

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

auft





www.bloeksen.com.tr info@bloeksen.com.tr

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







# BIOEKSEN AR-GE TEKNOLOJILERI ANONIM ŞIRKETİ

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** 





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 <u>info@kiwa.com.tr</u> <u>www.kiwa.com.tr</u>

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





# 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** 





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 <u>info@kiwa.com.tr</u> <u>www.kiwa.com.tr</u>

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



#### 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.

: Huzur Mah. Metin Oktay Cad. Nurol Life Sitesi D Blok No:3/31, 34396 Sarıyer/İstanbul TÜRKİYE : Huzur Mahallesi Metin Oktay Caddesi Nurol Life No:3/10,
: Huzur Mahallesi Metin Oktay Caddesi Nurol Life No:3/10,
Sarıyer/İstanbul TÜRKİYE
Web: www.bioeksen.com.tr, E-mail: info@bioeksen.com.tr
: Bio-Speedy <sup>®</sup> Bordetella pertussis, B.parapertussis, B.bronchiseptica and B.holmesii Real-Time PCR Detection Kit
: Bio-Speedy <sup>®</sup> 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
: 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
: According to Annex III of the IVD Directive 98/79/EC
EC declaration of conformity under manufacturer responsibility
: 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.

	IOEKSEN AR GE TEKNOLOJILERI A.Ş. uzur Mah. Metiri Oktay Ced. Nuret Life D Blok
Signature:	No: 3/31 Saniya: 15 TXNBUL aslak V.D. 175 995 2653 TKI Sicil No: 904277-0 Mergis No: 0176 0932 8530 0001 nfo@bioeksen.com.tr - www.bioeksen.com.tr
Authorized Person	n: Canan Zöhre Ketre Kolukırık

Place of Issue: İstanbul Valid from: 25.05.2022





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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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 <sup>®</sup> Bacillus anthracis Real-Time PCR Detection Kit
Description	: Bio-Speedy <sup>®</sup> Bacillus anthracis Real-Time PCR Detection Kit
Ref No: BS-DTC-V-224-25 Ref No: BS-DTC-V-224-100	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
10	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 Gad, Norni Life D Blok No: 3/31, Sarver / ISTANSul Maslak V.D. 176 091 2003 Urc. Afcil No: 904277-0 Mersis No: 0176 0992 8530 0001 info@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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1	EN ISO 13485:2016	Medical devices - Quality management systems - Requirements for regulatory purposes
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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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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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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 <sup>®</sup> Gastroenteritis RT-qPCR MX-5T Viral Panel
Description	: Bio-Speedy <sup>®</sup> Gastroenteritis RT-qPCR MX-5T Viral Panel
Ref No: BS-GE-MX5T-25 Ref No: BS-GE-MX5T-100	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.

Signature:

BİOEKSEN AR GE TEKNOLOJILERİ A.Ş. Huzur Mah. Metin Oktay Cad. Nuret Vife D Biok No: 3/31 Sarıyel // STANBUU Maslak V.D. 176.093 2853 700 Sicil No: 904277-0 Mersis Go: 0176 0932 8530 0001 info@bioeksen.com.tr - www.bioeksen.com.tr Place of Issue: İstanbul Valid from: 25.05.2022







No.	Title of standards	Contents
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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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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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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 <sup>®</sup> Human Enterovirus (HEV) qPCR Detection Kit
Description	: Bio-Speedy <sup>®</sup> 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.

Signature:

BIOEKSEN AR GE TEKNOL OJILERI A.Ş. Huzur Mah. Metin Otkay Cad. Hatol Life D Blok No: 5/31 Sariyeri ISTANBOL Maslak V.D. 176 093 2853 ric. Sicji No: 904277-0 Motse 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





No.	Title of standards	Contents
1	EN ISO 13485:2016	Medical devices - Quality management systems - Requirements for regulatory purposes
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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
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11	CLSI EP17 A2: 2ED 2012	Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures
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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 <sup>®</sup> Legionella pneumophila qPCR Kit	
Description	: Bio-Speedy <sup>®</sup> 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.

Signature: BIOEKSEN AR GE TEKNOLOUILERIA.S. Huzur Mah. Metin Oktay Cat. Numerin DBiok No: 3/31 Sarver 1577,000 Maslak V.D. 176 0932,053 100 Sicil No: 904217-0 Mersis DE 0176 0932,0530 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



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	
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5	EN ISO 23640:2015	In vitro diagnostic medical devices – Evaluation of stability of in vitro diagnostic reagents	
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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 <sup>®</sup> Meningitis/Encephalitis qPCR MX-6T Bacterial Panel		
Description	: Bio-Speedy <sup>®</sup> 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		
x	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:

BIOEKSEN AR GE TEKNOLOJLERI A.Ş. Huzur Mah. Metin Oktay Gad, Nevel Life D Blok No: 3/31 Sarver / 15 PANBUL/ Maslak V.D. 176 093 2033 Cc. Sicil No: 904277-0 Mersis Ccl 0176 0932 8530 0001 info@bioeksen.com.tr - www.bioeksen.com.tr Place of Issue: İstanbul Valid from: 25.05.2022





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# 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	vNAT <sup>®</sup> Transfer Tube
Product Catalog Number(s)	BS-NA-513m-100
Basic UDI-DI	868187745NAEXT0672
Intended Purpose	$\nu$ NAT <sup>®</sup> Transfer Tube, 2 mL of viral nucleic acid extractive and preservative liquid. When clinical specimens suspected of respiratory tract infection are transferred in $\nu$ NAT <sup>®</sup> 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 $\nu$ NAT <sup>®</sup> 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 or 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) o 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	
N	BIOEKSEN AR GE TEKNOLOJILERI A.Ş. Huzur Mah. Metin Oktay Cad. Nurol Life D Biok No. 3/31, Sarujer IIS KANBUL Maslak V.D. 176 093 (853 Pic. Stoji No: 904277-0 Mercisi Bic. 61 (00932 8530 0001 info@bioebeen.com.tr - www.bioeksen.com.tr		Page <b>1</b>	



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### 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.	<ul> <li>7.5.5 Special Requirements for Sterile Medical Devices</li> <li>7.5.7 Special Requirements for Process Validation for Sterilization and Sterile Barrie Systems</li> <li>7.5.2 Special requirements for implantable medical devices</li> </ul>
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.



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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 (I)
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	-





#### 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 <sup>®</sup> Respiratory Tract Virus RT-qPCR Panel		
Description	: Bio-Speedy <sup>®</sup> 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

conformity. BiOE Huzur Maslat	KSEN AR GE TEKNOLOVILERI A.Ş. Mah. Merin Oktay Carl Antro Life D Blok No 3/31 Samuer 1974 NGUL V.D. 375,055 2553 (Jct. Signi No: 904277-0
Signature:	Mersie No: 0176 0932 8530 0001 bloeksen.com.tr - www.bioeksen.com.tr
Authorized Person:	Canan Zöhre Ketre Kolukırık Chairman of the Board

Place of Issue: İstanbul Valid from: 25.05.2022



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 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	





#### 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 <sup>®</sup> Sepsis qPCR MX-30T Panel		
Description	: Bio-Speedy <sup>®</sup> 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.

Signature:

BIOEKSEN AR GE TEKNOLO JILERI A.Ş. Huzur Mah. Metin Oktay Cad. Nurol the D Blok No: 3/31 Sariyer / STATSUL Masiak V.D. 176.053-2803 T/c. Sicil No: 904277-0 Mersis No: 9176.052-8530 0001 info@bioeksen.com.tr Place of Issue: İstanbul Valid from: 25.05.2022

Authorized Person: Canan Zöhre Ketre Kolukırık Chairman of the Board





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		





#### 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 <sup>®</sup> Brucella spp. qPCR Kit			
Description	: Bio-Speedy <sup>®</sup> 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:



Place of Issue: İstanbul Valid from: 25.05.2022





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		



#### 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 <sup>®</sup> COVID-19/Flu RT-qPCR	
Description	: Bio-Speedy <sup>®</sup> 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 TEKNOL OJILERI A.Ş. Huzur Mah. Metin Oktav Cad. Muro-Dife D Blok No: 3/31 Sariyer / ISTANBAU Maslak V.D. 176 2032854 Tio, 2051 No: 904277-0 Mersis No: 9176 0052 4530 1001 info@bioekstric.com.tr

Place of Issue: İstanbul Valid from: 25.05.2022

Authorized Person: Canan Zöhre Ketre Kolukırık

Chairman of the Board





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		





#### 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 <sup>®</sup> Tropical Fever RT-qPCR Panel		
Description	: Bio-Speedy <sup>®</sup> 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. BIOEKSEN AR GE TEKNOLOJILERIA.S.

Signature:	Maslak	Mah. Metin Oktay Cad. Nurol Life D Blok No: 3/31 Server / ISTANBUT V.D. 176 091/2853 No: Sicil No: 904277-0 Mersis No: 0176 0932 8530 0001 bioeksen.com.tr - www.bioeksen.com.tr
Authorized P	erson:	Canan Zöhre Ketre Kolukırık
		Chairman of the Board

Place of Issue: İstanbul Valid from: 25.05.2022



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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# 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 <sup>®</sup> vNAT <sup>®</sup> 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 <b>vNAT</b> <sup>®</sup> 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 <b>vNAT</b> <sup>®</sup> 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 Pers	on: Canan Zöhre Ketre Kolukırık	Date of Issue:	25.01.2023
Position:	Chairman of the Board	Place of Issue:	İstanbul
Seal/Signature:	No: 3/31 Sariyar / STARBUL		
	Maslak V.D. 176 093 1856 16 / Sicil No. 904277-0 Mersis No. 0176 9932 8530 0001 info@bioeksen.com.tr - www.bioeksen.com.tr		Page 1



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### 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.	<ul> <li>7.5.5 Special Requirements for Sterile Medical Devices</li> <li>7.5.7 Special Requirements for Process Validation for Sterilization and Sterile Barrier Systems</li> <li>7.5.9.2 Special requirements for implantable medical devices</li> </ul>
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.



DoC.016-Rev.04

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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 (I)
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	-





#### 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 <sup>®</sup> Gastroenteritis RT-qPCR MX-24T Panel					
Description	: Bio-Speedy <sup>®</sup> 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.

Signature:

BİOEKSEN AR GE TEKNOLO ÜLERİ A.Ş. Huzur Mah. Metin Oktav Gad. Hurdi Life D Blok No: 3/21. Sariyer HSTANBUL Maslak V.D. 176.093.2853 Life. Sicil No: 904277-0 Merais No: 01/6 0932 8530 0001 info@bizeksen.com.tr - www.bioeksen.com.tr Place of Issue: İstanbul Valid from: 25.05.2022





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 supplication the manufacturer (labelling) - Part 2: In vitro diagnostic medical devices - Information supplication supplication of the manufacture (labelling) - Part 2: In vitro diagnostic medication of the manufacture (labelling) - Part 2: In vitro diagnostic medication of the manufacture (labelling) - Part 2: In vitro diagnostic medication of the manufacture (labelling) - Part 2: In vitro diagnostic medication of the manufacture (labelling) - Part 2: In vitro diagnostic medication of the manufacture (labelling) - Part 2: In vitro diagnostic medication of the manufacture (labelling) - Part 2: In vitro diagnostic medication of the manufacture (labelling) - Part 2: In vitro diagnostic medication of the manufacture (labelling) - Part 2: In vitro diagnostic medication of the manufacture (labelling) - Part 2: In vitro diagnostic medication of the manufacture (labelling) - Part 2: In vitro diagnostic medication of the manufacture (labelling) - Part 2: In vitro diagnostic medication of the manufacture (labelling) - Part 2: In vitro diagnostic medication of the manufacture (labelling) - Part 2: In vitro diagnostic medication of the manufacture (labelling) - Part 2: In vitro diagnostic medication of the manufacture (labelling) - Part 2: In vitro diagnostic medication of the manufacture (labelling) - Part 2: In vitro diagnostic medication of the manufacture (labelling) - Part 2: In vitro diagnostic medication of the manufacture (labelling) - Part 2: In vitro diagnostic medication of the manufacture (labelling) - Part 2: In vitro diagnostic medication of the manufacture (labelling) - Part 2: In vitro diagnostic medication of the manufacture (labelling) - Part 2: In vitro diagnostic medication of the manufacture (labelling) - Part 2: In vitro diagnostic medication of the manufacture (labelling) - Part 2: In vitro diagnostic medication of the manufacture (labelling) - Part 2: In vitro diagnostic medication of the manufacture (labelling) - Part 2: In vitr				
8	EN ISO 15223-1:2021 Medical devices - Symbols to be used with medical devices 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	17 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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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** Quantity Quantity Quantity Quantity Component Target Channel (20 µL/Rxn) (20 µL/Rxn) Component (20 µL/Rxn) (20 µL/Rxn) 25 Rxns 100 Rxns 25 Rxns 100 Rxns Sapovirus (GI/GII/GIV/GV) FAM Internal Control (Human RNase P gene) HEX SA Oligo Mix 1 x 125 ul 1 x 500 ul PC-SA 1 x 100 ul 1 x 100 ul RO) Adenovirus CY5 FAM Giardia lamblia HEX GCE Oligo Mix 1 x 125 μL 1 x 500 μL PC-GCE 1 x 100 μL 1 x 100 μL Entamoeba histolytica RO) CY5 Cryptosporidium spp. Yersinia enterocolitica FAM HEX Plesiomonas shigelloides YPC Oligo Mix 1 x 125 μL 1 x 500 μL PC-YPC 1 x 100 μL 1 x 100 μL ROX CY5 Cyclospora cayetanensis FAM Astrovirus Norovirus (GI/GII) HEX ANR Oligo Mix 1 x 125 μL 1 x 500 µL PC-ANR 1 x 100 µL 1 x 100 μL ROX Rotavirus (A) CY5 Salmonella spp. FAM Campylobacter spp HFX CVVS Oligo Mix 1 x 125 μL 1 x 500 μL PC-CVVS 1 x 100 μL 1 x 100 μL Vibrio parahaemolyticus ROX Vibrio cholerae CY5 Shigella/Enteroinvasive E. coli (EIEC) FAM HEX ET1 Oligo Mix 1 x 125 μL 1 x 500 μL PC-ET1 1 x 100 μL 1 x 100 μL Enteroaggregative E. coli (EAEC) ROX Shiga toxin producing E. coli (STEC Enteropathogenic E. coli (EPEC) FAM HEX ET2 Oligo Mix 1 x 125 μL $1 \times 500 \ \mu L$ PC-ET2 $1 \times 100 \ \mu L$ 1 x 100 μL ROX Enterotoxigenic E. coli (ETEC) CY5 Clostridium difficile toxin B FAM HEX CTX Oligo Mix 1 x 125 µL 1 x 500 μL PC-CTX 1 x 100 µL 1 x 100 µL Clostridium difficile toxin A RO CY5 Clostridium difficile Binary toxin A/B 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 Negative (No Template) Control NTC 1 x 1000 μL 1 x 1000 uL (Nuclease-free Water)

#### Table 2. Storage Requirements and Shelf Life

Component	Transport Condition	Storage Condition	Shelf Life	
2X Prime Script Mix		-22 to -18 °C		
Oligo Mix	-22 °C to +8 °C	-22 to -18 °C		12 Months
NTC		-22 to -18 °C / +2 to +8 °C	12 Months	
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			
<ol><li>Adjustable micropipettes and compatible pipette tips (nuclease-free)</li></ol>			the reaction volume			
3.	Centrifuge		Extra components recommended to use:			
4.	Vortex	8.	Biosafety cabinet for PCR setup			
5.	Nuclease-free water/viral transport medium/serum physiologic	9.	Cold tube rack (for microcentrifuge tubes and PCR tubes/strips)			
6.	1.5- or 2-mL microcentrifuge tubes (nuclease-free)	10.	PPE (Personal Protective Equipment)			

#### 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-513-100) 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.

			Sample Tra	nsfer Method	Extraction Method	
	NO	Specimen Type	Sterile Container	vNAT <sup>®</sup> Transfer Tube	Zybio EXM3000 Nucleic Acid Isolation System	LOD (cp/mL)
	1	Rectal swab	-	$\checkmark$	$\checkmark$	28-100
	2	Stool	$\checkmark$	-	$\checkmark$	28-100

The RT-qPCR is carried out in 20 µL reaction volume using the CFX96 Touch<sup>™</sup>/CFX96<sup>™</sup> Dx/CFX Opus 96<sup>™</sup>/CFX Opus 96<sup>™</sup> 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.
- 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).

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For in vitro diagnost For laboratory profe Table 5. Real-Time P	ssional use only					
Reaction S	Setup		RT-qPCR Pr ™/CFX96™ Dx/CFX Opus 96 etic Induction Cycler (Mic) (J	5™/CFX Opus 96™ Dx (I	•	QR Code for Thermal Protocol
Reagent	Volume/Rxn	Step	Cycle No.	Temperature	Duration	
2X Prime Script Mix		Reverse Transcription	1 Cycle	52 °C	5 min	
Litt inte oonpermit	10 µL	Pre-Incubation	1 Cycle	95 °C	10 sec	
		Denaturation	12 Touch Down Cycles:	95 °C	1 sec	
Oligo Mix	5 μL	Annealing and Extension	1 °C decrement in annealing temperature per cycle	67 °C to 56 °C	30 sec	6.53
Tomplato Nuclaia		Denaturation		95 °C	1 sec	
Template Nucleic Acid	5 μL	Annealing and Extension		55 °C	30 sec	
Total Reaction Volume	20 µL	Detection (Reading)	35 Cycles	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: <a href="https://www.ugentec.com/fastfinder">https://www.ugentec.com/fastfinder</a>. 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	Burnaca	Expected Results and Cq Values		
Name		Purpose	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	I IC	To monitor the integrity of nucleic acid extraction and RT-qPCR from each	Detected (Cq≤33)	If target Cq≤35, conclude it as IC is	
Internal/Extraction Control	IC.	sample	If IC Cq>33 check the target Cq	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 Resu	ults			
Target	Internal Control	Report		
Positive (+)	Positive (+)	Report it as <b>POSITIVE</b> for the target	25≤Cq≤35 = Low positive	
			18≤Cq<25 = Positive	
Positive (+)	Negative (-)	Report it as <b>POSITIVE</b> for the target	11≤Cq<18 = High positive	
			Cq<11 = Very high positive	
Negative (-)	Positive (+)	Report it as <b>NEGATIVE</b> for the target		
		INVALID Result: Sampling/extraction/inhibition problem		
Negative (-) Negative (-)		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.

Revision Date: 2022-07-22/ Rev.08 Published Date: 2021-08-20 3



#### 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	漛	Keep away from sunlight
IVD	In vitro diagnostic medical device	REF	Catalogue number	澎	Protect from heat and radioactive sources
***	Manufacturer	NON	Non-sterile		Do not use if package is damaged and consult <i>instructions for use</i>
$\square$	Use-by date		Consult instructions for use or consult electronic instructions for use	Ť	Keep dry
CONTROL -	Negative control	$\triangle$	Caution	<u>††</u>	Keep upright
CONTROL +	Positive control	X	Temperature limit	Σ	Contains sufficient for <n> tests</n>
CONTROL	Control				

#### 11. 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: <a href="mailto:support@bioeksen.com.tr">support@bioeksen.com.tr</a>

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-NA-513m-100

# **v**NAT® Transfer Tube

## Instructions for Use (IFU)

### 1. PRODUCT DESCRIPTION

Table 1	. Produ	ct overview
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Product Name	vNAT <sup>®</sup> 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 vNAT <sup>®</sup> 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 <sub>3</sub> 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
<b>v</b> NAT <sup>®</sup> <i>Transfer Tube</i>	Cell lysis and nucleic acid storage	100 tubes each containing 2 mL of vNAT® reagent

#### Table 3. Storage requirements and shelf life

Component	Transport Conditions	Storage Conditions	Shelf Life
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: <a href="https://www.cdc.gov/coronavirus/2019-ncov/lab/guidelines-clinical-specimens.html">https://www.cdc.gov/coronavirus/2019-ncov/lab/guidelines-clinical-specimens.html</a>.

