Life
2X Prime Script Mix	(-22) °C – (+8) °C	(-22) °C – (-18) °C	12 months
Oligo Mix		(-22) °C – (-18) °C	
NTC		(-22) °C – (-18) °C before opening, (+2) °C – (+8) °C after first thaw	
PC		(-22) °C – (-18) °C before opening, (+2) °C – (+8) °C after first thaw	

* Following the first opening, each reagent stored at storage temperature can be used until the expiration date indicated on the tube. The kit's expiration date is determined by the expiration date of the reagents.

Table 3. Required Components Not Included in the Package

Required Components Not Included in the Package
1. Real-Time PCR Instrument
2. Bioeksen **νNAT® Transfer Tube** (Cat. No: BS-NA-513m) or nucleic acid preparation instruments and nucleic acid preparation consumables
3. Micropipettes and compatible filtered pipette tips (nuclease-free) suitable for transferring 1-10 µL, 10-100 µL, and 100-1000 µL of liquid
4. A centrifuge or Mini-spin
5. Vortex
6. Reaction tubes,PCR strips, PCR plates and caps/films specific to qPCR instruments and compatible with the reaction volume

Table 4. Intended Use, Test Principle, and Analytical Specifications

Function	Aid to diagnosis	**Sample Type(s)**	**Table 5**
Analyte(s)	**Table 1**	**Nucleic Acid Preparation Method(s)**	Bioeksen **νNAT® Transfer Tube** Zybio EXM3000 Nucleic Acid Isolation System Adaltis EXTRAlab and MDXlab
Qualitative/Quantitative	Qualitative	**Validated qPCR Instrument(s)**	Bio Molecular Systems: Magnetic Induction Cycler (Mic)/Mic IVD Bio-Rad: CFX96 Touch/Dx, CFX Opus 96/Dx, CFX384 Touch, CFX Opus 384 Qiagen: Rotor-Gene Q 5-Plex/MDx Roche: LightCycler 96 Thermo Fisher Scientific: QuantStudio 5/5 Dx/6/7/12k Flex/Pro, StepOne Plus, Applied Biosystems 7500/7500 Fast Adaltis: AmpliLab, MDXlab HiMedia: InstaQ 96 Bioer: Linegene 9600 Plus Atila Biosystems: Fujirebio Co-Dx: Co-Dx Box Tianlong: Gentier 96E Sansure: SLAN-96P Azure: Cielo
Test Principle	Reverse transcription and Real-Time PCR (RT-qPCR)	**Inclusivity and Exclusivity**	Validated on the reference strains and the field isolates.
Automated/Manual	Manual		
Intended Users	Laboratory professionals trained in the techniques of qPCR and in vitro diagnostic procedures	**Limit of Detection (LoD)**	**Table 5**

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Target Population	Individuals with the suspected infection	Sensitivity and Specificity	99.93% and 99.14%

Table 5. Collection, Storage, Transfer and Nucleic Acid Preparation Method of Clinical Specimens

Sample Type**	Sample Transfer	Sample Storage	Nucleic Acid Preparation Method	LoD (cp/mL)
Combined nasopharyngeal and oropharyngeal swab samples ***	**vNAT® Transfer Tube** (Cat. No: BS-NA-513m)	3 months at (+2) °C – (+8) °C 1 year at (-20) °C	Nucleic acid preparation is not needed, samples can be used directly in RT-qPCR	250
	Transport Medium (without antibiotics)	3 days at (+2) °C – (+8) °C 1 year at (-20) °C	**Nucleic acid preparation instruments:** 1) Zybio EXM3000, 2) Adaltis EXTRAlab, 3) Adaltis MDXlab	125
Bronchoalveolar lavage (BAL), sputum, and nasopharyngeal aspirate (NAP) samples	Preservative-free sterile containers/tubes	3 days at (+2) °C – (+8) °C 1 year at (-20) °C	**Nucleic acid preparation consumables:** Bioeksen Bio-Speedy® Rapid Nucleic Acid Extraction Kit (Cat. No: ZFNAE01)	500

** Clinical specimens should be collected by a healthcare provider in accordance with national/international clinical specimen collection regulations.
*** If dry swab samples are received, put them into the **vNAT® Transfer Tube** for nucleic acid isolation.

1. APPLICATION PROTOCOL

1. Program the qPCR device using the QR Code/Link as indicated in Table 6.
2. Take the PCR kit out of the -20°C freezer.
3. Pipette (Sample Count + 3) *5 µL of RTV Oligo Mix 1 into an empty eppendorf tube. (i.e Sample Count = 3, pipette 5*(3+3) = 30 µL of RTV Oligo Mix)
4. Add (Sample Count + 3) *10 µL of 2X Prime Script Mix into RTV Oligo Mix 1. (i.e Sample Count = 3, pipette 10*(3+3) = 60 µL of 2X Prime Script Mix)
5. Vortex the master mix to homogenize.
6. Repeat Steps 3, 4 and 5 for all master mixes (4 master mixes in total).
7. Pipette 15 µL of each master mix into relative PCR tube, or wells to be used (including all samples, NTC and PC).
8. Pipette 5 µL of extracted/isolated sample into relative PCR tube, or wells.
9. Pipette 5 µL of NTC into the Negative Control PCR tube, or wells.
10. Pipette 5 µL of PC-RTV 1 into the relative PC tube, or wells. Repeat for all PC.
11. Close the cap of the strips, or PCR tubes or seal PCR plate. Label to avoid confusion during spin-centrifuge.
12. Spin-centrifuge the strips, or PCR tubes and PCR plate.
13. Open the lid of the instrument. Place the strips, or PCR tubes and PCR plate.
14. Close the lid and start the instrument.