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

One minute after the sampling, the sample in the vNAT\* *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<sup>\*</sup> *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.



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#### 3.1 Shelf-life and shipping stability

Since the swab samples are placed into the  $vNAT^{\circ}$  Transfer Tube immediately after its initial opening, stability studies were carried out only for the unopened  $vNAT^{\circ}$  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  $vNAT^{\circ}$  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 vNAT® 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<sup>®</sup> Respiratory ID-3 Panel (Cat No: BS-RIDP-3) was used to evaluate the stability of the stored  $vNAT^{e}$  Transfer Tubes. Negative clinical samples were collected using freshly produced  $vNAT^{e}$  Transfer Tubes. Subsequently, the samples were pooled together and subjected to 24 tests using the Bio-Speedy<sup>®</sup> 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  $18.31 \pm 0.74$ . 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, 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<sup>®</sup> Respiratory ID-3 Panel, which is 250 copies/mL.

Weekly testing was conducted on five vNAT<sup>®</sup> 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 vNAT<sup>®</sup> 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<sup>®</sup> 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  $vNAT^{\circ}$  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  $vNAT^{\circ}$  Transfer Tubes was determined to be 105 months at 30 °C.

#### Table 5. Stability study results at 50 °C.

			t =	0		t = Week 113						
Analyte	Analyte		IC		Detection Rate	Analyte		IC		Detection Rate		
	Cq	± SD	Cq	± SD	Detection Rate	Cq	± SD	Cq	± SD	Detection Rate		
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	25.97 0.54		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.

			t =	0		t = Week 113						
Analyte	Analyte		IC		Detection Rate	Analyte		IC		Detection Rate		
	Cq	± SD	Cq	± SD	Detection Rate	Cq	± SD	Cq	± SD	Detection Rate		
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		

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	Rhinovirus	24.42	0.45	18.38	0.53	15/15	25.64	0.76	18.75	0.66	15/15
P	arainfluenza 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

			t =	0		t = Week 113						
Analyte	Anal	yte	IC		Detection Pote	Analyte		IC		Detection Rate		
	Cq	± SD	Cq	± SD	Detection Rate	Cq	± SD	Cq	± SD	Detection Rate		
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 vNAT® Transfer Tube

The Bio-Speedy<sup>®</sup> 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  $\nu$ NAT<sup>®</sup> Transfer Tubes. Negative clinical samples were collected using the  $\nu$ NAT<sup>®</sup> Transfer Tubes. Subsequently, each sample was subjected to 5 tests using the Bio-Speedy<sup>®</sup> 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, 081050CF), 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<sup>®</sup> 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<sup>®</sup> 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 vNAT® 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 vNAT® 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.

		t = 0						t = Day 4				t = Day 5				
Analyte	Ana	Analyte		с	Hit	Ana	lyte	IC		Hit	Analyte		IC		Hit	
	Cq	± SD	Cq	± SD	Rate	Cq	± SD	Cq	± SD	Rate	Cq	± SD	Cq	± SD	Rate	
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 8. Stability results of nasopharyngeal swab samples at 30 °C

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

			t = 0			t = Day 120					
Analyte	Anal	yte	IC	IC		Analyte		IC		Hit Rate	
	Cq	± SD	Cq	± SD	Hit Rate	Cq	± SD	Cq	± SD	The Nate	
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

			t = 0					t = Day 4					t = Day 5		
Analyte	Ana	lyte	ŀ	с	Hit	Ana	lyte	IC		Hit	Anal	yte	ŀ	с	Hit
	Cq	± SD	Cq	± SD	Rate	Cq	± SD	Cq	± SD	Rate	Cq	± SD	Cq	± SD	Rate
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

			t = 0					t = Day 120		
Analyte	Anal	yte	IC	:	Hit Rate	Analy	yte	IC		Hit Rate
	Cq	± SD	Cq	± SD	The Note	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

			t = 0					t = Day 4					t = Day 5		
Analyte	Ana	lyte	I	с	Hit	Ana	lyte	IC		Hit	Anal	yte	ŀ	с	Hit
	Cq	± SD	Cq	± SD	Rate	Cq	± SD	Cq	± SD	Rate	Cq	± SD	Cq	± SD	Rate
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

			t = 0					t = Day 120		
Analyte	Anal	yte	IC		Hit Rate	Anal	yte	IC		Hit Rate
	Cq	± SD	Cq	± SD	The Note	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

			t = 0					t = Day 4					t = Day 5		
Analyte	Ana	lyte	ŀ	с	Hit	Ana	lyte	IC		Hit	Anal	yte	ŀ	С	Hit
	Cq	± SD	Cq	± SD	Rate	Cq	± SD	Cq	± SD	Rate	Cq	± SD	Cq	± SD	Rate
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



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For professional use only. Table 15. Stability results of oral swab samples at 4 °C

			t = 0					t = Day 120		
Analyte	Anal	yte	IC	:	Hit Rate	Anal	yte	IC		Hit Rate
	Cq	± SD	Cq	± SD	The Nate	Cq	± SD	Cq	± SD	The Nate
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<sup>®</sup> Respiratory Tract RT-qPCR MX-24L Panel (Cat No: BS-SY-MX24L) or Bio-Speedy<sup>®</sup> 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  $vNAT^{\circ}$  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  $vNAT^{\circ}$  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  $10^2 \cdot 10^6$  units/mL when cultivated from the samples in the UTM. All the concentrations resulted in negative results for the samples in the  $vNAT^{\circ}$  Transfer Tubes indicating successful inactivation by the  $vNAT^{\circ}$  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  $\nu$ NAT® Transfer Tubes showed negative results, indicating successful inactivation of the analytes by the  $\nu$ NAT® reagent.

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

Amelida	11	Spiked N	/ledia	Cle	an Media
Analyte	Unit	UTM	<b>v</b> NAT®	UTM	<b>v</b> NAT®
Group A Streptococcus	cfu/mL	2.1x10 <sup>5</sup>	Not detected	Not detected	Not detected
Streptococcus pneumoniae	cfu/mL	8.6x10 <sup>5</sup>	Not detected	Not detected	Not detected
Mycoplasma pneumoniae	cfu/mL	8x10 <sup>4</sup>	Not detected	Not detected	Not detected
Chlamydophila pneumoniae	cfu/mL	1.2x10⁵	Not detected	Not detected	Not detected
Haemophilus influenzae	cfu/mL	2.4x10 <sup>5</sup>	Not detected	Not detected	Not detected
SARS-CoV-2	TCID50/mL	3.2x10 <sup>4</sup>	Not detected	Not detected	Not detected
Influenza A	PFU/mL	8.9x10⁵	Not detected	Not detected	Not detected
RSV A	TCID50/mL	8.6x10 <sup>4</sup>	Not detected	Not detected	Not detected
Adenovirus	PFU/mL	9.5x10⁵	Not detected	Not detected	Not detected
Rhinovirus	TCID50/mL	9.1x10 <sup>4</sup>	Not detected	Not detected	Not detected
Parainfluenza virus 3	PFU/mL	8.3x10 <sup>5</sup>	Not detected	Not detected	Not detected

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



Auchar	11	Spiked N	1edia	Cle	an Media
Analyte	Unit	UTM	<b>v</b> NAT®	UTM	<b>v</b> NAT®
Group A Streptococcus	cfu/mL	8.1x10 <sup>3</sup>	Not detected	Not detected	Not detected
Streptococcus pneumoniae	cfu/mL	9.2x10 <sup>3</sup>	Not detected	Not detected	Not detected
Mycoplasma pneumoniae	cfu/mL	9.7x10 <sup>2</sup>	Not detected	Not detected	Not detected
Chlamydophila pneumoniae	cfu/mL	3.3x10 <sup>3</sup>	Not detected	Not detected	Not detected
Haemophilus influenzae	cfu/mL	1.7x10 <sup>3</sup>	Not detected	Not detected	Not detected
SARS-CoV-2	TCID50/mL	8.6x10 <sup>2</sup>	Not detected	Not detected	Not detected
Influenza A	PFU/mL	9.1x10 <sup>3</sup>	Not detected	Not detected	Not detected
RSV A	TCID50/mL	8.6x10 <sup>2</sup>	Not detected	Not detected	Not detected
Adenovirus	PFU/mL	9.7x10 <sup>3</sup>	Not detected	Not detected	Not detected
Rhinovirus	TCID50/mL	3.8x10 <sup>2</sup>	Not detected	Not detected	Not detected
Parainfluenza virus 3	PFU/mL	7.5x10 <sup>3</sup>	Not detected	Not detected	Not detected

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

Australia	11-14	Spiked N	/ledia	Cle	an Media
Analyte	Unit	UTM	<b>v</b> NAT®	UTM	<b>v</b> NAT®
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

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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	淡	Protect from heat and radioactive sources
Х	Use-by date	REF	Catalogue number		Do not use if package is damaged and consult instructions for use
X	Temperature limit	NON	Non-sterile	÷	Keep dry
$\triangle$	Caution	i	Consult instructions for use or consult electronic instructions for use		
<u>tt</u>	Keep it upright	2	Do not re-use		

#### **6 MANUFACTURER AND TECHNICAL SUPPORT**



#### Bioeksen AR GE Teknolojileri A.Ş

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Technical Support: <a href="mailto:support@bioeksen.com.tr">support@bioeksen.com.tr</a>

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-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



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## Package Insert

Component	Intended Use	2	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 amplificat FAM: Is481 ge HEX: Human (IC-Intern	ne	1 x 125 μL	1 x 500 μL
Bor 2 Oligo Mix	FAM: h/51001 g ROX: /51001 ge CY5: ptxP gen	ne	1 x 125 μL	1 x 500 μL
NTC	Negative Contr		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
able 2. Transport Condition,	Storage Condition, and Shelf Life of the Component	nts		
Component	Transport Condition		Condition*	Shelf Life
2X qPCR Mix Oligo Mix NTC PC Following the first opening, ea	(-22) °C – (+8) °C ch reagent stored at storage temperature can be used	(-22) °C (-22) °C – (-18) °C before openin (-22) °C – (-18) °C before openin	ng, (+2) °C – (+8) °C after fir	st thaw
xpiration date of the reagents.				,
able 3. Required Componen	ts Not Included in the Package	Not Included in the Package		
4. A centrifuge or Mini-s	ihuu			
able 4. Intended Use, Test P	rips, PCR plates and caps/films specific to qPCR instrun rinciple, and Analytical Specifications	·		
6. Reaction tubes, PCR st		nents and compatible with the reaction v Sample Type(s)	rolume Table 5	
6. Reaction tubes,PCR st able 4. Intended Use, Test P	inciple, and Analytical Specifications	·		
6. Reaction tubes,PCR st Table 4. Intended Use, Test Pr Function	rinciple, and Analytical Specifications Aid to diagnosis	Sample Type(s)	Table 5           vNAT® Transfer Tube           Zybio EXM3000 Nucleic	1DXlab Magnetic Induction Dx, CFX Opus 96/Dx, Is 384 5-Plex/MDx c: QuantStudio 5/5 tepOne Plus, Applied Fast tab
6. Reaction tubes,PCR st able 4. Intended Use, Test Pr Function Analyte(s)	Aid to diagnosis Table 1	Sample Type(s) Nucleic Acid Extraction Method(s)	Table 5         vNAT® Transfer Tube         Zybio EXM3000 Nucleic         Adaltis EXTRAlab and M         Bio Molecular Systems:         Cycler (Mic)/Mic IVD         Bio-Rad: CFX96 Touch/         CFX384 Touch, CFX Opt         Qiagen: Rotor-Gene Q:         Roche: LightCycler 96         Thermo Fisher Scientifi         Dx/6/7/12k Flex/Pro, SI         Biosystems 7500/7500         Adaltis: AmpliLab, MDX         HiMedia: InstaQ 96         Bioer: Linegene 9600 PI         Atila Biosystems: Fujire         Co-Dx: Co-Dx Box         Tianlong: Gentier 96E         Sansure: SLAN-96P         Azure: Cielo	1DXlab Magnetic Induction Dx, CFX Opus 96/Dx, Is 384 5-Plex/MDx c: QuantStudio 5/5 tepOne Plus, Applied Fast tlab
6. Reaction tubes,PCR st able 4. Intended Use, Test P Function Analyte(s) Qualitative/Quantitative	Aid to diagnosis Table 1 Qualitative	Sample Type(s) Nucleic Acid Extraction Method(s)	Table 5         vNAT® Transfer Tube         Zybio EXM3000 Nucleic         Adaltis EXTRAlab and M         Bio Molecular Systems:         Cycler (Mic)/Mic IVD         Bio-Rad: CFX96 Touch/         CFX384 Touch, CFX Opt         Qiagen: Rotor-Gene Q.S         Roche: LightCycler 96         Thermo Fisher Scientifi         Dx/6/7/12k Flex/Pro, St         Biosystems 7500/7500         Adaltis: AmpliLab, MDX         HIMedia: InstaQ 96         Bioer: Linegene 9600 Pl         Atila Biosystems: Fujire         Co-Dx: Co-Dx Box         Tianlong: Gentier 96E         Sansure: SLAN-96P	1DXlab Magnetic Induction Dx, CFX Opus 96/Dx, Is 384 5-Plex/MDx c: QuantStudio 5/5 tepOne Plus, Applied Fast tlab
6. Reaction tubes,PCR st able 4. Intended Use, Test Pr Function Analyte(s) Qualitative/Quantitative Test Principle	Aid to diagnosis         Aid to diagnosis         Table 1         Qualitative         Real-Time PCR (qPCR)	Sample Type(s) Nucleic Acid Extraction Method(s) Validated qPCR Instrument(s)	Table 5         vNAT® Transfer Tube         Zybio EXM3000 Nucleic         Adaltis EXTRAlab and M         Bio Molecular Systems:         Cycler (Mic)/Mic IVD         Bio-Rad: CFX96 Touch/         CFX384 Touch, CFX Opt         Qiagen: Rotor-Gene Q !         Roche: LightCycler 96         Thermo Fisher Scientifit         Dx/6/7/12k Flex/Pro, St         Biosystems 7500/7500         Adaltis: AmpliLab, MDX         HiMedia: InstaQ 96         Bioer: Linegene 9600 Pl         Atila Biosystems: Fujire         Co-Dx: Co-Dx Rox         Tianlong: Gentier 96E         Sansure: SLAN-96P         Azure: Cielo         Validated on the referee	1DXlab Magnetic Induction Dx, CFX Opus 96/Dx, Is 384 5-Plex/MDx c: QuantStudio 5/5 tepOne Plus, Applied Fast tlab

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

\*\* 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<sup>®</sup> Transfer Tube for nucleic acid isolation.

#### 1. APPLICATION PROTOCOL

- Program the qPCR device using the QR Code/Link as indicated in Table 6. 1.
- Take the PCR kit out of the -20°C freezer. 2.
- 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) 3.
- 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) 4.
- 5. Vortex the master mix to homogenize.
- 6. Repeat steps 3,4 and 5 for all master mixes. (Total 2 master mixes).
- Pipette 15 µL of master mix into all PCR tubes, or wells to be used (including all samples, NTC and PC). 7
- 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.
- Pipette 5  $\mu\text{L}$  of PC-Bor 1 into the Positive Control tubes, or wells. Repeat for all PC. 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.
- 13. Open the lid of the instrument. Place the strips, or PCR tubes or PCR plate.
- Close the lid and start the instrument. 14.

Table 6. Real Time qPCR Program Details

					RT-qPCR Pr	ogram			
Reaction Set	đr	Bio Molecular Systems: M Rad: CFX96 Touch/Dx, CF Roche: LightCycle	0	384 Touch, CFX (	Dpus 384,	Qiagen: Rotor-Gene Q 5- QuantStudio 5/5 Dx/6/7/ Biosystems 7500/7500 Fast InstaQ 96, Bioer: Linegene 9 Tianlong: Gentie	12k Flex/Pro , Adaltis: Am 9600 Plus, At	, StepOne Plus, , pliLab, MDXlab, ila Biosystems: I	Applied HiMedia:
Reagent	Volume/ Rxn	Step	Cycle No.	Temperature	Duration	Step	Cycle No.	Temperature	Duration
	10 1	Enzyme Activation	1 Cycle	52 °C	3 min	Enzyme Activation	1 Cycle	52 °C	3 min
2X qPCR Mix	10 µL	Pre-Incubation	1 Cycle	95 °C	10 sec	Pre-Incubation	1 Cycle	95 °C	10 sec
		Denaturation	12 Touchdown	95 °C	1 sec	Denaturation			
Oligo Mix	5 μL	Annealing and Extension	Cycles: 1 °C decrement in annealing	67 °C to 56 °C	15 sec	Annealing and Extension		95 °C	1 sec
			temperature per cycle			0	40 Cycles	55 °C	15 sec
Template Nucleic	E ul	Denaturation		95 °C	1 sec				
Acid/NTC/PC	5 μL	Annealing and Extension	30 Cycles	55 °C	15 sec	Detection (Reading)		FAM/HEX/R	
Total Reaction Volume	20 µL	Detection (Reading)	ou cycles	FAM/HEX/R	OX/CY5	Detection (Reading)		FAINI/TIEA/K	0//13



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 <a href="mailto-support@bioeksen.com.tr">support@bioeksen.com.tr</a>.

#### Table 7. Threshold Levels for Calculating Cq Values

		Real Time PCR Instrument											
	Analyte	Bio-Rad CFX		с	Cielo Ligh		ntCycler 96	er 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	200	30	20000	30	0.05	30	0.2	30	0.02	40	20000	30
	Control)	200	50	20000	50	0.05	50	0.2	50	0.02	40	20000	50
	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 Inter	pretation			
Positive (+)	Positive (+) or Negative (-)	Results are valid	Protocol 1	If 26 <cq "low="" positive"<br="" ≤30="">If 16<cq≤26 "positive"<br="">If Cq≤16 "High Positive"</cq≤26></cq>			
Positive (+)	Positive (+) of negative (-)	Target is detected	Protocol 2	If 34 <cq "low="" positive"<br="" ≤40="">If 22<cq≤34 "positive"<br="">If Cq≤22 "High Positive"</cq≤34></cq>			
Negative (-)	Positive (+)	Results are valid Target is not detected					
Target	Results Interpretation		Actio	on			
Bordetella pertussis	IS481 and ptxP should be positive	Re	port as Bordetella	pertussis POSITIVE			
Bordetella parapertussis	IS1001 should be positive	Repo	rt as <i>Bordetella pa</i> l	rapertussis POSITIVE			
Bordetella holmesii	IS481 and hIS1001 should be positive	Re	port as <i>Bordetella</i> p	oholmesi POSITIVE			
Bordetella branchiseptica	IS1001 and IS481 should be positive*	Repor	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

		Expected Results and Cq Values							
Control Type	Purpose	Prot	ocol 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)				
	Nucleic acid extraction and	Detected	Detection insignificant	Detected	Detection insignificant				
Internal Control	sampling control	If "Not Detected" check the target Cq If "Detected" IC is valid		If " <b>Not Detected</b> " check the target Cq	If "Detected" IC is valid				

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

- 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.
- Reagent Problem: If all Internal Controls, Positive Controls and targets in the run are "Not Detected". 3. 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

- False-negative results may occur if inadequate number (below the LoD) of organisms are present in the specimen. 1.
- Mutations within the target regions could affect primer and/or probe binding, resulting in failure to detect the presence of agents. 2.
- 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 3. pathogens and inhibit PCR.
- 4. False-negative results may occur if a specimen is improperly collected, transported, or handled.
- 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.
- 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.

P1	P10.Ek02-Rev.06/01.10.2024 PIS.002												
For in vitro diagnostic use only. 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	淡	Protect from heat and radioactive sources							
	***	Manufacturer	NON	Non-sterile	8	Do not use if package is damaged and consult <i>Instructions for Use</i>							
	$\square$	Expiration Date YYYY-MM	i	Consult Instructions for Use or consult electronic Instructions for Use	Ť	Keep dry							
	CONTROL -	Negative Control	$\triangle$	Caution	<u>tt</u>	Keep upright							
	CONTROL +	Positive Control	X	Temperature limit	Σ	Contains sufficient for <i><n></n></i> tests							
	CONTROL	Control											

#### MANUFACTURER AND TECHNICAL SUPPORT 5.

Bioeksen AR GE Teknolojileri A.Ş

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Web: www.bioeksen.com.tr, e-mail: info@bioeksen.com.tr,

Technical Support: <a href="mailto:support@bioeksen.com.tr">support@bioeksen.com.tr</a>

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-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**

able 1. Kit Content							
Component		Intended U	se		25 Reactions	100 Reactions	
2X Prime Script Mix	Optimized read	dy-to-use mix	for RT-qPCR assay		1 x 125 μL	1 x 500 μL	
HEV Oligo Mix	FAM	acid amplifica I: Human Ento man (IC-Inter			1 x 62,5 μL	1 x 250 μL	
NTC		Negative Con			1 x 1000 μL	1 x 1000 μL	
PC-HEV		ositive Contro			1 x 100 μL	1 x 100 μL	
ole 2. Transport Condition	, Storage Condition, and Shelf Life of th	ne Compone	nts		· · ·	•	
Component	Transport Condition			Storage Condition		Shelf Life	
2X Prime Script Mix				(-22) °C – (-18)			
Oligo Mix	(-22) °C − (+8) °C		(22) % (18) %	(-22) °C – (-18)		12 Months	
PC NTC					C - (+8) °C after first thaw C - (+8) °C after first thaw		
iration date of the reagents	nts Not Included in the Package			late indicated on the		is determined b	
<ol> <li>Micropipettes and c</li> <li>A centrifuge or Mini</li> <li>Vortex</li> <li>Reaction tubes,PCR</li> </ol>	nsfer Tube (Cat. No: BS-NA-513m) or nucle ompatible filtered pipette tips (nuclease-fre -spin strips, PCR plates and caps/films specific to Principle, and Analytical Specifications	ee) suitable fo	or transferring 1-10 $\mu$	L, 10-100 μL, and 100	0-1000 μL of liquid		
unction	Aid to diagnosis		Sample Type(s)		Table 5		
nalyte(s)	Table 1		Nucleic Acid Extrac	ction Method(s)	Bioeksen vNAT <sup>®</sup> Transfer Tube Zybio EXM3000 Nucleic Acid Isolation System Adaltis EXTRAlab and MDXlab		
Qualitative/Quantitative	Qualitative		Validated qPCR Ins	:trument(s)	Bio Molecular Systems: M Cycler (Mic)/Mic IVD Bio-Rad: CFX96 Touch/Dx, CFX384 Touch, CFX Opus 38 Qiagen: Rotor-Gene Q 5-Ple Roche: LightCycler 96 Thermo Fisher Scientific: Dx/6/7/12k Flex/Pro, Step 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	CFX Opus 96/ 4 x/MDx QuantStudio S One Plus, Appl	
est Principle	Reverse Transcription and Real-Time PCR	(RT-qPCR)	Inclusivity and Excl	lusivity	Validated on the reference	strains and the fi	
utomated/Manual	Manual				isolates		
ntended Users	Laboratory professionals trained in the teo qPCR and in vitro diagnostic procedures.	chniques of	Limit of Detection	(LoD)	Table 5		
arget Population	Individuals with the suspected infection		Sensitivity and Spe	-	100.00% and 100.00%		
	and Transfer of Clinical Specimens / Nu					1	
Sample Type**	Sample Transfer		n <b>ple Storage</b> at (+2) °C – (+8) °C		cid Preparation Method extraction is not needed.	LoD (cp/r	
ombined nasopharyngeal a oropharyngeal swab***		1 ye	ear at (-20) °C t (+2) °C – (+8) °C	The samples ca	n be used directly in RT-qPCR. paration instruments: 1) Zybio	)	
Si opniai yngear swan	(CDC SOP#: DSR-052-05)		ear at (-20) °C		ltis EXTRAlab, 3) Adaltis MDXIa	125	

- Pipette 7,5 µL of master mix into all PCR tubes, or wells to be used (including all samples, NTC and PC). 6.
- 7. Pipette 2,5 µL of each isolated/ extracted sample into the relative PCR tube, or well.
- Pipette 2,5 µL of NTC into the Negative Control PCR tube, or well. 8.
- 9 Pipette 2,5  $\mu\text{L}$  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.
- Open the lid of the instrument. Place the strips, PCR tubes or PCR plate. 12.
- 13. Close the lid and start the instrument. Table 6. Real-Time qPCR Program Details

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

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

#### **INTERPRETATION OF THE ASSAY RESULTS** 2.

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

		Real Time PCR Instrument											
A	Analyte	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
Humar	n 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 "low="" positive"<br="" ≤30="">If 16<cq≤26 "positive"<br="">If Cq≤16 "High Positive"</cq≤26></cq>			

Revision Date: 2024-10-23/Rev.03 Published Date: 2023-10-04



For in vitro diagnostic For professional use o				bi 🖉 eksen			
			Protocol 2	If 34 <cq "low="" positive"<br="" ≤40="">If 22<cq≤34 "positive"<br="">If Cq≤22 "High Positive"</cq≤34></cq>			
Negative (-)         Positive (+)         Results are valid           Target is not detected         Target is not detected         Target is not detected							

#### Table 9. Expected Performance of Kit Controls

		Expected Results and Cq Values							
Control Type	Purpose	Prot	ocol 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)				
	Nucleic acid extraction and	Detected	Detection insignificant	Detected	Detection insignificant				
Internal Control	sampling control	If " <b>Not Detected</b> " check the target Cq	If "Detected" IC is valid	If " <b>Not Detected</b> " check the target Cq	If "Detected" IC is valid				

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

 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.

- 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           IVD         In vitro diagnostic medical device		Batch code	漛	Keep away from sunlight	
IVD			Catalogue number	·淡·	Protect from heat and radioactive sources	
	Manufacturer	NON	Non-sterile	8	Do not use if package is damaged and consult Instructions for Use	
2	Expiration Date YYYY-MM		Consult Instructions for Use or consult electronic Instructions for Use	Ť	Keep dry	
CONTROL -	Negative Control	$\triangle$	Caution	<u>tt</u>	Keep upright	
CONTROL +	Positive Control	X	Temperature limit	Σ	Contains sufficient for <n> tests</n>	
CONTROL	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 inform us about product-related incidents at "vigilance@bioeksen.com.tr" within 24 hours.

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

2X qPCR Mix (-22) *	ing, (+2) °C – (+8) °C after first the tube. The kit's expiration d 100-1000 μL of liquid	thaw late is determined by Acid Isolation System DXlab	
BA Oligo Mix       FAM: Bacillus anthracis HEX: Human (IC-Internal Control)         PC-BA       Positive Control (PC)         NTC       Negative (No Template) Control         able 2. Transport Condition, Storage Condition, and Shelf Life of the Components       Storage         Component       Transport Condition         Storage       (-22) °C - (+8) °C         Oligo Mix       (-22) °C - (+8) °C         NTC       (-22) °C - (-18) °C before open (	1 x 100 μL           1 x 1000 μL           1 x 1000 μL           C - (-18) °C           'C - (-18) °C           ing, (+2) °C - (+8) °C after first           ing, (+2) °C - (+8) °C after first           the tube. The kit's expiration d           100-1000 μL of liquid           n volume           Table 5           Zybio EXM3000 Nucleic / Adaltis EXTRAlab and MI           Bio Molecular Systems	1 x 100 μL         1 x 1000 μL         Shelf Life         12 Months         thaw         date is determined by         Acid Isolation System         DXIab	
HEX: Human (IC-Internal Control)         PC-BA       Positive Control (PC)         NTC       Negative (No Template) Control         able 2. Transport Condition, Storage Condition, and Shelf Life of the Components       Storage         Component       Transport Condition       Storage         2X qPCR Mix       (-22) °C - (+8) °C       (-22) °C - (-18) °C before open         Oligo Mix       (-22) °C - (-18) °C before open       (-22) °C - (-18) °C before open         PC       Components Not Included in the Package       Required Components Not Included in the Package         Required Components Not Included in the Package         1       Real-Time PCR Instrument       Required Components Not Included in the Package       Include in the Package         1. Real-Time PCR 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         4. A centrifuge or Mini-spin       So Vortex       Geaction tubes, PCR strips, PCR plates and caps/films specific to qPCR instruments and compatible with the reaction tubes, PCR strips, PCR plates and caps/films specific to qPCR instruments and compatible with the reaction tubes, PCR strips, PCR plates and caps/films specific to qPCR instruments and compatible with the reaction tubes, PCR strips, PCR plates and caps/films specific to qPCR instruments and compatible with the reaction tubes, PCR strips, PCR plates and caps/films specific to qPCR instru	1 x 100 μL           1 x 1000 μL           1 x 1000 μL           C - (-18) °C           'C - (-18) °C           ing, (+2) °C - (+8) °C after first           ing, (+2) °C - (+8) °C after first           the tube. The kit's expiration d           100-1000 μL of liquid           n volume           Table 5           Zybio EXM3000 Nucleic / Adaltis EXTRAlab and MI           Bio Molecular Systems	1 x 100 μL         1 x 1000 μL         Shelf Life         12 Months         thaw         date is determined by         Acid Isolation System         DXIab	
PC-BA       Positive Control (PC)         NTC       Negative (No Template) Control         able 2. Transport Condition, Storage Condition, and Shelf Life of the Components       Component         Component       Transport Condition         2X qPCR Mix       (-22)°         Oligo Mix       (-22)°C - (+8) °C         NTC       (-22)°C - (-18) °C before open         PC       (-22)°C - (-18) °C before open         Following the first opening, each reagent stored at storage temperature can be used until the expiration date indicated on to prization date of the reagents.         able 3. 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         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 able 4. Intended Use, Test Principle, and Analytical Specifications         Function       Aid to diagnosis       Sample Type(s)	1 x 1000 μL         e Condition*         C - (-18) °C         'C - (-18) °C         ing, (+2) °C - (+8) °C after first         ing, (+2) °C - (+8) °C after first         the tube. The kit's expiration d         100-1000 μL of liquid         n volume         Table 5         Zybio EXM3000 Nucleic /         Adaltis EXTRAlab and ME         Bio Molecular Systems	1 x 1000 μL  Shelf Life  12 Months t thaw date is determined by  Acid Isolation System DXlab	
NTC       Negative (No Template) Control         ble 2. Transport Condition, Storage Condition, and Shelf Life of the Components       Storage         Component       Transport Condition       Storage         2X qPCR Mix       (-22)°C       (-22)°C         Oligo Mix       (-22)°C - (+8) °C       (-22)°C         NTC       (-22)°C - (-18)°C before open       (-22)°C - (-18)°C before open         PC       (-22)°C - (-18)°C before open       (-22)°C - (-18)°C before open         Following the first opening, each reagent stored at storage temperature can be used until the expiration date indicated on the piration date of the reagents.       (-22)°C - (-18)°C before open         ble 3. Required Components Not Included in the Package       Required Components Not Included in the Package         1. Real-Time PCR Instrument       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       .         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       .         5. Vortex       .       .       .         6. Reaction tubes, PCR strips, PCR plates and caps/films specific to qPC	1 x 1000 μL         e Condition*         C - (-18) °C         'C - (-18) °C         ing, (+2) °C - (+8) °C after first         ing, (+2) °C - (+8) °C after first         the tube. The kit's expiration d         100-1000 μL of liquid         n volume         Table 5         Zybio EXM3000 Nucleic /         Adaltis EXTRAlab and ME         Bio Molecular Systems	1 x 1000 μL  Shelf Life  12 Months t thaw date is determined by  Acid Isolation System DXlab	
ble 2. Transport Condition, Storage Condition, and Shelf Life of the Components         Component       Transport Condition       Storage         2X qPCR Mix       (-22) °C       (-22) °C         Oligo Mix       (-22) °C - (+8) °C       (-22) °C         NTC       (-22) °C - (-18) °C before open       (-22) °C - (-18) °C before open         Following the first opening, each reagent stored at storage temperature can be used until the expiration date indicated on the piration date of the reagents.       Required Components Not Included in the Package         Following the first opening, each reagent and nucleic acid preparation consumables       Required Components Not Included in the Package         1.       Real-Time PCR Instrument       Nucleic acid preparation instruments and nucleic acid preparation consumables       3.         3.       Micropipettes and compatible filtered pipette tips (nuclease-free) suitable for transferring 1-10 µL, 10-100 µL, and         4.       A centrifuge or Mini-spin       S.         5.       Vortex       6.       Reaction tubes, PCR strips, PCR plates and caps/films specific to qPCR instruments and compatible with the reaction         5.       Vortex       6.       Reaction tubes, PCR strips, PCR plates and caps/films specific to qPCR instruments and compatible with the reaction         6.       Reaction tubes, PCR strips, PCR plates and caps/films specific to qPCR instruments and compatible with the reaction <t< td=""><td>e Condition* C – (-18) °C C – (-18) °C ing, (+2) °C – (+8) °C after first ing, (+2) °C – (+8) °C after first the tube. The kit's expiration d 100-1000 μL of liquid n volume Table 5 Zybio EXM3000 Nucleic / Adaltis EXTRAlab and MI Bio Molecular Systems</td><td>Shelf Life 12 Months thaw date is determined by Acid Isolation System DXlab</td></t<>	e Condition* C – (-18) °C C – (-18) °C ing, (+2) °C – (+8) °C after first ing, (+2) °C – (+8) °C after first the tube. The kit's expiration d 100-1000 μL of liquid n volume Table 5 Zybio EXM3000 Nucleic / Adaltis EXTRAlab and MI Bio Molecular Systems	Shelf Life 12 Months thaw date is determined by Acid Isolation System DXlab	
Component         Transport Condition         Storage           2X qPCR Mix         (-22)°C         (-21)°C         (-22)°C         (-22)°C         (-21)°C         (-22)°C         (-22)°C         (-21)°C         (-22)°C         (-21)°C         (-22)°C         (-21)°C <td>C – (-18) °C C – (-18) °C ing, (+2) °C – (+8) °C after first ing, (+2) °C – (+8) °C after first the tube. The kit's expiration d 100-1000 μL of liquid n volume Table 5 Zybio EXM3000 Nucleic <i>i</i> Adaltis EXTRAlab and MI Bio Molecular Systems</td> <td>12 Months thaw tate is determined by Acid Isolation System</td>	C – (-18) °C C – (-18) °C ing, (+2) °C – (+8) °C after first ing, (+2) °C – (+8) °C after first the tube. The kit's expiration d 100-1000 μL of liquid n volume Table 5 Zybio EXM3000 Nucleic <i>i</i> Adaltis EXTRAlab and MI Bio Molecular Systems	12 Months thaw tate is determined by Acid Isolation System	
2X qPCR Mix       (-22) °C - (+8) °C         Oligo Mix       (-22) °C - (-18) °C before open         PC       (-22) °C - (-18) °C before open         Following the first opening, each reagent stored at storage temperature can be used until the expiration date indicated on the piration date of the reagents.         bible 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         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         bibe 4. Intended Use, Test Principle, and Analytical Specifications         Function       Aid to diagnosis	C – (-18) °C C – (-18) °C ing, (+2) °C – (+8) °C after first ing, (+2) °C – (+8) °C after first the tube. The kit's expiration d 100-1000 μL of liquid n volume Table 5 Zybio EXM3000 Nucleic <i>i</i> Adaltis EXTRAlab and MI Bio Molecular Systems	12 Months thaw tate is determined by Acid Isolation System	
Oligo Mix       (-22) °C - (+8) °C       (-22) °C - (-18) °C before open         PC       (-22) °C - (-18) °C before open       (-22) °C - (-18) °C before open         Following the first opening, each reagent stored at storage temperature can be used until the expiration date indicated on temperature date of the reagents.       (-22) °C - (-18) °C before open         spiration date of the reagents.       able 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.         3. Micropipettes and compatible filtered pipette tips (nuclease-free) suitable for transferring 1-10 µL, 10-100 µL, and         4. A centrifuge or Mini-spin       5.         5. Vortex       6.         6. Reaction tubes, PCR strips, PCR plates and caps/films specific to qPCR instruments and compatible with the reaction able 4. Intended Use, Test Principle, and Analytical Specifications         Function	C – (-18) °C ing, (+2) °C – (+8) °C after first ing, (+2) °C – (+8) °C after first the tube. The kit's expiration d 100-1000 μL of liquid n volume Table 5 Zybio EXM3000 Nucleic / Adaltis EXTRAlab and MI Bio Molecular Systems	t thaw t thaw date is determined by date is determined by date is determined by date by date is determined by date is determined by date is determined by date is determined by date is determined by date is determined by date is determined by date is determined by date is determined by date is determined by date is determined by	
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NTC       (-22) °C - (+8) °C         PC       (-22) °C - (-18) °C before open         Following the first opening, each reagent stored at storage temperature can be used until the expiration date indicated on the piration date of the reagents.       (-22) °C - (-18) °C before open         ble 3. Required Components Not Included in the Package       Required Components Not Included in the Package         1. Real-Time PCR Instrument       Required Components Not Included in the Package         3. Micropipettes and compatible filtered pipette tips (nuclease-free) suitable for transferring 1-10 μL, 10-100 μL, and         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         ble 4. Intended Use, Test Principle, and Analytical Specifications         Function       Aid to diagnosis	ing, (+2) °C – (+8) °C after first ing, (+2) °C – (+8) °C after first the tube. The kit's expiration d 100-1000 μL of liquid n volume Table 5 Zybio EXM3000 Nucleic / Adaltis EXTRAlab and MI Bio Molecular Systems	t thaw t thaw date is determined by date is determined by date is determined by date by date is determined by date is determined by date is determined by date is determined by date is determined by date is determined by date is determined by date is determined by date is determined by date is determined by date is determined by	
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iollowing the first opening, each reagent stored at storage temperature can be used until the expiration date indicated on the priz	the tube. The kit's expiration d 100-1000 μL of liquid n volume Table 5 Zybio EXM3000 Nucleic <i>i</i> Adaltis EXTRAlab and MI Bio Molecular Systems	date is determined by Acid Isolation System DXlab	
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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         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         ble 4. Intended Use, Test Principle, and Analytical Specifications         function       Aid to diagnosis	Table 5 Zybio EXM3000 Nucleic / Adaltis EXTRAlab and MI Bio Molecular Systems	DXlab	
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         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         ble 4.       Intended Use, Test Principle, and Analytical Specifications         function       Aid to diagnosis	Table 5 Zybio EXM3000 Nucleic / Adaltis EXTRAlab and MI Bio Molecular Systems	DXlab	
<ol> <li>Real-Time PCR Instrument</li> <li>Nucleic acid preparation instruments and nucleic acid preparation consumables</li> <li>Micropipettes and compatible filtered pipette tips (nuclease-free) suitable for transferring 1-10 μL, 10-100 μL, and</li> <li>A centrifuge or Mini-spin</li> <li>Vortex</li> <li>Reaction tubes, PCR strips, PCR plates and caps/films specific to qPCR instruments and compatible with the reaction</li> <li>ble 4. Intended Use, Test Principle, and Analytical Specifications</li> <li>Aid to diagnosis</li> </ol>	Table 5 Zybio EXM3000 Nucleic / Adaltis EXTRAlab and MI Bio Molecular Systems	DXlab	
<ol> <li>Nucleic acid preparation instruments and nucleic acid preparation consumables</li> <li>Micropipettes and compatible filtered pipette tips (nuclease-free) suitable for transferring 1-10 μL, 10-100 μL, and</li> <li>A centrifuge or Mini-spin</li> <li>Vortex</li> <li>Reaction tubes, PCR strips, PCR plates and caps/films specific to qPCR instruments and compatible with the reaction ble 4. Intended Use, Test Principle, and Analytical Specifications</li> <li>unction</li> <li>Aid to diagnosis</li> <li>Sample Type(s)</li> </ol>	Table 5 Zybio EXM3000 Nucleic / Adaltis EXTRAlab and MI Bio Molecular Systems	DXlab	
<ul> <li>A centrifuge or Mini-spin</li> <li>Vortex</li> <li>Reaction tubes, PCR strips, PCR plates and caps/films specific to qPCR instruments and compatible with the reaction on the specifications</li> <li>Intended Use, Test Principle, and Analytical Specifications</li> <li>Aid to diagnosis</li> </ul>	Table 5 Zybio EXM3000 Nucleic / Adaltis EXTRAlab and MI Bio Molecular Systems	DXlab	
5.       Vortex         6.       Reaction tubes, PCR strips, PCR plates and caps/films specific to qPCR instruments and compatible with the reaction         ble 4. Intended Use, Test Principle, and Analytical Specifications         unction       Aid to diagnosis         Sample Type(s)	Table 5         Zybio EXM3000 Nucleic A         Adaltis EXTRAlab and MI         Bio Molecular Systems	DXlab	
6.       Reaction tubes,PCR strips, PCR plates and caps/films specific to qPCR instruments and compatible with the reaction         ole 4. Intended Use, Test Principle, and Analytical Specifications         unction       Aid to diagnosis         Sample Type(s)	Table 5         Zybio EXM3000 Nucleic A         Adaltis EXTRAlab and MI         Bio Molecular Systems	DXlab	
Sample 4. Intended Use, Test Principle, and Analytical Specifications       Aid to diagnosis     Sample Type(s)	Table 5         Zybio EXM3000 Nucleic A         Adaltis EXTRAlab and MI         Bio Molecular Systems	DXlab	
unction     Aid to diagnosis     Sample Type(s)	Zybio EXM3000 Nucleic A Adaltis EXTRAlab and MI Bio Molecular Systems	DXlab	
	Zybio EXM3000 Nucleic A Adaltis EXTRAlab and MI Bio Molecular Systems	DXlab	
nalyte(s) Table 1 Nucleic Acid Extraction Method(s)	Adaltis EXTRAlab and MI Bio Molecular Systems	DXlab	
	Bio Molecular Systems		
		: Magnetic Induction	
Qualitative/Quantitative Qualitative Validated qPCR Instrument(s)	Bio-Rad: CFX96 Touch/ CFX384 Touch, CFX Opus Qiagen: Rotor-Gene Q 5- Roche: LightCycler 96 Thermo Fisher Scienti Dx/6/7/12k Flex/Pro, S Biosystems 7500/7500 F Adaltis: AmpliLab, MDXIa HiMedia: InstaQ 96 Bioer: Linegene 9600 Plu Atila Biosystems: Fujireb Co-Dx: Co-Dx Box Tianlong: Gentier 96E Sansure: SLAN-96P Azure: Cielo	s 384 -Plex/MDx ific: QuantStudio 5 itepOne Plus, Appli ast ab	
Test Principle Real-Time PCR (qPCR)	Validated on the referen	ice strains and the fie	
Automated/Manual Manual Inclusivity and Exclusivity	isolates		
ntended Users Professional use Limit of Detection (LoD)	Table 5		
Farget Population         Individuals with the suspected infection         Sensitivity and Specificity	100.00% and 100.00%		
ble 5. Collection, Storage, and Transfer of Clinical Specimens / Nucleic Acid Preparation Methods			
	ic Acid Preparation Method	LoD (cp/m	
Whole blood and serum FDLA-treated tube	preparation instruments: 1) Z	Zybio	
3 days at (+2) °C – (+8) °C	EXM3000, 2) Adaltis EXTRAlab		
1 year at (-20) °C Nucleic acid p	reparation consumables: Bioeksen 15 pid 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) \*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.
- $\textbf{9.} \qquad \text{Pipette 2,5 } \mu \text{L of PC-BA into the Positive Control tube, or well.}$
- 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 gPCR Program Details