Table 6. Real-Time qPCR Program Details

Reaction Setup		RT-qPCR Program							
		Protocol 1: Bio Molecular Systems: Magnetic Induction Cycler (Mic)/Mic IVD, Bio-Rad: CFX96 Touch/Dx, CFX Opus 96/Dx, CFX384 Touch, CFX Opus 384, Roche: LightCycler 96, Co-Dx: Co-Dx Box, Azure: Cielo				**Protocol 2:** Qiagen: Rotor-Gene Q 5-Plex/MDx, Thermo Fisher Scientific: QuantStudio 5/5 Dx/6/7/12k Flex/Pro, StepOne Plus, Applied Biosystems 7500/7500 Fast, Adaltis: AmpliLab, MDXlab, HiMedia: InstaQ 96, Bioer: Linegene 9600 Plus, Atila Biosystems: FujirebioTianlong: Gentier 96E, Sansure: SLAN-96P			
Reagent	**Volume/Rxn**	**Step**	**Cycle No.**	**Temperature**	**Duration**	**Step**	**Cycle No.**	**Temperature**	**Duration**
2X Prime Script Mix	10 µL	**Reverse Transcription**	1 Cycle	52 °C	3 min	**Reverse Transcription**	1 Cycle	52 °C	3 min
		Pre-Incubation	1 Cycle	95 °C	10 sec	**Pre-Incubation**	1 Cycle	95 °C	10 sec
Oligo Mix	5 µL	**Denaturation**	12 Touchdown Cycles: 1 °C decrement in annealing temperature per cycle	95 °C	1 sec	**Denaturation**	40 Cycles	95 °C	1 sec
		Annealing and Extension		67 °C to 56 °C	15 sec	**Annealing and Extension**		55 °C	15 sec
Template Nucleic Acid/NTC/PC	5 µL	**Denaturation**	30 Cycles	95 °C	1 sec	**Detection (Reading)**		FAM/HEX/ROX/CY5	
		Annealing and Extension		55 °C	15 sec				
Total Reaction Volume	**20 µL**	**Detection (Reading)**		FAM/HEX/ROX/CY5					

WARNING: The qPCR program file should be downloaded from the QR code on the left or from the link below.

https://www.bioeksen.com.tr/files/L_TD_43B

2. INTERPRETATION OF THE ASSAY RESULTS

Cq values of the results obtained from PCR instruments indicated in **Table 7** are calculated referring to the relative RFU threshold levels and Cq cut-offs. Auto-threshold and default options are used for devices not included in **Table 7**. For all targets that do not exceed the Cq cut-off, the shape of the amplification curve must be analyzed, and Cq values of the sigmoidal curves must be determined. Non-sigmoidal curves must be reported as "negative". The PCR results can be reported manually, as indicated in **Table 8**, or using the "**Sigmoida**" software for BMS Magnetic Induction Cycler (Mic)/Mic IVD and Bio-Rad CFX instruments. Sigmoida software sorts each target as positive or negative. To obtain the "**Sigmoida**" software installer, please send an e-mail to support@bioeksen.com.tr.

Table 7. Threshold Levels for Calculating Cq Values

Analyte	Real Time PCR Instrument											
	Bio-Rad CFX		Cielo		LightCycler 96		Mic/Mic IVD and Co-Dx Box		Rotor-Gene Q****		QuantStudio 5/5 Dx/6/7/12k Flex/Pro	
	RFU	Cq Cut-off	RFU	Cq Cut-off	RFU	Cq Cut-off	RFU	Cq Cut-off	RFU	Cq Cut-off	RFU	Cq Cut-off
SARS-CoV-2	200	30	20000	30	0.05	30	0.5	30	0.02	40	20000	30

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Human (IC-Internal Control)	200	30	20000	30	0.05	30	0.5	30	0.02	40	20000	30
Influenza B	750	30	75000	30	0.1	30	0.5	30	0.05	40	75000	30
Influenza A	200	30	20000	30	0.05	30	0.5	30	0.02	40	20000	30
Human Coronavirus 229E/ OC43	750	30	75000	30	0.1	30	0.5	30	0.05	40	20000	30
Human Parainfluenza 1/2	750	30	75000	30	0.1	30	0.5	30	0.05	40	20000	30
Human Coronavirus NL63/ HKU1	750	30	75000	30	0.1	30	0.5	30	0.05	40	20000	30
Human Parainfluenza 3/4	750	30	75000	30	0.1	30	0.5	30	0.05	40	20000	30
Respiratory Syncytial Virus A/B	750	30	75000	30	0.1	30	0.5	30	0.05	40	20000	30
Human Metapneumovirus	750	30	75000	30	0.1	30	0.5	30	0.05	40	20000	30
Human Enterovirus	750	30	75000	30	0.1	30	0.5	30	0.05	40	20000	30
Human Adenovirus	200	30	20000	30	0.05	30	0.5	30	0.02	40	20000	30
Human Bocavirus	750	30	75000	30	0.1	30	0.5	30	0.05	40	20000	30
Human Rhinovirus	200	30	20000	30	0.05	30	0.5	30	0.02	40	20000	30

**** Defined threshold with specific settings of "Outlier Removal = 0", "Dynamic Tube = On", and "Slope Correct = Off"

Table 8. Interpretation of Patient Results

Target	Internal Control (IC)	Result Interpretation		
Positive (+)	**Positive (+)** or **Negative (-)**	Results are valid Target is detected	**Protocol 1**	If 26<Cq ≤30 "Low Positive" If 16<Cq≤26 "Positive" If Cq≤16 "High Positive"
			Protocol 2	If 34<Cq ≤40 "Low Positive" If 22<Cq≤34 "Positive" If Cq≤22 "High Positive"
Negative (-)	**Positive (+)**	Results are valid Target is not detected		

Table 9. Expected Performance of Kit Controls

Control Type	Purpose	Expected Results and Cq Values			
		Protocol 1		Protocol 2	
		IC (HEX)	Target	IC (HEX)	Target
Negative Control	Contamination control during RT-qPCR	**Not Detected**	**Not Detected**	**Not Detected**	**Not Detected**
Positive Control	Reagent stability control	**Detected** (Cq≤30)	**Detected** (Cq≤30)	**Detected** (Cq≤40)	**Detected** (Cq≤40)
Internal Control	Nucleic acid extraction and sampling control	**Detected**	Detection insignificant	**Detected**	Detection insignificant
		If "**Not Detected**" check the target Cq	If "**Detected"** IC is valid	If "**Not Detected**" check the target Cq	If "**Detected"** IC is valid

If a control does not work as expected (**Table 9**), apply the procedures described below.

1. **Contamination Problem:** If a target in the Negative Control reaction is "**Detected**".
   Recommended action: Repeat the run, paying attention to the "Warnings and Limitations" section.

2. **Invalid Internal Control Problem:** If the Internal Control (IC) and all other targets of a sample are "**Not Detected**".
   Recommended action: Sampling was not successfully done, or there was a problem during the sample transportation or extraction. Re-test the sample. If the problem repeats, a new sample from the same patient should be collected and tested again.

3. **Reagent Problem**: If all Internal Controls, Positive Controls and targets in the run are "**Not Detected**".
   Recommended action: The run is considered invalid. Re-test the PC. If the problem repeats, please reach out to the manufacturer for further assistance.