rable 6. Real-Time q	ren riogia								
					qPCR Pro	gram			
Reaction Set	ир	Bio Molecular Systen Rad: CFX96 Touch/D Roche: Light		X384 Touch, CF	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, HiMed 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
		Enzyme Activation	1 Cycle	52 °C	3 min	Enzyme Activation	1 Cycle	52 °C	3 min
2X qPCR Mix	5 μL	Pre-Incubation	1 Cycle	95 °C	10 sec	Pre-Incubation	1 Cycle	95 °C	10 sec
		Denaturation	12 Touchdown	95 °C	1 sec	Denaturation			
Oligo Mix		Annealing and	Cycles: 1 °C decrement in annealing 67 °C to 56 °C 15 sec Annealing and Extensi	Annealing and Extension		95 °C	1 sec		
		Extension	temperature per cycle				40 Cycles	55 °C	15 sec
Tomplato Nuclaio		Denaturation		95 °C	1 sec				
Template Nucleic Acid/NTC/PC	2,5 μL	Annealing and Extension	30 Cycles	55 °C	15 sec	Detection (Reading)		FAM/H	IEX
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 <u>support@bioeksen.com.tr.</u>

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

ſ							Real Time P	CR Instru	ument				
	Analyte	Bi	o-Rad CFX	(	Cielo Ligh		LightCycler 96		Mic/Mic IVD and Co-Dx Box		r-Gene Q***	QuantStudio 5/5 Dx/6/7/12k Flex/Pro	
		RFU	RFU Cq Cut-off		Cq Cut-off	RFU	Cq Cut-off	RFU	Cq Cut-off	RFU	Cq Cut-off	RFU	Cq Cut-off
ſ	Human (IC-Internal Control)	200			30	0.05	30	0.2	30	0.02	40	20000	30
ſ	Bacillus anthracis	200	30	20000	30	0.05	30	0.2	30	0.02	40	20000	30
	<b>being thread with accelerating of </b> $(0.014)$ <b>being Demonstration 200 being thread thread with accelerating of </b> $(0.014)$ <b>being thread with accelerating of </b> $(0.014)$ <b>being thread thread with accelerating of </b> $(0.014)$ <b>being thread thread with accelerating of </b> $(0.014)$ <b>being thread thread with accelerating of </b> $(0.014)$ <b>being thread thread with accelerating of </b> $(0.014)$ <b>being thread thread with accelerating of </b> $(0.014)$ <b>being thread thread with accelerating of </b> $(0.014)$ <b>being thread thread thread thread thread with accelerating of <math>(0.014)</math> <b>being thread</b></b>												

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

#### **Table 8. Interpretation of Patient Results** Internal Control (IC) **Result Interpretation** Target If 26<Cq ≤30 "Low Positive" Protocol 1 If 16<Cq≤26 "Positive" If Cq≤16 "High Positive" Results are valid Positive (+) Positive (+) or Negative (-) Target is detected If 34<Cq ≤40 "Low Positive" Protocol 2 If 22<Cq≤34 "Positive" If Cq≤22 "High Positive" Results are valid Negative (-) Positive (+) Target is not detected



PIS.009

**Table 9. Expected Performance of Kit Controls Expected Results and Cq Values** Protocol 2 Control Type Purpose Protocol 1 IC (HEX) Target IC (HEX) Target Contamination control **Negative Control** Not Detected Not Detected Not Detected Not Detected during qPCR **Positive Control** Detected (Cq≤40) Reagent stability control Detected (Cq≤30) Detected (Cq≤30) Detected (Cq≤40) Detected **Detection insignificant** Detected Detection insignificant Nucleic acid extraction and **Internal Control** If "Not Detected" check the If "Not Detected" check the sampling control If "Detected" IC is valid If "Detected" IC is valid target Cq target Cq

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.

- 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.
  - Filtered and nuclease-free pipette tips should be used for sample transfer.
     The components in the kit should not be used together with different LOT numbers or characteristic of the same new local together.
  - The components in the kit should not be used together with different LOT numbers or chemicals of the same name but from different manufacturers.
     <u>The caps of the reaction tubes must not be opened after the PCR run.</u> The PCR tubes should be placed in a bag and thrown away after the bag is tightly closed.
  - 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	类	Keep away from sunlight
IVD	In vitro diagnostic medical device	REF	Catalogue number	·淡·	Protect from heat and radioactive sources
	Manufacturer	NON	Non-sterile	8	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	Ť	Keep dry
CONTROL -	Negative Control	$\triangle$	Caution	<u>tt</u>	Keep upright
CONTROL +	Positive Control	X	Temperature limit	Σ	Contains sufficient for <n> tests</n>
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 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: <a href="mailto:support@bioeksen.com.tr">support@bioeksen.com.tr</a>

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-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**

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 500 μL		
,	Storage Condition, and Shelf Life of the Componen	!	1 x 250 μL	1 x 250 μL	
Component	Transport Condition		Storage Condition*		Shelf Life
2X Prime Script Mix			(-22) °C – (-18) °C		
Oligo Mix	-		(-22) °C – (-18) °C		
NTC	(-22) °C − (+8) °C	(-22) °C – (-18) °C befo	re opening, (+2) °C – (+	-8) °C after first thaw	12 Months
PC	-	(-22) °C – (-18) °C befo	re opening, (+2) °C – (+	-8) °C after first thaw	
	nent <b>fer Tube</b> (Cat. No: BS-NA-513m) or nucleic acid prepa npatible filtered pipette tips (nuclease-free) suitable fo				
<ol> <li>Micropipettes and con</li> <li>A centrifuge or Mini-sy</li> <li>Vortex</li> <li>Reaction tubes, PCR str</li> </ol>	fer Tube (Cat. No: BS-NA-513m) or nucleic acid prepa npatible filtered pipette tips (nuclease-free) suitable fo pin ips, PCR plates and caps/films specific to qPCR instrum	r transferring 1-10 μL, 1	0-100 μL, and 100-1000	Ο μL of liquid	
<ol> <li>Micropipettes and con</li> <li>A centrifuge or Mini-si</li> <li>Vortex</li> <li>Reaction tubes, PCR str</li> <li>ble 4. Intended Use, Test Print</li> </ol>	fer Tube (Cat. No: BS-NA-513m) or nucleic acid prepa npatible filtered pipette tips (nuclease-free) suitable fo bin ips, PCR plates and caps/films specific to qPCR instrum inciple, and Analytical Specifications	r transferring 1-10 μL, 1 nents and compatible wi	0-100 μL, and 100-1000	Ο μL of liquid	
<ol> <li>Micropipettes and con</li> <li>A centrifuge or Mini-sy</li> <li>Vortex</li> <li>Reaction tubes, PCR str</li> </ol>	fer Tube (Cat. No: BS-NA-513m) or nucleic acid prepa npatible filtered pipette tips (nuclease-free) suitable fo pin ips, PCR plates and caps/films specific to qPCR instrum	r transferring 1-10 μL, 1	0-100 μL, and 100-1000 th the reaction volume Tab Inction Bion Zyb	Ο μL of liquid	id Isolation System

Validated qPCR Instrument(s)

**Inclusivity and Exclusivity** 

Limit of Detection (LoD)

Sensitivity and Specificity

Sample Storage

3 months at (+2) °C – (+8) °C

1 year at (-20) °C

3 days at (+2) °C – (+8) °C

1 year at (-20) °C

3 days at (+2) °C − (+8) °C

1 year at (-20) °C

\*\*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<sup>®</sup> Transfer Tube for nucleic acid isolation.

Sample Type\*\*

Combined nasopharyngeal, and

oropharyngeal swabs\*\*\*

Bronchoalveolar lavage (BAL)

and nasopharyngeal aspirate

Qualitative/Quantitative

Test Principle

Intended Users

**Target Population** 

Automated/Manual

Qualitative

Manual

Reverse Transcription and Real-Time PCR (RT-qPCR)

Laboratory professionals trained in the techniques

of gPCR and in vitro diagnostic procedures. Individuals with the suspected infection

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

**vNAT®** Transfer Tube

(Cat. No: BS-NA-513m)

Viral Transport Medium (VTM)

(CDC SOP#: DSR-052-05)

Preservative-free sterile

containers/tubes

Revision Date: 2024-11-18/Rev.04

Published Date: 2023-10-04



1

LoD (cp/mL)

250

125

500

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

isolates

Table 5

**Nucleic Acid Preparation Method** 

Nucleic acid preparation is not required.

The sample can be used directly in qPCR.

Nucleic acid preparation instruments: 1) Zybio

EXM3000, 2) Adaltis EXTRAlab, 3) Adaltis MDXlab Nucleic acid preparation consumables: Bioeksen Bio-

Speedy<sup>®</sup> Rapid Nucleic Acid Extraction Kit (Cat. No:

ZFNAE01)

%100.00 ve %100.00

Validated on the reference strains and the field



#### 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

				R	T-qPCR Pr	ogram				
Reaction Set	up	Bio Molecular Systems: Mag Rad: CFX96 Touch/Dx, CFX 0 Roche: LightCycler 9	Dpus 96/Dx, CFX38	cler (Mic)/Mic IV 4 Touch, CFX Opt	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, MDXIab, HiMedia InstaQ 96, Bioer: Linegene 9600 Plus, Atila Biosystems: FujirebioTianlong: Gentier 96E, Sansure: SLAN-96P					
Reagent	Volume/ Rxn	Step	Cycle No.	Temperature	Durati on	Step	Cycle No.	Temperature	Duration	
		Reverse Transcription	1 Cycle	52 °C	3 min	Reverse Transcription	1 Cycle	52 °C	3 min	
2X Prime Script Mix	10 µL	Pre-Incubation	1 Cycle	95 °C	10 sec	Pre-Incubation	1 Cycle	95 °C	10 sec	
		Denaturation	12 Touchdown	95 °C	1 sec	Denaturation				
Oligo Mix	5 μL	5 μL	Annealing and Extension	Cycles: 1 °C decrement in annealing	67 °C to 56 °C	15 sec	Annealing and Extension		95 °C	1 sec
		5	temperature per cycle				40 Cycles	55 °C	15 sec	
Template Nucleic	5 μL	Denaturation		95 °C	1 sec					
Acid/NTC/PC	5 μι	Annealing and Extension	30 Cycles	55 °C	15 sec	Detection (Reading)		<b>ΕΔΙΛΙ/ΗΕΧ/</b> Β	08/095	
Acid/NTC/PC           Total Reaction           Volume	Detection (Reading)	50 cycles	FAM/HEX/RO	X/CY5	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 <u>support@bioeksen.com.tr</u>.

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

		Real Time PCR Instrument											
Analyte	Bi	o-Rad CFX	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		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 Inte	rpretation
Positive (+)	Positive (+) or Negative (-)	Results are valid	Protocol 1	If 26 <cq "low="" positive"<br="" ≤30="">If 16<cq≤26 "positive"<br="">If Cq≤16 "High Positive"</cq≤26></cq>
Positive (+)	Positive (+) () Negative (-)	Target is detected	Protocol 2	If 34 <cq "low="" positive"<br="" ≤40="">If 22<cq≤34 "positive"<br="">If Cq≤22 "High Positive"</cq≤34></cq>
Negative (-)	Positive (+)		Results	are valid
Revision Date: 2024-11-18/Rev. Published Date: 2023-10-04	.04			2



P10.Ek02-Rev.06/01.10.2024 eksen For in vitro diagnostic use only. For professional use only Target is not detected Table 9. Expected Performance of Kit Controls **Expected Results and Cq Values** Protocol 2 **Control Type** Purpose Protocol 1 IC (HEX) Target IC (HEX Target Contamination control **Negative Control** Not Detected Not Detected Not Detected Not Detected during RT-qPCR **Positive Control** Reagent stability control Detected (Cq≤30) Detected (Cq≤30) Detected (Cq≤40) Detected (Cq≤40) Detection insignificant Detected Detected Detection insignificant Nucleic acid extraction and **Internal Control** If "Not Detected" check the If "Not Detected" check the If "Detected" IC is valid If "Detected" IC is valid sampling control target Cq target Cq If a control does not work as expected (Table 9), apply the procedures described below. Contamination Problem: If a target in the Negative Control reaction is "Detected". 1. Recommended action: Repeat the run, paying attention to the "Warnings and Limitations" section. Invalid Internal Control Problem: If the Internal Control (IC) and all other targets of a sample are "Not Detected". 2 repeats, a new sample from the same patient should be collected and tested again. Reagent Problem: If all Internal Controls, Positive Controls and targets in the run are "Not Detected". 3 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 False-negative results may occur if inadequate number (below the LoD) of organisms are present in the specimen. 1. 2 Mutations within the target regions could affect primer and/or probe binding, resulting in failure to detect the presence of agents. 3. inactivate some pathogens and inhibit PCR. 4. False-negative results may occur if a specimen is improperly collected, transported, or handled. 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. 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. Waste disposal must be carried out in accordance with local, state, and federal regulations. 12. 13. Proper personal protective equipment including lab coats, gowns, gloves, eye protection, and a biological safety cabinet are recommended for manipulation of clinical specimens. in a biohazard waste stockpot. The micropipettes used for pipetting PCR mixes and template nucleic acids should be separate. Filtered and nuclease-free pipette tips should be used. 15. 16. Maintenance/ calibration interval should be determined for all instruments and equipment used with the kit. **EXPLANATION OF SYMBOL** 4.

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

- 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

- 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

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	淡	Protect from heat and radioactive sources
***	Manufacturer	NON	Non- <i>sterile</i>		Do not use if package is damaged and consult Instructions for Use
	Expiration Date YYYY-MM	-I	Consult Instructions for Use or consult electronic Instructions for Use	Ť	Keep dry
CONTROL -	Negative Control	$\overline{\mathbb{A}}$	Caution	<u>tt</u>	Keep upright
CONTROL +	Positive Control	<u> </u>	Temperature limit	Σ	Contains sufficient for <n> tests</n>
CONTROL	Control				

#### MANUFACTURER AND TECHNICAL SUPPORT 5.

### Bioeksen AR GE Teknolojileri A.Ş

Address: Huzur Mah. Metin Oktay Cad. Nurol Life Sitesi D Blok No:3/31, 34396 Sarıyer/İstanbul-TÜRKİYE

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.

For in vitro diagnostic use only. For professional use only. Cat No: BS-SE-MX30T-25/BS-SE-MX30T-100 Ordering Ref No: Sepsis-P1-T-25/Sepsis-P1-T-100

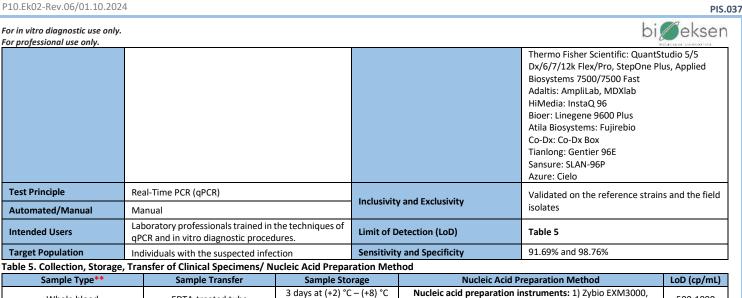
# Sepsis qPCR MX-30T Panel

## Package Insert



Component		Target		25 Reactions	100 Reactions		
2X gPCR Mix		Optimized ready-to-use n	nix for gPCR assay	2 x 1000 μL	7 x 1250 μL		
SPVC Oligo Mix		FAM : Staphylococ HEX : Pseudomo ROX: VanA-Vancomy CY5: Candida	<i>cus aureus</i> <i>nas</i> spp. cin resistance	1 x 125 μL	1 x 500 μL		
CRVS Oligo Mix		FAM: Candida g HEX: Human (IC-Inte ROX: VanB-Vancomy CY5: Staphylocod	rnal Control) cin resistance	1 x 125 μL	1 x 500 μL		
KPAC Oligo Mix		FAM: Pseudomonas HEX: Candida a ROX: Klebsiella pn CY5: Acinetobacter	lbicans eumoniae	1 x 125 μL	1 x 500 μL		
HKOC Oligo Mix		FAM: Haemophilus HEX: Klebsiella ROX: Candida pa CY5: OXA-48-Carbaper	oxytoca rapsilosis	1 x 125 μL	1 x 500 μL		
CRE Oligo Mix		FAM: KPC-Carbapene HEX: NDM-Carbapene ROX: VIM-Carbapene CY5: IMP-Carbapene	em resistance em resistance	1 x 125 μL	1 x 500 μL		
LEMC Oligo Mix		FAM: Listeria mono HEX: Enterococcu ROX: mecA/mecC-Meth CY5: Candida tr	is faecalis icillin resistance	1 x 125 μL	1 x 500 μL		
SES Oligo Mix		FAM: Stenotrophomor ROX: Enterobacter CY5: Streptococ	iaceae spp.	1 x 125 μL	1 x 500 μL		
ENES Oligo Mix		FAM: Enterococcu HEX: Escherich ROX: Neisseria mu CY5: Streptococcus	nia coli eningitidis	1 x 125 μL	1 x 500 μL		
NTC		Negative Co		1 x 1000 μL	1 x 1000 μL		
C-SPVC / PC-CRVS / PC-KPAC PC-CRE / PC-LEMC / PC-SES	/ PC-ENES	Positive Contr	ol (PC)	1 x 100 μL	1 x 100 μL		
	n, Storage	Condition and Shelf Life of The Component					
Component		Transport Condition		ondition*	Shelf Life		
2X qPCR Mix				- (-18) °C			
Oligo Mix		(-22) °C − (+8) °C		– (-18) °C	. 12 Months		
NTC			(-22) °C – (-18) °C before openin				
PC ollowing the first opening, piration date of the reagent	-	t stored at storage temperature can be used u	(-22) $^{\circ}C$ – (-18) $^{\circ}C$ before openin ntil the expiration date indicated on t				
ble 3. Required Compone		-	lot Included in the Package				
<ol> <li>Micropipettes and of</li> <li>A centrifuge or Min</li> <li>Vortex</li> <li>Reaction tubes, PCR</li> </ol>	ation instru compatible f i-spin strips, PCR	ments and nucleic acid preparation consumabl iltered pipette tips (nuclease-free) suitable for plates and caps/films specific to qPCR instrume	transferring 1-10 $\mu\text{L},$ 10-100 $\mu\text{L},$ and :				
· · ·		and Analytical Specifications		Table C			
Function Analyte	Aid to dia Table 1		Sample Type(s) Nucleic Acid Extraction Method(s)	Table 5 Zybio EXM3000 Nucleic			
Qualitative/Quantitative Qualitative			Validated qPCR Instrument(s)	Bio Molecular Systems: Cycler (Mic)/Mic IVD	Alab and MDXlab ar Systems: Magnetic Induction /Mic IVD (96 Touch/Dx, CFX Opus 96/Dx, ch, CFX Opus 384 or-Gene Q 5-Plex/MDx Cycler 96		

PIS.037



Whole blood EDTA-treated tube 500-1000 1 year at (-20) °C 2) Adaltis EXTRAlab, 3) Adaltis MDXlab Nucleic acid preparation consumables: Bio-Speedy® Rapid Positive blood culture Blood culture bottle Room temperature 100-500 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.
- Take the PCR kit out of the -20°C freezer. 2.
- 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)
- 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) 4.
- 5. Vortex the master mix to homogenize.
- Repeat Steps 3, 4 and 5 for all master mixes (8 master mixes in total). 6.
- 7. Pipette 15 µL of each master mix into relative PCR tube, or wells to be used (including all samples, NTC and PC).
- Pipette 5 µL of extracted/isolated sample into relative PCR tube, or wells. 8.
- 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

					qPCR Pro	gram															
Reaction	Setup	Bio Molecular Systems: M Rad: CFX96 Touch/Dx, CF Roche: LightCycle	0	384 Touch, CFX C	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, MDXIab, 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												
	40.1	Enzyme Activation	1 Cycle	52 °C	3 min	Enzyme Activation	1 Cycle	52 °C	3 min												
2X qPCR Mix	10 µL	Pre-Incubation	1 Cycle	95 °C	10 sec	Pre-Incubation	1 Cycle	95 °C	10 sec												
		Denaturation	12 Touchdown	95 °C	1 sec	Denaturation															
Oligo Mix	5 μL	5 μL	5 μL	5 μL	5 μL	5 μL	5 μL	5 μL	5 μL	5 μL	5 μL	5 μL	5 μL	Annealing and Extension	Cycles: 1 °C decrement in annealing	67 °C to 56 °C	15 sec	Annealing and Extension		95 °C	1 sec
		· · · · · · · · · · · · · · · · · · ·	temperature per cycle				40 Cycles	55 °C	15 sec												
Template		Denaturation		95 °C	1 sec																
Nucleic Acid/NTC/PC	Nucleic 5 μL	Annealing and Extension	30 Cycles	55 °C	15 sec	Detection (Reading)		FAM/HEX/I	ROX/CY5												
Total Reaction Volume	20 µL	Detection (Reading)		FAM/HEX/R	OX/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 <a href="mailto:support@bioeksen.com.tr">support@bioeksen.com.tr</a>. Table 7. Threshold Levels and Cq Cut-offs for Calculating Cq Values

						Real Time	PCR Inst	trument				
Analyte	Bio-F	Rad CFX	Cie	elo	Light	Cycler 96		/lic IVD and -Dx Box	Rotor-0	Gene Q***	-	tudio 5/5 2k 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 (+)	ve (+) Positive (+) or Negative (-) Results are valid	Protocol Results are valid	If 26 <cq "low="" positive"<br="" ≤30="">If 16<cq≤26 "positive"<br="">If Cq≤16 "High Positive"</cq≤26></cq>			
Positive (+)	Positive (+) of Negative (-)	Target is detected Protocol	If 34 <cq "low="" positive"<br="" ≤40="">If 22<cq≤34 "positive"<br="">If Cq≤22 "High Positive"</cq≤34></cq>			
Negative (-)	Positive (+)		ts are valid s not detected			

#### Table 9. Expected Performance of Kit Controls

		Expected Results and Cq Values						
Control Type	Purpose	Prote	ocol 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)			
	Nucleic acid extraction and	Detected	Detection insignificant	Detected	Detection insignificant			
Internal Control	sampling control	If " <b>Not Detected</b> " check the target Cq	If "Detected" IC is valid	If " <b>Not Detected</b> " 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.

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.

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.



eksen

### For in vitro diagnostic use only.

For professional use only. 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  $\geq$ 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	HON	Non-sterile	<b>@</b>	Do not use if package is damaged and consult <i>Instructions for Use</i>
	Expiration Date YYYY-MM	i	Consult Instructions for Use or consult electronic Instructions for Use	Ý	Keep dry
CONTROL -	Negative Control	$\triangle$	Caution	<u>tt</u>	Keep upright
CONTROL +	Positive Control	X	Temperature limit	Σ	Contains sufficient for <n> tests</n>
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

Phone: +90 (212) 285 10 17, Fax: +90 (212) 285 10 18 Web: <u>www.bioeksen.com.tr</u>, e-mail: <u>info@bioeksen.com.tr</u>,

Technical Support: <a href="mailto:support@bioeksen.com.tr">support@bioeksen.com.tr</a>

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

Cat No: BS-NA-513m-100

# vNAT® Transfer Tube

## **Package Insert**

### 1. KIT CONTENT

#### Table 1. Kit Content

Component	Desci	Amount	
VNAT <sup>®</sup> Transfer Tube	Microbial nucleic acid stor	100 Tubes	
Table 2. Storage Requirements and S	helf Life		
Component	Transport Conditions	Storage Conditions	Shelf Life
vNAT <sup>®</sup> Transfer Tube	(+2) °C to (+50) °C	(+15) °C to (+30) °C	60 months

#### 2. INTENDED USE

vNAT \* Transfer Tube, 2 mL of nucleic acid extraction and preservation liquid. The vNAT\* Transfer Tube is intended for single use. When clinical specimens suspected of infections are transferred in the vNAT \* 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 vNAT\* Transfer Tube allows from sample to RT-qPCR in a minute.

#### 3. ANALYTICAL SPECIFICATIONS

vNAT® 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 vNAT <sup>®</sup> 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 vNAT<sup>®</sup> 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 vNAT® 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	<b>淡</b>	Protect from heat and radioactive sources
	Use-by date	REF	Catalogue number		Do not use if package is damaged and consult instructions for use
X	Temperature limit	MON	Non-sterile	Ť	Keep dry
$\triangle$	Caution	Ĩ	Consult instructions for use or consult electronic instructions for use		
<u></u>	Keep it upright	2	Do not re-use		

#### 7. 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: <a href="mailto:support@bioeksen.com.tr">support@bioeksen.com.tr</a>

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**

			Intended U	Use			25 Reactions	100 Reaction
2X Prime Script N			Optimized ready-to-use mi		PCR assav		1 x 500 μL	2 x 1000 μL
SA Oligo Mix		Sp	pecific nucleic acid amplific FAM: Sapovirus (GI, HEX: Human (IC-Inte	cation and /GII/GIV/C ernal Cont	d detection: GV)		1 x 125 μL	1 x 500 μL
ANR Oligo Mix	x		CY5: Adenoviru FAM: Astro HEX: Norovirus ROX: Rotavir	virus s (GI/GII)			1 x 125 μL	1 x 500 μL
NTC			Negative Co				1 x 1000 μL	1 x 1000 μL
PC-SA/PC-ANF	R		Positive Contr				1 x 100 μL	1 x 100 μL
le 2. Storage Req								
Component		Transport Co	ondition		Storage Cond			Shelf Life
2X Prime Script	Mix				(-22) °C – (+			
Oligo Mix		(-22) °C − (	(+8) °C		(-22) °C – (+	-8) °C		12 Months
NTC		( ) 0 (			C – (-18) °C before opening, (+			12 111011110
PC				(-22) °C	C – (-18) °C before opening, (+	-2) °C – (+8	°C after first thaw	
		ch reagent stored at storage te	mperature can be used ur	ntil the exp	piration date indicated on the	e tube. The	kit's expiration date	is determined b
iration date of the le 3. Required Co	0	s Not Included in the Packag	ge					
1. Real-Time P			Required Components N	lot Include	ed in the Package			
<ol> <li>A centrifuge</li> <li>Vortex</li> <li>Reaction tub</li> </ol>		pin rips, PCR plates and caps/films	specific to qPCR instrume	ents and co	ompatible with the reaction v	volume		
		inciple and Analytical Specif	fications					
le 4. Intended Us		inciple and Analytical Specif	fications	Sample	Type(s)	Table 5		
		inciple and Analytical Specif Aid to diagnosis Table 1	fications		Type(s) Acid Extraction Methods	Zybio E	<b>Fransfer Tube</b> (M3000 Nucleic Acid	
le 4. Intended Us inction halyte(s)	ie, Test Pr	Aid to diagnosis	fications	Nucleic		VNAT® Zybio E2 Adaltis Bio Mol Cycler ( Bio-Rad CFX384 Qiagen: Roche: Thermo Dx/6/7/ Biosysta Adaltis: HiMedia Bioer: L Atila Bio Co-Dx: Q	Transfer Tube KM3000 Nucleic Acid EXTRAlab and MDXIa ecular Systems: Magi Mic)/Mic IVD : CFX96 Touch/Dx, CF Touch, CFX Opus 384 Rotor-Gene Q 5-Plex LightCycler 96 Fisher Scientific: Qui 12k Flex/Pro, StepOr ems 7500/7500 Fast AmpliLab, MDXIab a: InstaQ 96 inegene 9600 Plus systems: Fujirebio Co-Dx Box g: Gentier 96E :: SLAN-96P	b netic Induction TX Opus 96/Dx, 4 (/MDx antStudio 5/5
le 4. Intended Us unction	ie, Test Pr	Aid to diagnosis Table 1		Validat	Acid Extraction Methods	VNAT® Zybio E Adaltis Bio Mol Cycler ( Bio-Rad CFX384 Qiagen: Roche: I Thermo Dx/6/7/ Biosyste Adaltis: HiMedia Bioer: L Atila Bio Co-Dx: Q Tianlon Sansure Azure: Q	Transfer Tube KM3000 Nucleic Acid EXTRAIab and MDXIa ecular Systems: Magi Mic)/Mic IVD : CFX96 Touch/Dx, CF Touch, CFX Opus 384 Rotor-Gene Q 5-Plex LightCycler 96 Fisher Scientific: Qua 12k Flex/Pro, StepOr fusher Scientific: Qua instaQ 96 inegene 9600 Plus bystems: Fujirebio Co-Dx Box g: Gentier 96E :: SLAN-96P Cielo ed on the reference s	b netic Induction FX Opus 96/Dx, /MDx antStudio 5/5 ne Plus, Applied
le 4. Intended Us Inction halyte(s) ualitative/Quantita	ie, Test Pr	Aid to diagnosis Table 1 Qualitative		Validat	ed qPCR Instrument(s)	VNAT® Zybio E Adaltis Bio Mol Cycler ( Bio-Rad CFX384 Qiagen: Roche: I Thermo Dx/6/7/ Biosyste Adaltis: HiMedia Bioer: L Atila Bio Co-Dx: ( Tianlon) Sansure Azure: (	Transfer Tube KM3000 Nucleic Acid EXTRAIab and MDXIa ecular Systems: Magi Mic)/Mic IVD : CFX96 Touch/Dx, CF Touch, CFX Opus 384 Rotor-Gene Q 5-Plex LightCycler 96 Fisher Scientific: Qua 12k Flex/Pro, StepOr fusher Scientific: Qua instaQ 96 inegene 9600 Plus bystems: Fujirebio Co-Dx Box g: Gentier 96E :: SLAN-96P Cielo ed on the reference s	b netic Induction FX Opus 96/Dx, /MDx antStudio 5/5 ne Plus, Applied
le 4. Intended Us Inction halyte(s) ualitative/Quantita est Principle Itomatic/Manual	ie, Test Pr	Aid to diagnosis Table 1 Qualitative Reverse Transcription and Re Manual Laboratory professionals trai	eal-Time PCR (RT-qPCR)	Nucleic Validate	ed qPCR Instrument(s)	VNAT® Zybio E Adaltis Bio Mol Cycler ( Bio-Rad CFX384 Qiagen: Roche: I Thermo Dx/6/7/ Biosyste Adaltis: HiMedia Bioer: L Atila Bio Co-Dx: Q Tianlon Sansure Azure: Q	Transfer Tube KM3000 Nucleic Acid EXTRAIab and MDXIa ecular Systems: Magi Mic)/Mic IVD : CFX96 Touch/Dx, CF Touch, CFX Opus 384 Rotor-Gene Q 5-Plex LightCycler 96 Fisher Scientific: Qua 12k Flex/Pro, StepOr fusher Scientific: Qua instaQ 96 inegene 9600 Plus bystems: Fujirebio Co-Dx Box g: Gentier 96E :: SLAN-96P Cielo ed on the reference s	b netic Induction FX Opus 96/Dx, /MDx antStudio 5/5 ne Plus, Applied
le 4. Intended Us Inction halyte(s) ualitative/Quantita est Principle utomatic/Manual tended Users	ie, Test Pr	Aid to diagnosis Table 1 Qualitative Reverse Transcription and Re Manual Laboratory professionals trai qPCR and in vitro diagnostic	eal-Time PCR (RT-qPCR) ined in the techniques of procedures.	Nucleic Validate Inclusiv Limit of	ed qPCR Instrument(s)	vNAT*         Zybio El         Zybio El         Adaltis         Bio Mol         Cycler (         Bio-Rad         CFX384         Qiagen:         Roche:         Thermo         Dx/6/7/         Biosyste         Adaltis:         HiMedia         Bioer: L         Atila Bio         Co-Dx: Q         Tianlon         Sansure         Azure: Q         Validate         isolates	Transfer Tube KM3000 Nucleic Acid EXTRAIab and MDXIa ecular Systems: Magi Mic)/Mic IVD : CFX96 Touch/Dx, CF Touch, CFX Opus 384 Rotor-Gene Q 5-Plex LightCycler 96 Fisher Scientific: Qua 12k Flex/Pro, StepOr fusher Scientific: Qua instaQ 96 inegene 9600 Plus bystems: Fujirebio Co-Dx Box g: Gentier 96E :: SLAN-96P Cielo ed on the reference s	b netic Induction FX Opus 96/Dx, /MDx antStudio 5/5 ne Plus, Applied
le 4. Intended Us Inction halyte(s) ualitative/Quantita est Principle utomatic/Manual tended Users Irget Population	ative	Aid to diagnosis Table 1 Qualitative Reverse Transcription and Re Manual Laboratory professionals trai	eal-Time PCR (RT-qPCR) ined in the techniques of procedures. ed infection	Nucleic Validate Inclusiv Limit of Sensitiv	ed qPCR Instrument(s) vity and Exclusivity f Detection vity and Specificity	vNAT*         Zybio El         Zybio El         Adaltis         Bio Mol         Cycler (         Bio-Rad         CFX384         Qiagen:         Roche:         Thermo         Dx/6/7/         Biosyste         Adaltis:         HiMedia         Bioer: L         Atila Bio         Co-Dx: Q         Tianlon         Sansure         Azure: Q         Validate         isolates	Transfer Tube (M3000 Nucleic Acid EXTRAlab and MDXIa ecular Systems: Mag Mic)/Mic IVD : CFX96 Touch/Dx, Cf Touch, CFX Opus 384 Rotor-Gene Q 5-Plex LightCycler 96 Fisher Scientific: Qui 12k Flex/Pro, StepOr ems 7500/7500 Fast AmpliLab, MDXIab a: InstaQ 96 inegene 9600 Plus posystems: Fujirebio Co-Dx Box g: Gentier 96E : SLAN-96P Cielo	b netic Induction FX Opus 96/Dx, /MDx antStudio 5/5 ne Plus, Applied
le 4. Intended Us inction halyte(s) ualitative/Quantita est Principle utomatic/Manual tended Users irget Population	ative	Aid to diagnosis Table 1 Qualitative Reverse Transcription and Re Manual Laboratory professionals trai qPCR and in vitro diagnostic Individuals with the suspected	eal-Time PCR (RT-qPCR) ined in the techniques of procedures. ed infection	Nucleic Validate Inclusiv Limit of Sensitiv	ed qPCR Instrument(s) vity and Exclusivity f Detection vity and Specificity	<ul> <li>vNAT*</li> <li>Zybio E: Adaltis</li> <li>Bio Mol Cycler ( Bio-Rad CFX384</li> <li>Qiagen: Roche:</li> <li>Thermo Dx/6/7/ Biosyste</li> <li>Adaltis:</li> <li>HiMedia</li> <li>Bioer: L</li> <li>Atila Bio</li> <li>Co-Dx: 0</li> <li>Tianlon,</li> <li>Sansure</li> <li>Azure: 0</li> <li>Validate</li> <li>isolates</li> <li>Table 5</li> <li>98.93%</li> </ul>	Transfer Tube (M3000 Nucleic Acid EXTRAlab and MDXla ecular Systems: Mag Mic)/Mic IVD : CFX96 Touch/Dx, Cf Touch, CFX Opus 384 Rotor-Gene Q 5-Plex LightCycler 96 Fisher Scientific: Qui 12k Flex/Pro, StepOr ems 7500/7500 Fast AmpliLab, MDXlab a: InstaQ 96 inegene 9600 Plus psystems: Fujirebio Co-Dx Box g: Gentier 96E : SLAN-96P Cielo ed on the reference s	b netic Induction FX Opus 96/Dx, /MDx antStudio 5/5 ne Plus, Applied