3. WARNINGS AND LIMITATIONS

1. False-negative results may occur if inadequate number (below the LoD) of organisms are present in the specimen.
2. Mutations within the target regions could affect primer and/or probe binding, resulting in failure to detect the presence of agents.
3. The use of cotton or calcium alginate swabs or swabs with wooden sticks can lead to false negative results since they may contain substances that inactivate some pathogens and inhibit PCR.
4. False-negative results may occur if a specimen is improperly collected, transported, or handled.
5. The clinical specimens shall be collected by a healthcare provider in accordance with the national/international specimen collection guidelines.
6. Test procedures should be performed by personnel trained in the use of the kit.
7. Sample tubes should always be kept closed except for liquid transfers.
8. Filtered and nuclease-free pipette tips should be used for sample transfer.
9. The components in the kit should not be used together with different LOT numbers or chemicals of the same name but from different manufacturers.
10. ***The caps of the reaction tubes must not be opened after the PCR run.*** The PCR tubes should be placed in a bag and thrown away after the bag is tightly closed.
11. The surfaces of the workbenches should be wiped with freshly diluted 10% bleach (0.5% NaClO) at the beginning and end of each day.
12. Waste disposal must be carried out in accordance with local, state, and federal regulations.
13. Proper personal protective equipment including lab coats, gowns, gloves, eye protection, and a biological safety cabinet are recommended for manipulation of clinical specimens.
14. Immediately clean up any spill containing potentially infectious material with 0.5-1% (w/v) sodium hypochlorite (10-20% v/v bleach). Dispose of cleaning materials in a biohazard waste stockpot.
15. The micropipettes used for pipetting PCR mixes and template nucleic acids should be separate. Filtered and nuclease-free pipette tips should be used.
16. Maintenance/ calibration interval should be determined for all instruments and equipment used with the kit.

4. EXPLANATIONS OF SYMBOLS

Symbol	Title of Symbol	Symbol	Title of Symbol	Symbol	Title of Symbol
CE	European Conformity CE Mark	LOT	Batch code		Keep away from sunlight
IVD	*In vitro* diagnostic medical device	REF	Catalog number		Protect from heat and radioactive sources

For in vitro diagnostic use only.
For professional use only.

	Manufacturer		Non-sterile		Do not use if package is damaged and consult *Instructions for Use*
	Expiration Date YYYY-MM		Consult *Instructions for Use* or consult electronic *Instructions for Use*		Keep dry
	Negative Control		Caution		Keep upright
	Positive Control		Temperature limit		Contains sufficient for <*n*> tests
	Control				

5. MANUFACTURER AND TECHNICAL SUPPORT

Bioeksen AR GE Teknolojileri A.Ş
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Web: www.bioeksen.com.tr, **e-mail:** info@bioeksen.com.tr,
Technical Support: support@bioeksen.com.tr

Notice to User: Please send an e-mail to **vigilance@bioeksen.com.tr** about product-related incidents, within 24 hours.

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For professional use only.
Cat No: BS-LP-25/BS-LP-100
Ordering Ref No: LPNEU-T-25/LPNEU-T-100

Legionella pneumophila qPCR Kit

Package Insert

Table 1. Kit Content

Component	Intended Use	25 Reactions	100 Reactions
2X qPCR Mix	Optimized ready-to-use mix for RT-qPCR assay	1 x 125 µL	1 x 500 µL
LP Oligo Mix	Specific nucleic acid amplification and detection: **FAM**: *Legionella pneumophila* **HEX:** Human (Internal Control)	1 x 62.5 µL	1 x 250 µL
NTC	Negative Control	1 x 1000 µL	1 x 1000 µL
PC-LP	Positive Control (PC)	1 x 100 µL	1 x 100 µL

Table 2. Transport Condition, Storage Condition, and Shelf Life of the Components

Component	Transport Condition	Storage Condition*	Shelf Life
2X qPCR Mix	(-22) – (+8) °C	(-22) – (-18) °C	12 Months
Oligo Mix		(-22) – (-18) °C	
PC		(-22) °C – (-18) °C before opening, (+2) °C – (+8) °C after first thaw	
NTC		(-22) °C – (-18) °C before opening, (+2) °C – (+8) °C after first thaw	

* Following the first opening, each reagent stored at storage temperature can be used until the expiration date indicated on the tube. The kit's expiration date is determined by the expiration date of the reagents.

Table 3. Required Components Not Included in the Package

Required Components Not Included in the Package
1. Real-Time PCR Instrument
2. Bioeksen **vNAT® Transfer Tube** (Cat. No: BS-NA-513m) or nucleic acid preparation instruments and nucleic acid preparation consumables
3. Micropipettes and compatible filtered pipette tips (nuclease-free) suitable for transferring 1-10 µL, 10-100 µL, and 100-1000 µL of liquid
4. A centrifuge or Mini-spin
5. Vortex
6. Reaction tubes,PCR strips, PCR plates and caps/films specific to qPCR instruments and compatible with the reaction volume

Table 4. Intended Use, Test Principle, and Analytical Specifications

Function	Aid to diagnosis	**Sample Type(s)**	**Table 5**
Analyte(s)	**Table 1**	**Nucleic Acid Extraction Method(s)**	Bioeksen **vNAT® Transfer Tube** Zybio EXM3000 Nucleic Acid Isolation System Adaltis EXTRAlab and MDXlab
Qualitative/Quantitative	Qualitative	**Validated qPCR Instrument(s)**	Bio Molecular Systems: Magnetic Induction Cycler (Mic)/Mic IVD Bio-Rad: CFX96 Touch/Dx, CFX Opus 96/Dx, CFX384 Touch, CFX Opus 384 Qiagen: Rotor-Gene Q 5-Plex/MDx Roche: LightCycler 96 Thermo Fisher Scientific: QuantStudio 5/5 Dx/6/7/12k Flex/Pro, StepOne Plus, Applied Biosystems 7500/7500 Fast Adaltis: AmpliLab, MDXlab HiMedia: InstaQ 96 Bioer: Linegene 9600 Plus Atila Biosystems: Fujirebio Co-Dx: Co-Dx Box Tianlong: Gentier 96E Sansure: SLAN-96P Azure: Cielo
Test Principle	Real-Time PCR (qPCR)	**Inclusivity and Exclusivity**	Validated on the reference strains and the field isolates
Automated/Manual	Manual		
Intended Users	Laboratory professionals trained in the techniques of qPCR and in vitro diagnostic procedures	**Limit of Detection (LoD)**	**Table 5**
Target Population	Individuals with the suspected infection	**Sensitivity and Specificity**	%100.00 ve %100.00

Table 5. Collection, Storage, and Transfer of Clinical Specimens / Nucleic Acid Preparation Methods

Sample Type**	Sample Transfer	Sample Storage	Nucleic Acid Preparation Method	LoD (cp/mL)
Combined nasopharyngeal, and oropharyngeal swabs***	**vNAT® Transfer Tube** (Cat. No: BS-NA-513m)	3 months at (+2) °C – (+8) °C 1 year at (-20) °C	Nucleic acid preparation is not required. The sample can be used directly in qPCR.	250
	Viral Transport Medium (VTM) (CDC SOP#: DSR-052-05 (without antibiotic))	3 days at (+2) °C – (+8) °C 1 year at (-20) °C	**Nucleic acid preparation instruments:** 1) Zybio EXM3000,2) Adaltis EXTRAlab, 3) Adaltis MDXlab **Nucleic acid preparation consumables:** Bioeksen Bio- Speedy® Rapid Nucleic Acid Extraction Kit (Cat. No: ZFNAE01)	125
Bronchoalveolar lavage (BAL) and nasopharyngeal aspirate	Preservative-free sterile containers/tubes	3 days at (+2) °C – (+8) °C 1 year at (-20) °C		500

**Clinical specimens should be collected by a healthcare provider in accordance with national/international clinical specimen collection regulations.

Revision Date: 2024-11-19/Rev.03
Published Date: 2023-10-04

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*** If dry swab samples are received, put them into the **vNAT® Transfer Tube** for nucleic acid isolation.

1. APPLICATION PROTOCOL

1. Program the qPCR device using the QR Code/Link as indicated in **Table 6**.
2. Take the PCR kit out of the -20°C freezer.
3. Pipette (Sample Count + 3) *2.5 µL of LP Oligo Mix into an empty eppendorf tube. (i.e Sample Count = 3, pipette 2.5*(3+3) = 15 µL of LP Oligo Mix)
4. Add (Sample Count + 3) *5 µL of 2X qPCR Mix into the tube prepared in Step 3. (i.e Sample Count = 3, pipette 5*(3+3) = 30 µL of 2X qPCR Mix)
5. Vortex the master mix to homogenize.
6. Pipette 7.5 µL of master mix into all PCR tubes, or wells to be used (including all samples, NTC and PC).
7. Pipette 2.5 µL of each isolated/ extracted sample into the relative PCR tube, or well.
8. Pipette 2.5 µL of NTC into the Negative Control PCR tube, or well.
9. Pipette 2.5 µL of PC-LP into the Positive Control tubes, or wells.
10. Close the cap of the strips, or PCR tubes or seal PCR plate. Label to avoid confusion during spin-centrifuge.
11. Spin-centrifuge the strips, or PCR tubes or PCR plates.
12. Open the lid of the instrument. Place the strips, PCR tubes or PCR plate.
13. Close the lid and start the instrument.

Table 6. Real Time qPCR Program Details

Reaction Setup		qPCR Program							
		Protocol 1: Bio Molecular Systems: Magnetic Induction Cycler (Mic)/Mic IVD, Bio-Rad: CFX96 Touch/Dx, CFX Opus 96/Dx, CFX384 Touch, CFX Opus 384, Roche: LightCycler 96, Co-Dx: Co-Dx Box, Azure: Cielo				**Protocol 2:** Qiagen: Rotor-Gene Q 5-Plex/MDx, Thermo Fisher Scientific: QuantStudio 5/5 Dx/6/7/12k Flex/Pro, StepOne Plus, Applied Biosystems 7500/7500 Fast, Adaltis: AmpliLab, MDXlab, HiMedia: InstaQ 96, Bioer: Linegene 9600 Plus, Atila Biosystems: FujirebioTianlong: Gentier 96E, Sansure: SLAN-96P			
Reagent	**Volume/Rxn**	**Step**	**Cycle No.**	**Temperature**	**Duration**	**Step**	**Cycle No.**	**Temperature**	**Duration**
2X qPCR Mix	5 µL	**Enzyme Activation**	1 Cycle	52 °C	3 min	**Enzyme Activation**	1 Cycle	52 °C	3 min
		Pre-Incubation	1 Cycle	95 °C	10 sec	**Pre-Incubation**	1 Cycle	95 °C	10 sec
Oligo Mix	2.5 µL	**Denaturation**	12 Touchdown Cycles: 1 °C decrement in annealing temperature per cycle	95 °C	1 sec	**Denaturation**	40 Cycles	95 °C	1 sec
		Annealing and Extension		67 °C to 56 °C	15 sec	**Annealing and Extension**		55 °C	15 sec
Template Nucleic Acid/NTC/PC	2.5 µL	**Denaturation**	30 Cycles	95 °C	1 sec	**Detection (Reading)**		FAM/HEX	
		Annealing and Extension		55 °C	15 sec				
Total Reaction Volume	**10 µL**	**Detection (Reading)**		FAM/HEX					

WARNING: The qPCR program file should be downloaded from the QR code on the left or from the link below.

https://www.bioeksen.com.tr/files/L_TD_43B

2. INTERPRETATION OF THE ASSAY RESULTS

Cq values of the results obtained from PCR instruments indicated in **Table 7** are calculated referring to the relative RFU threshold levels and Cq cut-offs. Auto-threshold and default options are used for devices not included in **Table 7**. For all targets that do not exceed the Cq cut-off, the shape of the amplification curve must be analyzed, and Cq values of the sigmoidal curves must be determined. Non-sigmoidal curves must be reported as "negative". The PCR results can be reported manually, as indicated in **Table 8**, or using the "**Sigmoida**" software for BMS Magnetic Induction Cycler (Mic)/Mic IVD and Bio-Rad CFX instruments. Sigmoida software sorts each target as positive or negative. To obtain the "**Sigmoida**" software installer, please send an e-mail to support@bioeksen.com.tr.

Table 7. Threshold Levels and Cq Cut-offs for Calculating Cq Values

Analyte	Real Time PCR Instrument											
	Bio-Rad CFX		**Cielo**		**LightCycler 96**		**Mic/Mic IVD and Co-Dx Box**		**Rotor-Gene Q****		**QuantStudio 5/5 Dx/6/7/12k Flex/Pro**	
	RFU	**Cq Cut-off**	**RFU**	**Cq Cut-off**	**RFU**	**Cq Cut-off**	**RFU**	**Cq Cut-off**	**RFU**	**Cq Cut-off**	**RFU**	**Cq Cut-off**
Legionella pneumophila	200	30	20000	30	0.05	30	0.2	30	0.05	40	20000	30
Human (IC-Internal Control)	200	30	20000	30	0.05	30	0.2	30	0.02	40	20000	30

**** Defined threshold with specific settings of "Outlier Removal = 0", "Dynamic Tube = On", and "Slope Correct = Off"

Table 8. Interpretation of Patient Results

Target	Internal Control (IC)	Result Interpretation		
Positive (+)	**Positive (+)** or **Negative (-)**	Results are valid Target is detected	**Protocol 1**	If 26<Cq ≤30 "Low Positive" If 16<Cq≤26 "Positive" If Cq≤16 "High Positive"
			Protocol 2	If 34<Cq ≤40 "Low Positive" If 22<Cq≤34 "Positive" If Cq≤22 "High Positive"
Negative (-)	**Positive (+)**	Results are valid Target is not detected		

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Table 9. Expected Performance of Kit Controls

Control Type	Purpose	Expected Results and Cq Values			
		Protocol 1		Protocol 2	
		IC (HEX)	Target	IC (HEX)	Target
Negative Control	Contamination control during qPCR	**Not Detected**	**Not Detected**	**Not Detected**	**Not Detected**
Positive Control	Reagent stability control	**Detected** (Cq≤30)	**Detected** (Cq≤30)	**Detected** (Cq≤40)	**Detected** (Cq≤40)
Internal Control	Nucleic acid extraction and sampling control	**Detected**	Detection insignificant	**Detected**	Detection insignificant
		If "**Not Detected**" check the target Cq	If "**Detected"** IC is valid	If "**Not Detected**" check the target Cq	If "**Detected"** IC is valid

If a control does not work as expected (**Table 9**), apply the procedures described below.