P10.Ek02-Rev.00	5/01.10.2024			PIS.067
For in vitro diag For professiona			bi	jeksen
Rectal Swab	<pre>***</pre>	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
	mens should be collected by a healthcare prov samples are received, put them into the <b>vNAT</b> *		ternational clinical specimen collection regulations. paration.	
1. APPLICA	TION 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.			(i.e Sample Count = 3, pipette $5^{*}(3+3) = 30 \mu$ L of SA Oligo Mix)	
4.	, , , ,	ript Mix into the tube prepared in S	Step 3. (i.e Sample Count = 3, pipette $10^{*}(3+3) = 60 \mu$ L 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 tube	s, or wells to be used (including all s	amples, NTC and PC).	
8.	Pipette 5 µL of each isolated/ extracted samp	le into the relative PCR tube, or we	41.	
9.	Pipette 5 μL of NTC into the Negative Control	PCR tube, or well.		
10.	Pipette 5 $\mu$ L of PC-SA into the Positive Contro	I 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

				R	F-qPCR Progra	ım			
Reaction Setu	ıp	CFX96 Touch/Dx, Cl	Protocol 1: ns: Magnetic Induction Cy FX Opus 96/Dx, CFX384 To ycler 96, Co-Dx: Co-Dx Box	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, MDXIab, 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
		Denaturation	12 Touchdown Cycles:	95 °C	1 sec	Denaturation			
Oligo Mix	5 μL	Annealing and Extension	1 °C decrement in annealing temperature per cycle	67 °C to 56 °C	15 sec	Annealing and Extension		95 ℃ 55 ℃	1 sec 15 sec
		Denaturation	. ,	95 °C	1 sec		40 Cycles	55 C	TO SEC
Template Nucleic Acid/NTC/PC	5 μL	Annealing and Extension	30 Cycles	55 °C	15 sec	Detection (Reading)		FAM/HEX/F	OX/CY5
Total Reaction Volume	20 µL	Detection (Reading)		FAM/HEX/I	ROX/CY5				



WARNING: The gPCR 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 <u>support@bioeksen.com.tr.</u>

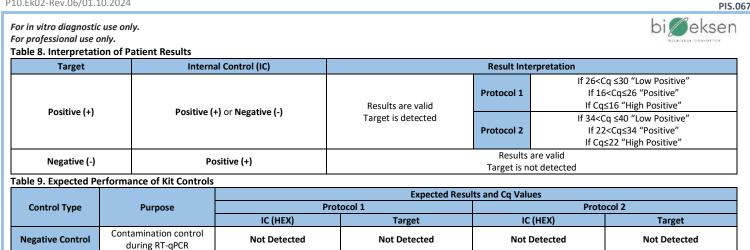
#### Table 7. Threshold Levels and Cq Cut-offs for Calculating Cq Values

	Real Time PCR Instrument											
Analyte	Bio-Rad CFX		с	ielo	LightCycler 96		-	/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"

**Positive Control** 

Internal Control



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

Reagent stability control

Nucleic acid extraction and

sampling control

Contamination Problem: If a target in the Negative Control reaction is "Detected". 1.

Recommended action: Repeat the run, paying attention to the "Warnings and Limitations" section.

Detected (Cq≤30)

Detected

If "Not Detected" check the

target Cq

Invalid Internal Control Problem: If the Internal Control (IC) and all other targets of a sample are "Not Detected". 2. 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.

Detected (Cq≤30)

Detection insignificant

If "Detected" IC is valid

Detected (Cq≤40)

Detected

If "Not Detected" check the

target Cq

Detected (Cq≤40)

Detection insignificant

If "Detected" IC is valid

Reagent Problem: If all Internal Controls, Positive Controls and targets in the run are "Not Detected". 3. 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

- False-negative results may occur if inadequate number (below the LoD) of organisms are present in the specimen. 1.
- Mutations within the target regions could affect primer and/or probe binding, resulting in failure to detect the presence of agents. 2.
- False-negative results may occur if a specimen is improperly collected, transported, or handled. 3.
- The clinical specimens shall be collected by a healthcare provider in accordance with the national/international specimen collection guidelines. 4.
- 5. Test procedures should be performed by personnel trained in the use of the kit.
- Sample tubes should always be kept closed except for liquid transfers. 6.
- 7. Filtered and nuclease-free pipette tips should be used for sample transfer.
- The components in the kit should not be used together with different LOT numbers or chemicals of the same name but from different manufacturers. 8.
- 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.
- Proper personal protective equipment including lab coats, gowns, gloves, eye protection, and a biological safety cabinet are recommended for manipulation of 12. clinical specimens.
- 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 13. 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.
- Maintenance/ calibration interval should be determined for all instruments and equipment used with the kit. 15.

#### **EXPLANATION OF SYMBOLS** Δ.

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	<b>REF</b> Catalogue number		淡	Protect from heat and radioactive sources
	Manufacturer	NON	Non-sterile	8	Do not use if package is damaged and consult <i>Instructions for Use</i>
	Expiration Date YYYY-MM		Consult Instructions for Use or consult electronic Instructions for Use	لم الم	Keep dry
CONTROL -	Negative Control	$\triangle$	Caution	<u>tt</u>	Keep upright
CONTROL +	Positive Control	<i>\</i>	Temperature limit	Σ	Contains sufficient for <n> tests</n>

n vitro diagnostic use professional use only.	only.				bissekse
CONTROL	Control				
Bioeksen / Address: H Phone: +9	0 (212) 285 10 17, Fax: +90 w.bioeksen.com.tr, e-mail:	ad. Nurol Life Sitesi D Bl ) (212) 285 10 18	ok No:3/31, 34396 Sarıyer/	stanbul-TÜRKİYE	
ce to User: Please info	rm us about product-relate	ed incidents at " <mark>vigilanc</mark>	<b>ce@bioeksen.com.tr</b> " within	1 24 hours.	

ALL RIGHTS RESERVED

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For in vitro diagnostic use only. 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



PIS.068

## **Package Insert**

Component		ntended U				100 Reactions
2X qPCR Mix	1		ix for qPCR assay		1 x 500 μL	2 x 1000 μL
LNS Oligo Mix	HEX: Huma ROX: Net	n (IC-Inter <i>isseria me</i>	ocytogenes rnal Control) eningitidis eneumoniae		1 x 125 μL	1 x 500 μL
HES Oligo Mix	ROX: Strep		influenzae agalactiae coli K1		1 x 125 μL	1 x 500 μL
PC-LNS / PC-HES	Posit	ive Contro	ol (PC)		1 x 100 μL	1 x 100 μL
NTC		gative Con			1 x 1000 μL	1 x 1000 μL
ole 2. Transport Condition, S	torage Condition, and Shelf Life of the O	Compone	nts			
Component	Transport Condition			Storage Condition	n*	Shelf Life
2X qPCR Mix				(-22) °C – (-18) °		
Oligo Mix	(-22) °C – (+8) °C			(-22) °C – (-18) °		12 Months
NTC	(22) c (10) c				C – (+8) °C after first thaw	
PC	reagent stored at storage temperature ca			C – (+8) °C after first thaw		
	Required Con ent n instruments and nucleic acid preparation	i consuma				
<ol> <li>A centrifuge or Mini-spi</li> <li>Vortex</li> <li>Reaction tubes, PCR stri</li> </ol>	ps, PCR plates and caps/films specific to qP		Ū			
	nciple and Analytical Specifications					
unction	Aid to diagnosis		Sample Type(s)		Table 5	
Analyte	Table 1		Nucleic Acid Ext	raction Method(s)	Zybio EXM3000 Nucleic Acid Adaltis EXTRAlab and MDXlab	
Qualitative/Quantitative	Qualitative		Validated qPCR I	Instrument(s)	Bio Molecular Systems: Magr Cycler (Mic)/Mic IVD Bio-Rad: CFX96 Touch/Dx, CF CFX384 Touch, CFX Opus 384 Qiagen: Rotor-Gene Q 5-Plex, Roche: LightCycler 96 Thermo Fisher Scientific: Qua Dx/6/7/12k Flex/Pro, StepOn Biosystems 7500/7500 Fast Adaltis: AmpliLab, MDXIab HiMedia: InstaQ 96 Bioer: Linegene 9600 Plus Atila Biosystems: Fujirebio Co-Dx: Co-Dx Box Tianlong: Gentier 96E Sansure: SLAN-96P Azure: Cielo	X Opus 96/Dx, /MDx intStudio 5/5
Test Principle	Real-Time PCR (qPCR)		Inclusivity and F	volucivity	Validated on the reference st	rains and the fie
est Fincipie	Manual		Inclusivity and E	xclusivity	isolates	
•	Manaa					
Automated/Manual ntended Users	Laboratory professionals trained techniques of qPCR and in vitro dia procedures		Limit of Detectio	on (LoD)	Table 5	
ntended Users arget Population	Laboratory professionals trained techniques of qPCR and in vitro dia procedures Individuals with the suspected infection	agnostic	Sensitivity and S	pecificity	Table 5           100.00% and 98.04%	
ntended Users arget Population	Laboratory professionals trained techniques of qPCR and in vitro dia procedures	agnostic	Sensitivity and S	pecificity		
ntended Users arget Population	Laboratory professionals trained techniques of qPCR and in vitro dia procedures Individuals with the suspected infection	agnostic	Sensitivity and S	pecificity		LoD (cp/m

P10.Ek02-Rev.06/01.1	L0.2024													PIS
For in vitro diagnostic u For professional use only													k	oi Øeks
									Nucleic acid preparation consumables: Bioeksen Bio- Speedy <sup>®</sup> Rapid Nucleic Acid Extraction Kit (Cat. No: ZFNAE01)					
Clinical specimens sh	nould be co	llected	l by a healthcar	e provide	er in accordance	e with nat	ional/inte	national	clinic	al specimen co	ollection r	egulations.		<u> </u>
<ol> <li>Take the PCR I</li> <li>Pipette (Samp</li> <li>Add (Sample C</li> <li>Vortex the ma</li> <li>Repeat Steps 3</li> <li>Pipette 15 μL o</li> <li>Pipette 5 μL o</li> </ol>	PCR device kit out of the le Count + 3) * ister mix to 3, 4 and 5 f of each ma f extracted f NTC into 1 f PC-LNS in of the strip the strip of the instru- nd start the	e using ne -20° 3) *5 µ *10 µL homo for all n ster m /isolate the Neg to the s, or PC ument. e instru <b>m</b>	L of LNS Oligo I of 2X qPCR Mix genize. naster mixes (2 ix into relative f ed sample into gative Control F PC tube or well: CR tubes or sea CR tubes and PC Place the strips ument.	Mix into a into the t PCR tube, relative P PCR tube, S. Repeat I PCR plat R plate. S, or PCR t	in empty epper sube prepared in or wells to be CR tube, or we or wells. for all PC. te. Label to avo subes and PCR	ndorf tube in Step 3. used (incl ells. id confusi plate.	(i.e Sample) uding all s on during R	e Count = amples, N spin-cent T-qPCR P	3, pip	m	) = 60 μL c	of 2X qPCR Mix	<)	er Scientific:
Reaction Setu	Protocol 1:       Qiagen: Rotor-Gene Q 5-Plex/MDx, Thermo Fisher Sci         Reaction Setup       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       Qiagen: Rotor-Gene Q 5-Plex/MDx, Thermo Fisher Sci         Image: Rotor-Gene Q 5-Plex/MDx, Thermo Fisher Sci       QuantStudio 5/5 Dx/6/7/12k Flex/Pro, StepOne Plus, A Biosystems 7500/7500 Fast, Adaltis: AmpliLab, MDXIab, InstaQ 96, Bioer: Linegene 9600 Plus, Atila Biosystem FujirebioTianlong: Gentier 96E, Sansure: SLAN-90							Plus, Applied Xlab, HiMedia: osystems:						
Reagent	Volume/ Rxn		Step		Cycle No.	Tem	perature	Durati on		Step		Cycle No.	Temper ature	Duration
2X qPCR Mix	10 µL		Enzyme Activat Pre-Incubatio		1 Cycle 1 Cycle		52 °C 95 °C	3 min 10 sec		Enzyme Act Pre-Incub		1 Cycle 1 Cycle	52 ℃ 95 ℃	3 min 10 sec
			Denaturation		12 Touchdow		95 °C	10 Sec 1 sec			Denaturation	I Cycle	55 0	10 300
Oligo Mix	5 μL	Anr	nealing and Exte	ension	Cycles: 1 °C decreme in annealing temperature per cycle	g 67 °C	to 56 °C	15 sec	А	Annealing and	Extensior	40 Cycles	95 ℃ 55 ℃	1 sec 15 sec
Template Nucleic	5 μL		Denaturation			-	95 °C	1 sec			-,			
Acid/NTC/PC Total Reaction Volume	20 μL		nealing and Extension (Read		30 Cycles		55 °C M/HEX/RC	15 sec		Detection (Reading)		FAM/HEX/ROX/CY5		
		L tps://w	WARNIN		PCR program fi	ile should	be downlo	oaded fro	m the	e QR code on t	he left or	from the link b	selow.	
INTERPRETATI	ON OF TH	HE AS	SAY RESULTS	5										
a values of the results otions are used for de gmoidal curves must <b>igmoida</b> " software fo <b>igmoida</b> " software in a <b>ble 7. Threshold Le</b>	vices not ir be determ or BMS Ma staller, plea	ncludeo iined. I gnetic ase ser	d in <b>Table 7</b> . Fo Non-sigmoidal o Induction Cycle nd an e-mail to <u>s</u>	r all targe curves mi er (Mic)/N support@	ets that do not ust be reporte Aic IVD and Bio Obioeksen.com	exceed th d as "neg p-Rad CFX	e Cq cut-c ative". Th	ff, the sh e PCR res	ape o sults o	of the amplification of the amplification of the second seco	ation curv ed manua	e must be and ally, as indicat	alyzed, and ed in <b>Tabl</b> e	Cq values of the cq val
							Real Ti	ne PCR II						ACAUNIT - F /F
Analyte		Bio-Rad CFX		Cielo		LightCycler 96		Mic/Mic IVD and Co-Dx Box		Rotor-Gene Q***		Dx/6/7	QuantStudio 5/5 Dx/6/7/12k Flex/Pro	
Listeria monocytog		<b>RFU</b> 750	Cq Cut-off 30	<b>RFU</b> 75000	Cq Cut-off 30	0.1	Cq Cut 30		FU ).5	Cq Cut-off 30	<b>RFU</b> 0.05	Cq Cut-off 40	<b>RFU</b> 20000	Cq Cut-off 30
luman (IC-Internal C		200	30	20000		0.05	30	(	).2	30	0.02	40	20000	30
Neisseria meningi		750	30	75000		0.1	30		).5	30	0.05	40	20000	30
Streptococcus pneun Haemophilus influe		1000 750	26 30	100000 75000		0.12	26 30		.75 ).5	26 30	0.08	34 40	75000 20000	26 30
Streptococcus agaia		750	30	75000		0.1	30		).5 ).5	30	0.05	40	20000	30

30

0.02

40

20000

30

2

Escherichia coli K1 750 30 75000 30 0.1 30 0.5 

## Revision Date: 2024-11-19/Rev.05

Published Date: 2023-10-04

**Positive Control** 

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Detected (Cq≤40)

Detection insignificant

If "Detected" IC is valid

#### For professional use only. Table 8. Interpretation of Patient Results

Target Interna		al Control (IC)	Result Interpretation					
			Results are valid	Protocol 1         If 26 <cq "low="" positive"<="" th="" ≤30="">           If 16<cq≤26 "positive"<="" td="">         If cq≤16 "High Positive"</cq≤26></cq>				
Positive (+)	Positive (	+) or Negative (-)	Target is detected	Protocol 2	If 34-Cq ≤40 "Low Positiv           Protocol 2         If 22 <cq≤34 "positive"<="" td="">           If Cq≤22 "High Positive"         If Cq≤22 "High Positive"</cq≤34>			
Negative ()			Results are valid					
Negative (-)	P	ositive (+)	Target is not detected					
able 9. Expected Pe	erformance of Kit Controls							
		Expected Results and Cq Values						
Control Type	Purpose	Pro	otocol 1	Protocol 2				
		IC (HEX)	Target	IC (HEX)		Target		
Negative Control	Contamination control during aPCR	Not Detected	Not Detected	Not Detecte	ed	Not Detected		

**Internal Control** If "Not Detected" check the If "Not Detected" check the sampling control If "Detected" IC is valid target Cq

Detected (Cq≤30)

Detected

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

Reagent stability control

Nucleic acid extraction and

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.

Invalid Internal Control Problem: If the Internal Control (IC) and all other targets of a sample are "Not Detected". 2. 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.