1. **Contamination Problem:** If a target in the Negative Control reaction is "**Detected**".
   Recommended action: Repeat the run, paying attention to the "Warnings and Limitations" section.

2. **Invalid Internal Control Problem:** If the Internal Control (IC) and all other targets of a sample are "**Not Detected**".
   Recommended action: Sampling was not successfully done, or there was a problem during the sample transportation or extraction. Re-test the sample. If the problem repeats, a new sample from the same patient should be collected and tested again.

3. **Reagent Problem**: If all Internal Controls, Positive Controls and targets in the run are "**Not Detected**".
   Recommended action: The run is considered invalid. Re-test the PC. If the problem repeats, please reach out to the manufacturer for further assistance.

3. WARNINGS AND LIMITATIONS

1. False-negative results may occur if inadequate number (below the LoD) of organisms are present in the specimen.
2. Mutations within the target regions could affect primer and/or probe binding, resulting in failure to detect the presence of agents.
3. The use of swabs with wooden sticks, cotton or calcium alginate swabs can lead to false negative results since they may contain substances that inactivate some pathogens and inhibit PCR.
4. False-negative results may occur if a specimen is improperly collected, transported, or handled.
5. The clinical specimens shall be collected by a healthcare provider in accordance with the national/international specimen collection guidelines.
6. Test procedures should be performed by personnel trained in the use of the kit.
7. Sample tubes should always be kept closed except for liquid transfers.
8. Filtered and nuclease-free pipette tips should be used for sample transfer.
9. The components in the kit should not be used together with different LOT numbers or chemicals of the same name but from different manufacturers.
10. ***The caps of the reaction tubes must not be opened after the PCR run.*** The PCR tubes should be placed in a bag and thrown away after the bag is tightly closed.
11. The surfaces of the workbenches should be wiped with freshly diluted 10% bleach (0.5% NaClO) at the beginning and end of each day.
12. Waste disposal must be carried out in accordance with local, state, and federal regulations.
13. Proper personal protective equipment including lab coats, gowns, gloves, eye protection, and a biological safety cabinet are recommended for manipulation of clinical specimens.
14. Immediately clean up any spill containing potentially infectious material with 0.5-1% (w/v) sodium hypochlorite (10-20% v/v bleach). Dispose of cleaning materials in a biohazard waste stockpot.
15. The micropipettes used for pipetting PCR mixes and template nucleic acids should be separate. Filtered and nuclease-free pipette tips should be used.
16. Maintenance/ calibration interval should be determined for all instruments and equipment used with the kit.

4. EXPLANATION OF SYMBOL

Symbol	Title of Symbol	Symbol	Title of Symbol	Symbol	Title of Symbol
CE	European Conformity CE Mark	LOT	Batch code		Keep away from sunlight
IVD	*In vitro* diagnostic *medical device*	REF	Catalogue number		Protect from heat and radioactive sources
	Manufacturer	NON STERILE	Non-sterile		Do not use if package is damaged and consult *Instructions for Use*
	Expiration Date YYYY-MM		Consult *Instructions for Use* or consult electronic *Instructions for Use*		Keep dry
CONTROL -	Negative Control		Caution		Keep upright
CONTROL +	Positive Control		Temperature limit	Σ	Contains sufficient for *<n>* tests
CONTROL	Control				

5. MANUFACTURER AND TECHNICAL SUPPORT

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Technical Support: support@bioeksen.com.tr

Notice to User: Please inform us about product-related incidents at "**vigilance@bioeksen.com.tr**" within 24 hours.

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Cat No: BS-TF-T-25/BS-TF-T-100
Ordering Ref No: FEVER-T-25/FEVER-T-100

Tropical Fever RT-qPCR Panel

Package Insert

Table 1. Kit Content

Component	Intended Use	25 Reactions	100 Reactions
2X Prime Script Mix	Optimized ready-to-use mix for RT-qPCR assay	2 x 1000 µL	7 x 1250 µL
TF Oligo Mix 1	Specific nucleic acid amplification and detection: **FAM:** Crimean-Congo Hemorrhagic Fever virus (CCHFV) **HEX:** Human (IC-Internal Control)	1 x 125 µL	1 x 500 µL
TF Oligo Mix 2	**FAM:** Dengue virus (DENV)	1 x 125 µL	1 x 500 µL
TF Oligo Mix 3	**FAM:** Ebola virus **ROX:** Hantavirus **CY5:** Mayaro Virus	1 x 125 µL	1 x 500 µL
TF Oligo Mix 4	**FAM:** Rift Valley virus **ROX:** *Trypanosoma cruzi* **CY5:** *Plasmodium* spp.	1 x 125 µL	1 x 500 µL
TF Oligo Mix 5	**FAM:** *Brucella* spp. **ROX:** *Coxiella burnetii* **CY5:** *Burkholderia pseudomallei*	1 x 125 µL	1 x 500 µL
TF Oligo Mix 6	**FAM:** *Salmonella* spp. **HEX:** *Rickettsia* spp. **ROX:** *Leptospira* spp. **CY5:** *Leishmania* spp.	1 x 125 µL	1 x 500 µL
TF Oligo Mix 7	**FAM:** West Nile Virus (WNV) **HEX:** Zika virus (ZIKV) **CY5:** *Streptococcus pneumoniae*	1 x 125 µL	1 x 500 µL
TF Oligo Mix 8	**FAM:** Yellow fever virus **ROX:** Chikungunya virus (CHIKV) **CY5:** Japanese Encephalitis (JE) virus	1 x 125 µL	1 x 500 µL
PC-TF 1 / PC-TF 2 / PC-TF 3 / PC-TF 4 PC-TF 5 / PC-TF 6 / PC-TF 7 / PC-TF 8	Positive Control (PC)	1 x 100 µL	1 x 100 µL
NTC	Negative Control	1 x 1000 µL	1 x 1000 µL

Table 2. Transport Condition, Storage Condition, and Shelf Life of the Components

Component	Transport Condition	Storage Condition*	Shelf Life
2X Prime Script Mix	(-22) °C – (+8) °C	(-22) °C – (-18) °C	12 Months
Oligo Mix		(-22) °C – (-18) °C	
PC		(-22) °C – (-18) °C before opening, (+2) °C – (+8) °C after first thaw	
NTC		(-22) °C – (-18) °C before opening, (+2) °C – (+8) °C after first thaw	

* Following the first opening, each reagent stored at storage temperature can be used until the expiration date indicated on the tube. The kit's expiration date is determined by the expiration date of the reagents.

Table 3. Required Components Not Included in the Package

Required Components Not Included in the Package
1. Real-Time PCR Instrument
2. Nucleic acid preparation instruments and nucleic acid preparation consumables
3. Micropipettes and compatible filtered pipette tips (nuclease-free) suitable for transferring 1-10 µL, 10-100 µL, and 100-1000 µL of liquid
4. A centrifuge or Mini-spin
5. Vortex
6. PCR Reaction tubes, or PCR strips and caps or PCR plates and seals specific to Real-Time PCR instruments and compatible with reaction volume

Table 4. Intended Use, Test Principle, and Analytical Specifications

Function	Aid to diagnosis	**Sample Type(s)**	**Table 5**
Analyte(s)	**Table 1**	**Nucleic Acid Extraction Method(s)**	Zybio EXM3000 Nucleic Acid Isolation System Adaltis EXTRAlab and MDXlab
Qualitative/Quantitative	Qualitative	**Validated Real-Time PCR Instruments**	Bio Molecular Systems: Magnetic Induction Cycler (Mic)/Mic IVD Bio-Rad: CFX96 Touch/Dx, CFX Opus 96/Dx, CFX384 Touch, CFX Opus 384 Qiagen: Rotor-Gene Q 5-Plex/MDx Roche: LightCycler 96 Thermo Fisher Scientific: QuantStudio 5/5 Dx/6/7/12k Flex/Pro, StepOne Plus, Applied Biosystems 7500/7500 Fast

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			Adaltis: AmpliLab, MDXlab HiMedia: InstaQ 96 Bioer: Linegene 9600 Plus Atila Biosystems: Fujirebio Co-Dx: Co-Dx Box Tianlong: Gentier 96E Sansure: SLAN-96P Azure: Cielo
Test Principle	Reverse Transcription and Real-Time PCR (RT-qPCR)	**Inclusivity and Exclusivity**	Validated on the reference strains and the field isolates
Automated/Manual	Manual		
Intended Users	Laboratory professionals trained in the techniques of qPCR and in vitro diagnostic procedures	**Limit of Detection (LoD)**	**Table 5**
Target Population	Individuals with the suspected infection	**Sensitivity and Specificity**	98.55% and 99.21%

Table 5. Collection, Storage and Transfer of Clinical Specimens / Nucleic Acid Preparation Methods

Sample Type**	Sample Transfer	Sample Storage	Nucleic Acid Preparation Method	LoD (cp/mL)
Whole blood, serum and plasma	EDTA-treated blood tube	3 days at (+2) °C – (+8) °C 1 year at (-20) °C	**Nucleic acid preparation instruments:** 1) Zybio EXM3000, 2) Adaltis EXTRAlab, 3) Adaltis MDXlab **Nucleic acid preparation consumables:** Bio-Speedy® Rapid Nucleic Acid Extraction Kit (Cat. No: ZFNAE01)	500-1000
Urine	Preservative-free sterile tubes/containers			1000-2000

**Clinical specimens should be collected by a healthcare provider in accordance with national/international clinical specimen collection regulations.

1. APPLICATION PROTOCOL

1. Program the qPCR device using the QR Code/Link as indicated in **Table 6.**
2. Take the PCR kit out of the -20°C freezer.
3. Pipette (Sample Count + 3) *5 µL of TF Oligo Mix 1 into an empty eppendorf tube. (i.e Sample Count = 3, pipette 5*(3+3) = 30 µL of TF Oligo Mix 1)
4. Add (Sample Count + 3) *5 µL of 2X Prime Script Mix into the tube prepared in Step 3. (i.e Sample Count = 3, pipette 5*(3+3) = 30 µL of 2X Prime Script Mix)
5. Vortex the master mix to homogenize.
6. Repeat Steps 3, 4 and 5 for all master mixes (8 master mixes in total).
7. Pipette 15 µL of each master mix into all PCR tubes, or wells to be used (including all samples, NTC and PC).
8. Pipette 5 µL of extracted sample(s) into the relative PCR tube, or well.
9. Pipette 5 µL of NTC into Negative Control PCR tube, or well.
10. Pipette 5 µL of PC-TF 1 into the relative Positive Control tube, or well. Repeat for all PC.
11. Close the cap of the strips, or PCR tubes or seal PCR plate. Label to avoid confusion during spin-centrifuge.
12. Spin-centrifuge the strips, or PCR tubes and PCR plate.
13. Open the lid of the instrument. Place the strips, or PCR tubes and PCR plate.
14. Close the lid and start the instrument.

Table 6. Real-Time qPCR Program Details

Reaction Setup		RT-qPCR Program							
		Protocol 1: Bio Molecular Systems: Magnetic Induction Cycler (Mic)/Mic IVD, Bio-Rad: CFX96 Touch/Dx, CFX Opus 96/Dx, CFX384 Touch, CFX Opus 384, Roche: LightCycler 96, Co-Dx: Co-Dx Box, Azure: Cielo				**Protocol 2:** Qiagen: Rotor-Gene Q 5-Plex/MDx, Thermo Fisher Scientific: QuantStudio 5/5 Dx/6/7/12k Flex/Pro, StepOne Plus, Applied Biosystems 7500/7500 Fast, Adaltis: AmpliLab, MDXlab, HiMedia: InstaQ 96, Bioer: Linegene 9600 Plus, Atila Biosystems: Fujirebio, Tianlong: Gentier 96E, Sansure: SLAN-96P			
Reagent	**Volume/Rxn**	**Step**	**Cycle No.**	**Temperature**	**Duration**	**Step**	**Cycle No.**	**Temperature**	**Duration**
2X Prime Script Mix	10 µL	**Reverse Transcription**	1 Cycle	52 °C	3 min	**Reverse Transcription**	1 Cycle	52 °C	3 min
		Pre-Incubation	1 Cycle	95 °C	10 sec	**Pre-Incubation**	1 Cycle	95 °C	10 sec
Oligo Mix	5 µL	**Denaturation**	12 Touchdown Cycles: 1 °C decrement in annealing temperature per cycle	95 °C	1 sec	**Denaturation**	40 Cycles	95 °C	1 sec
		Annealing and Extension		67 °C to 56 °C	15 sec	**Annealing and Extension**		55 °C	15 sec
Template Nucleic Acid/NTC/PC	5 µL	**Denaturation**	30 Cycles	95 °C	1 sec	**Detection (Reading)**		FAM/HEX/ROX/CY5	
		Annealing and Extension		55 °C	15 sec				
Total Reaction Volume	**20 µL**	**Detection (Reading)**		FAM/HEX/ROX/CY5					