Detected (Cq≤30)

Detection insignificant

Detected (Cq≤40)

Detected

target Cq

- Reagent Problem: If all Internal Controls, Positive Controls and targets in the run are "Not Detected". 3.
- 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

- False-negative results may occur if inadequate number (below the LoD) of organisms are present in the specimen. 1.
- 2. Mutations within the target regions could affect primer and/or probe binding, resulting in failure to detect the presence of agents.
- False-negative results may occur if a specimen is improperly collected, transported, or handled. 3.
- 4. The clinical specimens shall be collected by a healthcare provider in accordance with the national/international specimen collection guidelines.
- Test procedures should be performed by personnel trained in the use of the kit. 5.
- 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.
- 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. 9.
- 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.
- Waste disposal must be carried out in accordance with local, state, and federal regulations. 11.
- 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.
- Maintenance/ calibration interval should be determined for all instruments and equipment used with the kit. 15.

#### **EXPLANATION OF SYMBOLS** 4.

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	迷	Protect from heat and radioactive sources	
	Manufacturer	NON	Non-sterile	\$	Do not use if package is damaged and consult <i>Instructions for Use</i>	
$\Sigma$	Expiration Date YYYY-MM		Consult Instructions for Use or consult electronic Instructions for Use	Ť	Keep dry	
CONTROL -	Negative Control	$\triangle$	Caution	<u>tt</u>	Keep upright	
CONTROL +	Positive Control	X	Temperature limit	Σ	Contains sufficient for <n> tests</n>	
CONTROL	Control					

## 5. MANUFACTURER AND TECHNICAL SUPPORT



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Technical Support: <a href="mailto:support@bioeksen.com.tr">support@bioeksen.com.tr</a>.

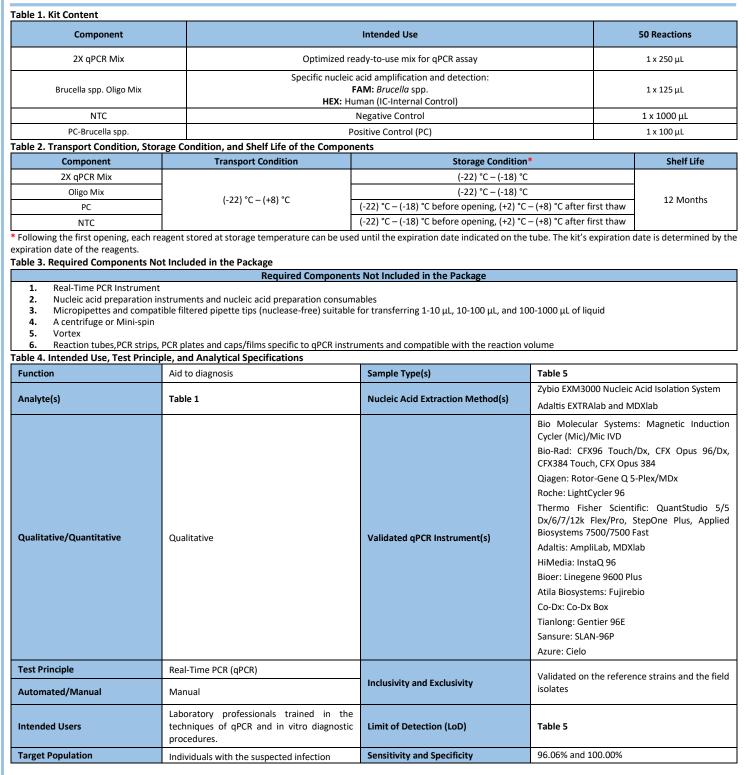
Notice to User: Please inform us about product-related incidents at "vigilance@bioeksen.com.tr" within 24 hours.

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For in vitro diagnostic use only. For professional use only. Cat No: BS-SP-B-12-50

## Brucella spp. qPCR Kit

## Package Insert





bi eksen Bio-Speedy<sup>®</sup> CE IVD



#### For professional use only. 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	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	Rapid Nucleic Acid Extraction Kit (Cat. No: ZFNAE01)	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  $\mu L$  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

				I	qPCR Pro	gram			
Reaction Set	up	Protocol 1:       Qiagen: Rotor-Gene Q 5-P         Bio Molecular Systems: Magnetic Induction Cycler (Mic)/Mic IVD, Bio-       QuantStudio 5/5 Dx/6/7/1         Rad: CFX96 Touch/Dx, CFX Opus 96/Dx, CFX384 Touch, CFX Opus 384,       Biosystems 7500/7500 Fast,         Roche: LightCycler 96, Co-Dx: Co-Dx Box, Azure: Cielo       InstaQ 96, Bioer: Linegene 9         Tianlong: Gentie       Tianlong: Gentie					rotocol 2: Plex/MDx, Thermo Fisher Scientific: .2k Flex/Pro, StepOne Plus, Applied Adaltis: AmpliLab, MDXlab, HiMedia: 600 Plus, Atila Biosystems: Fujirebio, r 96E, Sansure: SLAN-96P		
Reagent	Volume/ Rxn	Step	Cycle No.	Temperature	Durati on	Step	Cycle No.	Temper ature	Duration
		Enzyme Activation	1 Cycle	52 °C	3 min	Enzyme Activation	1 Cycle	52 °C	3 min
2X qPCR Mix	5 μL	Pre-Incubation	1 Cycle	95 °C	10 sec	Pre-Incubation	1 Cycle	95 °C	10 sec
		Denaturation	12 Touchdown	95 °C	1 sec	Denaturation			
Oligo Mix	2,5 μL	Annealing and Extension	Cycles: 1 °C decrement in annealing	67 °C to 56 °C	15 sec	Annealing and Extension		95 °C	1 sec
		5	temperature per cycle			9	40 Cycles	55 °C	15 sec
Template Nucleic	2,5 μL	Denaturation		95 °C	1 sec				
Acid/NTC/PC	2,3 μι	Annealing and Extension	30 Cycles	55 °C	15 sec	Detection (Reading)		ΕΛ	M/HEY
Total Reaction Volume	10 µL	Detection (Reading)	Socycles	FAM/HE	х	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 <u>support@bioeksen.com.tr</u>.

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

	Real Time PCR Instrument														
Bio-Rad CFX		Bio-Rad CFX		Bio-Rad CFX						Mic/	Mic IVD and			Quant	Studio 5/5
			Cielo	Light	Cycler 96	C	o-Dx Box	Rotor-	Gene Q***	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				
200	30	20000	30	0.05	30	0.2	30	0.02	40	20000	30				
200	30	20000	30	0.05	30	0.2	30	0.02	40	20000	30				
	<b>RFU</b> 200	RFU         Cq Cut-off           200         30	RFU         Cq Cut-off         RFU           200         30         20000	Cq Cut-off         RFU         Cq Cut-off           200         30         20000         30	RFU         Cq Cut-off         RFU         Cq Cut-off         RFU           200         30         20000         30         0.05	Bio-Rad CFX         LightCycler 96           RFU         Cq Cut-off         RFU         Cq Cut-off         RFU         Cq Cut-off           200         30         20000         30         0.05         30	Bio-Rad CFX         LightCielo         LightCielo         Mic/           RFU         Cq Cut-off         RFU         Cq Cut-off         RFU         Cq Cut-off         RFU           200         30         20000         30         0.05         30         0.2	Bio-Rad CFX         Image: Cielo         LightCycler 96         Mic/Mic IVD and Co-Dx Box           RFU         Cq Cut-off         RFU         Cq Cut-off         RFU         Cq Cut-off         Cq Cut-off           200         30         20000         30         0.05         30         0.2         30	Bio-Rad CFX         Light⊂ycler 96         Mic/Mic IVD and Co-Dx Box         Rotor- Rotor           RFU         Cq Cut-off         RFU         Cq Cut-off         RFU         Cq Cut-off         RFU           200         30         20000         30         0.05         30         0.2         30         0.02	Bio-Rad CFX         Light⊂ycler 96         Mic/Mic IVD and Co-Dx Box         Rotor-Gene Q***           RFU         Cq Cut-off         RFU         Cq Cut-off         RFU         Cq Cut-off         RFU         Cq Cut-off           200         30         20000         30         0.05         30         0.2         30         0.02         40	Bio-Rad CFX         Light⊂ycler 96         Mic/Mic IVD and Co-Dx Box         Rotor-Gene Q***         Quant Dx/6/7/           RFU         Cq Cut-off         RFU         Cut-off         RFU         Cut-off         RFU         Cut-off         RFU         Cut-off				

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

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able 8. Interpretati	on of Patient Re	sults						
Target		Internal	Control (IC)		Result Interp	retation		
				Results are valid	Protocol 1	Protocol 1 If 26 <cq "low="" positive"<br="" ≤30="">If 16<cq≤26 "positive"<br="">If Cq≤16 "High Positive"</cq≤26></cq>		
Positive (+)		Positive (+,	) or <b>Negative (-)</b>	Target is detected	Protocol 2 If 22 <cq≤34 "posi<="" td=""><td>Cq ≤40 "Low Positive" <cq≤34 "positive"<br="">≤22 "High Positive"</cq≤34></td></cq≤34>		Cq ≤40 "Low Positive" <cq≤34 "positive"<br="">≤22 "High Positive"</cq≤34>	
Negative (-)		Pos	sitive (+)		Results are Target is not o			
able 9. Expected Po	erformance of Ki	t Controls						
				Expected Res	esults and Cq Values			
Control Type	Purpos	e	Pi	otocol 1	Protocol 2		ocol 2	
			IC (HEX)	Target	IC (H	EX)	Target	
Negative Control	Contamination during qP		Not Detected	Not Detected	Not Det	ected	Not Detected	

Detected Detection insignificant Detected Detection insignificant Nucleic acid extraction and **Internal Control** If "Not Detected" check the If "Not Detected" check the sampling control If "Detected" IC is valid If "Detected" IC is valid target Cq target Cq

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

Reagent stability control

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

Detected (Cq≤30)

Invalid Internal Control Problem: If the Internal Control (IC) and all other targets of a sample are "Not Detected". 2 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.

Detected (Cq≤30)

Detected (Cq≤40)

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:

**Positive Control** 

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 Cg 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. WARNINGS AND LIMITATIONS 3.

#### False-negative results may occur if inadequate number (below the LoD) of organisms are present in the specimen. 1.

- 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.
- The clinical specimens shall be collected by a healthcare provider in accordance with the national/international specimen collection guidelines. 4.
- Test procedures should be performed by personnel trained in the use of the kit. 5.
- 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.
- The components in the kit should not be used together with different LOT numbers or chemicals of the same name but from different manufacturers. 8.
- 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.
- 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 13. 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	淡	Protect from heat and radioactive sources
	Manufacturer	NON	Non-sterile	8	Do not use if package is damaged and consult Instructions for Use
$\Sigma$	Expiration Date YYYY-MM		Consult Instructions for Use or consult electronic Instructions for Use	Ť	Keep dry

Revision Date: 2025-02-20/Rev.05

Published Date: 2023-10-04

PIS.073

Detected (Cq≤40)

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CONTROL -	Negative Control	$\triangle$	Caution	<u> </u>	Keep upright
CONTROL +	Positive Control	X	Temperature limit	Σ	Contains sufficient for <n> tests</n>
CONTROL	Control				

#### 5. MANUFACTURER AND TECHNICAL SUPPORT

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Technical Support: <a href="mailto:support@bioeksen.com.tr">support@bioeksen.com.tr</a>

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

PIS.073

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For in vitro diagnostic use only. 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

Component 2X Prime Script Mix		nded Use		25 Reactions	100 Reaction		
		use mix for RT-gPCR assay		1 x 1000 μL	4 x 1000 μL		
		mplification and detection:		2 % 1000 µL	. Α 1000 μι		
		SARS-CoV-2					
PTV Oligo Mix 1				1 x 12E ul	1 y E00 ul		
RTV Oligo Mix 1		IC-Internal Control)		1 x 125 μL	1 x 500 μL		
	-	Influenza B					
		nfluenza A					
	FAM: Human Co	ronavirus 229E/ OC43					
RTV Oligo Mix 2	HEX: Human	Parainfluenza 1/2		1 v 12E ul	1 × 500		
KTV Oligo Ivila z	ROX: Human Cor	onavirus NL63/ HKU1		1 x 125 μL	1 x 500 μl		
	CY5: Human	Parainfluenza 3/4					
	FAM: Respirator	v Syncytial Virus A/B					
	HEX: Human	Metapneumovirus		1 x 125 μL	1 x 500 μl		
RTV Oligo Mix 3	ROX: Hum	ROX: Human Enterovirus					
		CY5: Human Adenovirus					
RTV Oligo Mix 4		FAM: Human Bocavirus CY5: Human Rhinovirus					
NITO				4 4000 1	1 1000		
NTC	Negat	ive Control		1 x 1000 μL	1 x 1000 µ		
PC-RTV 1 / PC-RTV 2	Positive	Control (PC)		1 x 100 μL	1 x 100 μ		
PC-RTV 3 / PC-RTV 4				1 × 100 με	1 100 p		
ble 2. Transport Conditio	n, Storage Condition, and Shelf Life of the Compone	nts					
Component	Transport Condition	Storage Condi	tion*		Shelf Life		
2X Prime Script Mix		(-22) °C − (-18					
Oligo Mix		(-22) °C – (-18					
NTC	(-22) °C – (+8) °C	(-22) °C – (-18) °C before opening, (+2	1	ftor first thou	12 month		
PC		(-22) °C – (-18) °C before opening, (+2	, , ,				
	each reagent stored at storage temperature can be used						
4. A centrifuge or Mir	compatible filtered pipette tips (nuclease-free) suitable for	ration instruments and nucleic acid prepa or transferring 1-10 μL, 10-100 μL, and 100					
<ol> <li>A centrifuge or Mir</li> <li>Vortex</li> <li>Reaction tubes, PCF</li> </ol>	compatible filtered pipette tips (nuclease-free) suitable fo ni-spin strips, PCR plates and caps/films specific to qPCR instrur	or transferring 1-10 $\mu L$ , 10-100 $\mu L$ , and 100	)-1000 μL of liq				
<ol> <li>A centrifuge or Mir</li> <li>Vortex</li> <li>Reaction tubes, PCF</li> <li>ble 4. Intended Use, Test</li> </ol>	compatible filtered pipette tips (nuclease-free) suitable fo ni-spin a strips, PCR plates and caps/films specific to qPCR instrum <b>Principle, and Analytical Specifications</b>	pr transferring 1-10 $\mu$ L, 10-100 $\mu$ L, and 100 ments and compatible with the reaction vo	)-1000 μL of liq				
<ol> <li>A centrifuge or Mir</li> <li>Vortex</li> <li>Reaction tubes, PCF</li> <li>ble 4. Intended Use, Test</li> </ol>	compatible filtered pipette tips (nuclease-free) suitable fo ni-spin strips, PCR plates and caps/films specific to qPCR instrur	or transferring 1-10 $\mu L$ , 10-100 $\mu L$ , and 100	)-1000 μL of liq blume Table 5	ιuid			
<ol> <li>A centrifuge or Mir</li> <li>Vortex</li> <li>Reaction tubes, PCF</li> <li>ble 4. Intended Use, Test</li> <li>Function</li> </ol>	compatible filtered pipette tips (nuclease-free) suitable fo ni-spin a strips, PCR plates and caps/films specific to qPCR instrum <b>Principle, and Analytical Specifications</b>	pr transferring 1-10 $\mu$ L, 10-100 $\mu$ L, and 100 ments and compatible with the reaction vo	D-1000 μL of liq Diume Table 5 Bioeksen νΝα Zybio EXM30	iuid AT® Transfer Tube 000 Nucleic Acid Iso			
<ol> <li>A centrifuge or Mir</li> <li>Vortex</li> <li>Reaction tubes, PCF</li> </ol>	compatible filtered pipette tips (nuclease-free) suitable fo ni-spin strips, PCR plates and caps/films specific to qPCR instrum <b>Principle, and Analytical Specifications</b> Aid to diagnosis	or transferring 1-10 μL, 10-100 μL, and 100 ments and compatible with the reaction vo Sample Type(s) Nucleic Acid Preparation	)-1000 μL of liq plume Table 5 Bioeksen νΝ Zybio EXM30 Adaltis EXTR	uid AT® Transfer Tube 000 Nucleic Acid Iso Alab and MDXlab	olation Syster		
4. A centrifuge or Mir 5. Vortex 6. Reaction tubes, PCF ble 4. Intended Use, Test function	compatible filtered pipette tips (nuclease-free) suitable fo ni-spin strips, PCR plates and caps/films specific to qPCR instrum <b>Principle, and Analytical Specifications</b> Aid to diagnosis	or transferring 1-10 μL, 10-100 μL, and 100 ments and compatible with the reaction vo Sample Type(s) Nucleic Acid Preparation	D-1000 µL of liq D-1000 µL of liq D-1000 µL of liq D-100 µL of liq D-	AT® Transfer Tube DOD Nucleic Acid Is Alab and MDXlab ar Systems: Magne /Mic IVD (96 Touch/Dx, CFX ch, CFX Opus 384 or-Gene Q 5-Plex/N Cycler 96 er Scientific: Quan Flex/Pro, StepOne 7500/7500 Fast JilLab, MDXlab taQ 96 ene 9600 Plus ems: Fujirebio	olation Systen tic Induction Opus 96/Dx, MDx tStudio 5/5		
4. A centrifuge or Mir 5. Vortex 6. Reaction tubes, PCF ble 4. Intended Use, Test Function Analyte(s) Qualitative/Quantitative Fest Principle	compatible filtered pipette tips (nuclease-free) suitable for ni-spin strips, PCR plates and caps/films specific to qPCR instrum Principle, and Analytical Specifications Aid to diagnosis Table 1 Qualitative Reverse transcription and Real-Time PCR (RT-qPCR)	or transferring 1-10 μL, 10-100 μL, and 100 ments and compatible with the reaction vo Sample Type(s) Nucleic Acid Preparation Method(s)	Table 5 Bioeksen VN. Zybio EXM30 Adaltis EXTR. Bio Molecula Cycler (Mic)/ Bio-Rad: CFX CFX384 Touc Qiagen: Roto Roche: Light( Thermo Fish Dx/6/7/12k f Biosystems 7 Adaltis: Amp HiMedia: Ins Bioer: Linege Atila Biosyste Co-Dx: Co-Dy Tianlong: Ge Sansure: SLA Azure: Cielo	AT® Transfer Tube 200 Nucleic Acid Iso Alab and MDXlab ar Systems: Magne /Mic IVD (96 Touch/Dx, CFX ch, CFX Opus 384 or-Gene Q 5-Plex/N Cycler 96 er Scientific: Quan Flex/Pro, StepOne 7500/7500 Fast bil.ab, MDXlab traQ 96 ene 9600 Plus ems: Fujirebio x Box untier 96E N-96P	olation Syster tic Induction Opus 96/Dx, /IDx tStudio 5/5 Plus, Applied		
4. A centrifuge or Mir 5. Vortex 6. Reaction tubes, PCF ble 4. Intended Use, Test function Analyte(s) Qualitative/Quantitative	compatible filtered pipette tips (nuclease-free) suitable fo ni-spin estrips, PCR plates and caps/films specific to qPCR instrum Principle, and Analytical Specifications Aid to diagnosis Table 1 Qualitative	br transferring 1-10 μL, 10-100 μL, and 100         ments and compatible with the reaction volume         Sample Type(s)         Nucleic       Acid         Method(s)         Validated qPCR Instrument(s)         Inclusivity and Exclusivity	-1000 µL of liq -1000 µL of liq -1000 µL of liq Bioeksen vN/ Zybio EXM30 Adaltis EXTR Bio Molecula Cycler (Mic)/ Bio-Rad: CFX CFX384 Touc Qiagen: Rotc Roche: Light( Thermo Fish Dx/6/7/12k f Biosystems 7 Adaltis: Amp HiMedia: Ins Bioer: Linege Atila Biosyste Co-Dx: Co-Dy Tianlong: Ge Sansure: SLA Azure: Cielo Validated on	AT® Transfer Tube DOO Nucleic Acid Iso Alab and MDXlab ar Systems: Magne /Mic IVD (96 Touch/Dx, CFX ch, CFX Opus 384 or-Gene Q 5-Plex/N Cycler 96 er Scientific: Quan Flex/Pro, StepOne 7500/7500 Fast biLab, MDXlab ttaQ 96 ene 9600 Plus ems: Fujirebio x Box intier 96E N-96P	olation Syster tic Induction Opus 96/Dx, /IDx tStudio 5/5 Plus, Applied		