WARNING: The qPCR program file should be downloaded from the QR code on the left or from the link below.

https://www.bioeksen.com.tr/files/L_TD_43B

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2. INTERPRETATION OF THE ASSAY RESULTS

Cq values of the results obtained from PCR instruments indicated in **Table 7** are calculated referring to the relative RFU threshold levels and Cq cut-offs**.** Auto-threshold and default options are used for devices not included in **Table 7**. For all targets that do not exceed the Cq cut-off, the shape of the amplification curve must be analyzed, and Cq values of the sigmoidal curves must be determined. Non-sigmoidal curves must be reported as "negative". The PCR results can be reported manually, as indicated in **Table 8**, or using the "**Sigmoida**" software for BMS Magnetic Induction Cycler (Mic)/Mic IVD and Bio-Rad CFX instruments. Sigmoida software sorts each target as positive or negative. To obtain the "**Sigmoida**" software installer, please send an e-mail to support@bioeksen.com.tr.

Table 7. Threshold Levels and Cq Cut-offs for Calculating Cq Values

Analyte	Real Time PCR Instrument											
	Bio-Rad CFX		Cielo		LightCycler 96		Mic/Mic IVD and Co-Dx Box		Rotor-Gene Q****		QuantStudio 5/5 Dx/6/7/12k Flex/Pro	
	RFU	Cq Cut-off	RFU	Cq Cut-off	RFU	Cq Cut-off	RFU	Cq Cut-off	RFU	Cq Cut-off	RFU	Cq Cut-off
Crimean-Congo Hemorrhagic Fever virus (CCHFV)	750	30	75000	30	0.1	30	0.5	30	0.05	40	20000	30
Human (IC-Internal Control)	200	30	20000	30	0.05	30	0.2	30	0.02	40	20000	30
Dengue virus (DENV)	750	30	75000	30	0.1	30	0.5	30	0.05	40	20000	30
Ebola virus	750	30	75000	30	0.1	30	0.5	30	0.05	40	20000	30
Hantavirus	750	30	75000	30	0.1	30	0.5	30	0.05	40	20000	30
Mayaro Virus	1500	26	150000	26	0.15	30	0.75	26	0.1	34	75000	26
Rift Valley virus	750	30	75000	30	0.1	30	0.5	30	0.05	40	20000	30
Trypanosoma cruzi	750	30	75000	30	0.1	30	0.5	30	0.05	40	20000	30
Plasmodium spp.	750	30	75000	30	0.1	30	0.5	30	0.05	40	20000	30
Brucella spp.	750	30	75000	30	0.1	30	0.5	30	0.05	40	20000	30
Coxiella burnetii	750	30	75000	30	0.1	30	0.5	30	0.05	40	20000	30
Burkholderia pseudomallei	750	30	75000	30	0.1	30	0.5	30	0.05	40	20000	30
Salmonella spp.	750	30	75000	30	0.1	30	0.5	30	0.05	40	20000	30
Rickettsia spp.	750	30	75000	30	0.1	30	0.5	30	0.05	40	20000	30
Leptospira spp.	750	30	75000	30	0.1	30	0.5	30	0.05	40	20000	30
Leishmania spp.	750	30	75000	30	0.1	30	0.5	30	0.05	40	20000	30
West Nile Virus (WNV)	750	30	75000	30	0.1	30	0.5	30	0.05	40	20000	30
Zika virus (ZIKV)	750	30	75000	30	0.1	30	0.5	30	0.05	40	20000	30
Streptococcus pneumoniae	1500	26	150000	26	0.15	30	0.75	26	0.1	34	75000	26
Yellow fever virus	750	30	75000	30	0.1	30	0.5	30	0.05	40	20000	30
Chikungunya virus (CHIKV)	750	30	75000	30	0.1	30	0.5	30	0.05	40	20000	30
Japanese Encephalitis (JE) virus	750	30	75000	30	0.1	30	0.5	30	0.05	40	20000	30

**** Defined threshold with specific settings of "Outlier Removal = 0", "Dynamic Tube = On", and "Slope Correct = Off"

Table 8. Interpretation of Patient Results

Target	Internal Control (IC)	Result Interpretation		
Positive (+)	**Positive (+)** or **Negative (-)**	Results are valid Target is detected	**Protocol 1**	If 26<Cq ≤30 "Low Positive" If 16<Cq≤26 "Positive" If Cq≤16 "High Positive"
			Protocol 2	If 34<Cq ≤40 "Low Positive" If 22<Cq≤34 "Positive" If Cq≤22 "High Positive"
Negative (-)	**Positive (+)**	Results are valid Target is not detected		

Table 9. Expected Performance of Kit Controls

Control Type	Purpose	Expected Results and Cq Values			
		Protocol 1		Protocol 2	
		IC (HEX)	Target	IC (HEX)	Target
Negative Control	Contamination control during RT-qPCR	**Not Detected**	**Not Detected**	**Not Detected**	**Not Detected**
Positive Control	Reagent stability control	**Detected** (Cq≤30)	**Detected** (Cq≤30)	**Detected** (Cq≤40)	**Detected** (Cq≤40)
Internal Control	Nucleic acid extraction and sampling control	**Detected**	Detection insignificant	**Detected**	Detection insignificant
		If "**Not Detected**" check the target Cq	If "**Detected"** IC is valid	If "**Not Detected**" check the target Cq	If "**Detected"** IC is valid

If a control does not work as expected (**Table 9**), apply the procedures described below.

1. **Contamination Problem:** If a target in the Negative Control reaction is "**Detected**".
   Recommended action: Repeat the run, paying attention to the "Warnings and Limitations" section.

2. **Invalid Internal Control Problem:** If the Internal Control (IC) and all other targets of a sample are "**Not Detected**".
   Recommended action: Sampling was not successfully done, or there was a problem during the sample transportation or extraction. Re-test the sample. If the problem repeats, a new sample from the same patient should be collected and tested again.

3. **Reagent Problem**: If all Internal Controls, Positive Controls and targets in the run are "**Not Detected**".
   Recommended action: The run is considered invalid. Re-test the PC. If the problem repeats, please reach out to the manufacturer for further assistance.

3. WARNINGS AND LIMITATIONS

1. False-negative results may occur if inadequate number (below the LoD) of organisms are present in the specimen.
2. Mutations within the target regions could affect primer and/or probe binding, resulting in failure to detect the presence of agents.
3. False-negative results may occur if a specimen is improperly collected, transported, or handled.
4. The clinical specimens shall be collected by a healthcare provider in accordance with the national/international specimen collection guidelines.

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5. Test procedures should be performed by personnel trained in the use of the kit.
6. Sample tubes should always be kept closed except for liquid transfers.
7. Filtered and nuclease-free pipette tips should be used for sample transfer.
8. The components in the kit should not be used together with different LOT numbers or chemicals of the same name but from different manufacturers.
9. ***The caps of the reaction tubes must not be opened after the PCR run.*** The PCR tubes should be placed in a bag and thrown away after the bag is tightly closed.
10. The surfaces of the workbenches should be wiped with freshly diluted 10% bleach (0.5% NaClO) at the beginning and end of each day.
11. Waste disposal must be carried out in accordance with local, state, and federal regulations.
12. Proper personal protective equipment including lab coats, gowns, gloves, eye protection, and a biological safety cabinet are recommended for manipulation of clinical specimens.
13. Immediately clean up any spill containing potentially infectious material with 0.5-1% (w/v) sodium hypochlorite (10-20% v/v bleach). Dispose of cleaning materials in a biohazard waste stockpot.
14. The micropipettes used for pipetting PCR mixes and template nucleic acids should be separate. Filtered and nuclease-free pipette tips should be used.
15. Maintenance/ calibration interval should be determined for all instruments and equipment used with the kit.

4. EXPLANATIONS OF SYMBOLS

Symbol	Title of Symbol	Symbol	Title of Symbol	Symbol	Title of Symbol
CE	European Conformity CE Mark	LOT	Batch code		Keep away from sunlight
IVD	*In vitro* diagnostic medical device	REF	Catalog number		Protect from heat and radioactive sources
	Manufacturer	NON STERILE	Non-sterile		Do not use if package is damaged and consult *Instructions for Use*
	Expiration Date YYYY-MM		Consult *Instructions for Use* or consult electronic *Instructions for Use*		Keep dry
CONTROL -	Negative Control		Caution		Keep upright
CONTROL +	Positive Control		Temperature limit	Σ	Contains sufficient for <*n*> tests
CONTROL	Control				

5. MANUFACTURER AND TECHNICAL SUPPORT

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Web: www.bioeksen.com.tr, **e-mail:** info@bioeksen.com.tr,
Technical Support: support@bioeksen.com.tr

Notice to User: Please send an e-mail to **vigilance@bioeksen.com.tr** about product-related incidents, within 24 hours.

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Cat No: BS-NA-510-100/BS-NA-510-250/BS-NA-510-500/BS-NA-510-1000

vNAT® Viral Nucleic Acid Buffer

Package Insert

1. Product Content

Table 1: Product Content, Storage Requirements, and Shelf Life

Component	Amount				Transport Conditions	Storage Conditions	Shelf Life
vNAT® Viral Nucleic Acid Buffer	100 Test (1 X 10mL)	250 Test (1 X 25mL)	500 Test (1 X 50mL)	1000 Test (1 X 100mL)	2-50°C	15-30 °C	18 Months

2. Intended Use and Test Principle

The ***vNAT® Viral Nucleic Acid Buffer*** is a ***10x concentrated*** viral nucleic acid extractive and preservative liquid for nasopharyngeal swab, oropharyngeal swab, oral/saliva swab samples. The nucleic acid extractive and preservative liquid inactivates all viral, bacterial, or eukaryotic pathogens in the sample within 1 minutes after contact with the clinical specimen. The ***vNAT® Viral Nucleic Acid Buffer*** allows from sample to qPCR in a minute**.**

3. Analytical Specifications

vNAT® Viral Nucleic Acid Buffer is validated for detection kits produced by Bioeksen R&D Technologies Inc.

4. Sampling Protocol

Clinical samples are collected from individuals by a healthcare provider in accordance with the CDC Specimen Collection Guidelines: https://www.cdc.gov/coronavirus/2019-ncov/lab/guidelines-clinical-specimens.html.

5. Sample Transportation, Storage, and Application Protocol

The specimens in the ***vNAT® Viral Nucleic Acid Buffer*** can be stored at 2-8°C and ship to the laboratory on ice pack. If a specimen is frozen at -70°C or lower, ship overnight to the laboratory on dry ice. It is important that specimens are not exposed to continuous freeze-thaw exposure.

⚠ **WARNING:**

a) The VTM validated with the vNAT buffer is in accordance with the CDC directive and do not contain phenol-red (Preparation of viral transport medium, Centers for Disease Control and Prevention, SOP#: DSR-052-06).
b) The Amies medium should not contain charcoal.

Standard Protocol (Samples in VTM/Saline/Amies)

1. Vortex the sample tube at the highest speed for 3 seconds.
2. Transfer 100 µl of the ***vNAT® Viral Nucleic Acid Buffer*** into a clean tube.
3. Add 900 µL of the sample to the tube containing 100 µL ***vNAT® Viral Nucleic Acid Buffer***.
4. Mix the sample and the ***vNAT® Viral Nucleic Acid Buffer*** well by vortexing/shaking/pipetting.
5. Incubate the tube for 1 minute at room temperature.
6. 1000 µl mixture is ready to use in PCR reaction.

Protocol for Dry Swab Samples

1. Transfer the swab sample into a tube containing 100 µl ***vNAT® Viral Nucleic Acid Buffer*** + 900 µl nuclease-free water.
2. Apply the steps 1-6 of the "**Standard Protocol**".

6. Explanation of Symbol

Symbol	Title of Symbol	Symbol	Title of Symbol	Symbol	Title of Symbol
CE	European Conformity CE Mark	LOT	Batch code		Keep away from sunlight
IVD	*In vitro* diagnostic *medical device*	REF	Catalogue number		Protect from heat and radioactive sources
	Manufacturer	NON STERILE	Non-*sterile*		Keep dry
	Use-by date		Consult *instructions for use* or consult electronic *instructions for use*		Keep it upright
	Temperature limit	Σ	Contains sufficient for <*n*> tests		Caution

7. Manufacturer and Technical Support

Bioeksen R&D Technologies Incorporated Company
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Phone: +90 (212) 285 10 17, **Fax:** +90 (212) 285 10 18
Web: www.bioeksen.com.tr, **e-mail:** info@bioeksen.com.tr,
Technical Support: support@bioeksen.com.tr

Notice to User: Please inform us about product-related incidents at "**vigilance@bioeksen.com.tr**" within 24 hours.