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#### PIS.079

or professional use	0								
<b>Target Population</b>		viduals with the suspected info			y and Speci	ficity	99.93% and 99.149	%	
,		sfer and Nucleic Acid Prepa			nens				
Sample Ty	pe**	Sample Transfer		ple Storage			reparation Metho		LoD (cp/mL
Combined nasopha	aryngeal and	vNAT <sup>®</sup> Transfer Tube (Cat. No: BS-NA-513m)		it (+2) °C – (+8) °C ar at (-20) °C	Nucle	ic acid preparation	is not needed, sar ctly in RT-qPCR	nples can be	250
oropharyngeal sw	ab samples	Transport Medium		(+2) °C – (+8) °C	Nucleir	acid preparation	<u> </u>	hio FXM3000	
***		(without antibiotics)		ar at (-20) °C	itueien		lab, 3) Adaltis MD	,	125
Bronchoalveolar la	avage (BAL),	Preservative-free sterile 3 days at (+2		(+2) °C _ (+8) °C	Nucl	Nucleic acid preparation consumables: Bioeksen B		ioeksen Bio-	
sputum, and naso		containers/tubes		ar at (-20) °C	Spe	edy <sup>®</sup> Rapid Nuclei		it (Cat. No:	500
aspirate (NAP)		•	,		national ali		NAE01)		
		ected by a healthcare provider d, put them into the <b>vNAT<sup>®</sup> Tra</b>				nical specimen coll	ection regulations.		
					JII.				
		device using the QR Code/Lin	k as indicated in 1	Table 6					
	•	ut of the -20°C freezer.	k as maleated in i						
		ount + 3) *5 μL of RTV Oligo M	lix 1 into an empt	y eppendorf tube	. (i.e Sampl	e Count = 3, pipett	e 5*(3+3) = 30 μL α	of RTV Oligo Mix	)
		t + 3) *10 μL of 2X Prime Scrip	ot Mix into RTV Ol	igo Mix 1. (i.e Sai	nple Count	= 3, pipette 10*(3-	-3) = 60 μL of 2X Pi	rime Script Mix)	
		mix to homogenize.							
		and 5 for all master mixes (4 m ich master mix into relative PC		,	المع مال ممسي				
r i		racted/isolated sample into re	,		ing an sam	pies, ivit allu PCJ.			
0. FIP									
9. Pip				or wells.					
	ette 5 μL of NTO	C into the Negative Control PC RTV 1 into the relative PC tub	R tube, or wells.						
10. Pip 11. Clo	bette 5 $\mu$ L of NTC bette 5 $\mu$ L of PC- base the cap of th	C into the Negative Control PC RTV 1 into the relative PC tub e strips, or PCR tubes or seal P	R tube, or wells. e, or wells. Repea PCR plate. Label to	at for all PC.	n during spir	n-centrifuge.			
10. Pip 11. Clo 12. Spi	pette 5 $\mu$ L of NTC pette 5 $\mu$ L of PC- pse the cap of th in-centrifuge the	C into the Negative Control PC RTV 1 into the relative PC tub e strips, or PCR tubes or seal I e strips, or PCR tubes and PCR	R tube, or wells. e, or wells. Repea PCR plate. Label to plate.	nt for all PC. o avoid confusior	ı during spiı	n-centrifuge.			
10. Pip 11. Clo 12. Spi 13. Op	pette 5 μL of NTC pette 5 μL of PC- ose the cap of th in-centrifuge the pen the lid of the	C into the Negative Control PC RTV 1 into the relative PC tub e strips, or PCR tubes or seal I e strips, or PCR tubes and PCR e instrument. Place the strips,	R tube, or wells. e, or wells. Repea PCR plate. Label to plate.	nt for all PC. o avoid confusior	i during spir	n-centrifuge.			
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10. Pip 11. Clo 12. Spi 13. Op 14. Clo able 6. Real-Time Reaction 5 Reagent 2X Prime Script	eette 5 µL of NTG bette 5 µL of NTG bette 5 µL of PC- osse the cap of th in-centrifuge the een the lid of the ose the lid and st <b>qPCR Program</b> Setup Volume/Rxn	C into the Negative Control PC RTV 1 into the relative PC tub e strips, or PCR tubes or seal f e strips, or PCR tubes and PCR instrument. Place the strips, tart the instrument. Details Bio Molecular Systems: Ma Rad: CFX96 Touch/Dx, CFX Roche: LightCycler Step Reverse Transcription	CR tube, or wells. e, or wells. Repea PCR plate. Label to plate. or PCR tubes and Protocol 1: agnetic Induction Opus 96/Dx, CFX 96, Co-Dx: Co-Dx Cycle No. 1 Cycle	t for all PC. o avoid confusior PCR plate. Cycler (Mic)/Mic 384 Touch, CFX C 80x, Azure: Ciel Temperature 52 °C	IVD, Bio- pus 384, Duration 3 min	ogram Qiagen: Rotor- QuantStudio 5, Biosystems 7500, InstaQ 96, E Fujirebio1 Step Reverse Transcription	Gene Q 5-Plex/MD 5 Dx/6/7/12k Flex, 7500 Fast, Adaltis- ioer: Linegene 960 ianlong: Gentier 9 Cycle No. 1 Cycle 1 Cycle	x, Thermo Fishei /Pro, StepOne Pl : AmpliLab, MDX 10 Plus, Atila Bios 6E, Sansure: SLAI <b>Temperature</b> 52 °C	us, Applied lab, HiMed ystems: N-96P <b>Duratio</b> 3 min
10. Pip 11. Clo 12. Spi 13. Op 14. Clo able 6. Real-Time Reaction 5 Reagent 2X Prime Script	eette 5 µL of NTG bette 5 µL of NTG bette 5 µL of PC- osse the cap of th in-centrifuge the een the lid of the ose the lid and st <b>qPCR Program</b> Setup Volume/Rxn	C into the Negative Control PC RTV 1 into the relative PC tub e strips, or PCR tubes or seal f e strips, or PCR tubes and PCR instrument. Place the strips, tart the instrument. Details Bio Molecular Systems: Ma Rad: CFX96 Touch/Dx, CFX Roche: LightCycler Step Reverse Transcription Pre-Incubation Denaturation	R tube, or wells. e, or wells. Repea PCR plate. Label to plate. or PCR tubes and Protocol 1: agnetic Induction Opus 96/Dx, CFX 96, Co-Dx: Co-Dx Cycle No. 1 Cycle 1 Cycle 12 Touchdown	t for all PC. o avoid confusion PCR plate. Cycler (Mic)/Mic 384 Touch, CFX C 80x, Azure: Ciel Temperature 52 °C 95 °C	IVD, Bio- Duration 3 min 10 sec	Qiagen: Rotor- QuantStudio 5, Biosystems 7500, InstaQ 96, E FujirebioT Step Reverse Transcription Pre-Incubation	Gene Q 5-Plex/MD 5 Dx/6/7/12k Flex, 7500 Fast, Adaltis- ioer: Linegene 960 ianlong: Gentier 9 Cycle No. 1 Cycle 1 Cycle	x, Thermo Fisher /Pro, StepOne Pl : AmpliLab, MDX 10 Plus, Atila Bios 6E, Sansure: SLAI Temperature 52 °C 95 °C	us, Applied lab, HiMedi ystems: N-96P <b>Duration</b> 3 min 10 sec
10. Pip 11. Clo 12. Spi 13. Op 14. Clo able 6. Real-Time Reaction S Reagent 2X Prime Script Mix	bette 5 μL of NTG bette 5 μL of NTG bette 5 μL of PC- ose the cap of the in-centrifuge the en the lid of the ose the lid and st <b>qPCR Program</b> Setup 10 μL 5 μL	C into the Negative Control PC RTV 1 into the relative PC tub e strips, or PCR tubes or seal f e strips, or PCR tubes and PCR instrument. Place the strips, tart the instrument. Details Bio Molecular Systems: Ma Rad: CFX96 Touch/Dx, CFX Roche: LightCycler Step Reverse Transcription Pre-Incubation Denaturation	CR tube, or wells. e, or wells. Repeat PCR plate. Label to plate. or PCR tubes and Protocol 1: agnetic Induction Opus 96/Dx, CFX 96, Co-Dx: Co-Dx Cycle No. 1 Cycle 12 Touchdown Cycles: 1 °C decrement in annealing temperature	tt for all PC. o avoid confusion PCR plate. Cycler (Mic)/Mic 384 Touch, CFX C c Box, Azure: Ciel Temperature 52 °C 95 °C 95 °C	IVD, Bio- ppus 384, p Duration 3 min 10 sec 1 sec	Ogram Qiagen: Rotor- QuantStudio 5, Biosystems 7500, InstaQ 96, E Fujirebio1 Step Reverse Transcription Pre-Incubation Denaturation	Gene Q 5-Plex/MD 5 Dx/6/7/12k Flex, 7500 Fast, Adaltis- ioer: Linegene 960 ianlong: Gentier 90 Cycle No. 1 Cycle 1 Cycle	x, Thermo Fisher /Pro, StepOne Pl : AmpliLab, MDX 00 Plus, Atila Bios 6E, Sansure: SLAI Temperature 52 °C 95 °C 95 °C	us, Applied lab, HiMedi ystems: N-96P Duration 3 min 10 sec 1 sec
10. Pip 11. Clo 12. Spi 13. Op 14. Clo sable 6. Real-Time Reaction S Reagent 2X Prime Script Mix Oligo Mix	bette 5 μL of NTG bette 5 μL of NTG bette 5 μL of PC- sse the cap of th in-centrifuge the en the lid of the ose the lid and st <b>qPCR Program</b> Setup 10 μL	C into the Negative Control PC RTV 1 into the relative PC tub e strips, or PCR tubes or seal f e strips, or PCR tubes and PCR instrument. Place the strips, tart the instrument. Details Bio Molecular Systems: Ma Rad: CFX96 Touch/Dx, CFX Roche: LightCycler Step Reverse Transcription Pre-Incubation Denaturation Annealing and Extension	CR tube, or wells. e, or wells. Repeat PCR plate. Label to plate. or PCR tubes and Protocol 1: agnetic Induction Opus 96/Dx, CFX 96, Co-Dx: Co-Dx Cycle No. 1 Cycle 12 Touchdown Cycles: 1 °C decrement in annealing temperature	tt for all PC. o avoid confusion PCR plate. Cycler (Mic)/Mic 384 Touch, CFX C 80x, Azure: Ciel 52 °C 95 °C 95 °C 67 °C to 56 °C	IVD, Bio- ppus 384, Duration 3 min 10 sec 1 sec 15 sec	Ogram Qiagen: Rotor- QuantStudio 5, Biosystems 7500, InstaQ 96, E Fujirebio1 Step Reverse Transcription Pre-Incubation Denaturation	Gene Q 5-Plex/MD 5 Dx/6/7/12k Flex, 7500 Fast, Adaltis- ioer: Linegene 960 ianlong: Gentier 9 Cycle No. 1 Cycle 1 Cycle 40 Cycles	x, Thermo Fisher /Pro, StepOne Pl : AmpliLab, MDX 00 Plus, Atila Bios 6E, Sansure: SLAI Temperature 52 °C 95 °C 95 °C	us, Applied lab, HiMedi ystems: N-96P Duration 3 min 10 sec 1 sec 15 sec



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 <u>support@bioeksen.com.tr.</u>

#### Table 7. Threshold Levels for Calculating Cq Values

						Real Time PC	R Instrur	nent				
Analyte	Bi	o-Rad CFX	U	Cielo	Light	Cycler 96		lic IVD and -Dx Box	Rotor-Gene Q****			tudio 5/5 .2k 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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or in vitro diagnost or professional use (		ıly.											bi	Øekse	
Human (IC-Interr		rol) 2	200	30	20000	30	0.05	30	0.5	30	0.02	40	20000	30	
Influenza	a B	7	750	30	75000	30	0.1	30	0.5	30	0.05	40	75000	30	
Influenza	-		200	30	20000	30	0.05	30	0.5	30	0.02	40	20000	30	
luman Coronaviru			750	30	75000	30	0.1	30	0.5	30	0.05	40	20000	30	
Human Parainfl Iuman Coronaviru			750 750	30 30	75000 75000	30 30	0.1	<u> </u>	0.5	30 30	0.05	40 40	20000	30 30	
Human Coronavirus Human Parainfl			750 750	30	75000	30	0.1	30	0.5	30	0.05	40	20000	30	
Respiratory Syncyt			750	30	75000	30	0.1	30	0.5	30	0.05	40	20000	30	
Human Metapn			750	30	75000	30	0.1	30	0.5	30	0.05	40	20000	30	
Human Ente	rovirus	7	750	30	75000	30	0.1	30	0.5	30	0.05	40	20000	30	
Human Ader			200	30	20000	30	0.05	30	0.5	30	0.02	40	20000	30	
Human Boc			750	30	75000	30	0.1	30	0.5	30 30	0.05	40 40	20000	30	
Human Rhin ** Defined thresho			200	30 f "Outlior Pr	20000	30 "Dunamic	0.05 Tubo = Op"	30	0.5		0.02	40	20000	30	
ble 8. Interpretat		•			:110vai – 0 ,	, Dynamic	rube – Off ,	, and slope (	Lonect -	OII					
Target				rnal Contro	l (IC)					Result Inter	pretation				
					X - <i>i</i>							lf 26 <cq< td=""><td>≤30 "Low Posit</td><td>ive"</td></cq<>	≤30 "Low Posit	ive"	
										Protocol 1		If 16<0	Cq≤26 "Positive	e"	
Positive (+)			Positiv	e (+) or Neg	ative (-)			ts are valid					.6 "High Positiv		
				- ( ,			Target	is detected		Destand 2			≤40 "Low Posit		
									Protocol 2			Cq≤34 "Positive 2 "High Positiv			
				B						Results a	re valid	0422	6.1.1 031(19	-	
Negative (-)	Negative (-)			Positive (+)						Target is not					
ble 9. Expected P	erforma	nce of Ki	t Contro	ols											
								Expecte	d Result	s and Cq Value	S				
Control Type		Purpose	e		10 (115)()	Prot	ocol 1	<u> </u>				Protoco		<u>.</u>	
	Cont	amination	control		IC (HEX)			Target		IC (	HEX)		Tar	get	
Negative Control		uring RT-q			Not Detecte	ed	No	t Detected		Not D	etected		Not De	tected	
	÷.		ty contro	De	tected (Ca<	(30)	Dete	<b>cted</b> (Cq≤30)		Detecte	<b>(</b> Ca<40)				
Positive Control	Reag	erri stabilit	Ly CONTRO	00	Detected (Cq≤30)         Detected (Cq≤3					Detected (Cq≤40)         Detected (Cq≤4           Detected         Detection insignition			(04340)		
Positive Control					Detected			on insignifica	nt	Det	,		Detection in	,	
Internal Control	Nucleic sa work as e	c acid extra impling co expected ('	action a ontrol ( <b>Table 9</b> )	If "Not	Detected Detected" of target Cq procedures	check the described l	Detecti If " <b>Dete</b> pelow.	ected" IC is va		If "Not Detec	ected	the		nsignificant	
Recomme	Nucleic sa work as e nation Pr ended ac	c acid extra impling co expected ( roblem: If i ction: Repe	action an ontrol ( <b>Table 9</b> ) a target eat the p	If "Not , apply the p in the Nega	Detected Detected" of target Cq procedures tive Control attention to	check the described l l reaction is the "Warr	Detecti If " <b>Dete</b> pelow. s " <b>Detected</b> " ings and Lim	ected" IC is va '. hitations" sec	ilid tion.	If " <b>Not Detec</b> targ	ected ted" check	the	Detection ir	nsignificant	
Internal Control a control does not v 1. Contamin Recomme 2. Invalid In Recomme repeats, a 3. Reagent F	Nucleic sa work as e nation Pr ended ac ternal Co ended ac a new sa Problem	acid extra impling co expected (' <b>roblem:</b> If a <b>ction:</b> Repo <b>ction:</b> Repo <b>ction:</b> Sam mple from : If all Inter	action a ontrol ( <b>Table 9</b> ) a target eat the oblem: If opling wa o the sar	nd If "Not If "Not in the Nega run, paying i the Interna as not succe ne patient si ttrols, Positi	Detected Detected" c target Cq procedures tive Control attention to I Control (IC ssfully done hould be col	theck the described I reaction is the "Warr and all ot p or there llected and and target	Detecti If "Dete pelow. s "Detected" ings and Lim her targets o was a proble tested again s in the run a	cted" IC is va	tion. re " <b>Not</b> sample	If " <b>Not Detec</b> targ <b>Detected</b> ". transportation	ected ted" check et Cq or extract	ion. Re-to	Detection in If " <b>Detected</b> est the sample	" IC is valid	
Internal Control control does not v 1. Contamin Recomme 2. Invalid In Recomme repeats, a 3. Reagent F Recomme WARNINGS A 1. Fals 2. Mut	Nucleic sa work as e hation Pr ended ac ternal Co ended ac new sar Problem ended ac ND LIV i.e-negati tations v	c acid extra impling co expected (' roblem: If : tion: Repo ontrol Pro cition: Sam mple from : If all Inte: tion: The ition: The itinATION ive results vithin the !	action a ontrol (Table 9) a target eat the bblem: If opling wa the sar the sar run is co VS may occ target ro	If "Not If "Not in the Nega un, paying a the Interna as not succe he patient si itrols, Positi onsidered in cur if inadec ggions could	Detected Detected" of target Cq procedures tive Control attention to I Control (IC ssfully done hould be col ve Controls valid. Re-tes juate numbe affect prim	check the described I I reaction is the "Warr and all ot or there w llected and and target st the PC. I er (below t ier and/or	Detecti If "Detected" oelow. s "Detected" ings and Lin her targets of was a proble tested again s in the run a f the probler he LoD) of o probe bindin	cted" IC is va , itations" sec of a sample a m during the n. are "Not Deta m repeats, pla rganisms are rg, resulting in	tion. re " <b>Not</b> sample ected". ease rea present n failure	If " <b>Not Detec</b> targ <b>Detected</b> ". transportation ch out to the m in the specime to detect the p	or extract anufacture n. resence of	ion. Re-to er for fur f agents.	Detection in If "Detected est the sample ther assistance	" IC is valid	
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For in vitro diagnostic For professional use o					bi
•••	Manufacturer	MON	Non-sterile	8	Do not use if package is damaged and consult <i>Instructions for Use</i>
2	Expiration Date YYYY-MM		Consult Instructions for Use or consult electronic Instructions for Use	Ť	Keep dry
CONTROL -	Negative Control	$\triangle$	Caution	<u>tt</u>	Keep upright
CONTROL +	Positive Control	X	Temperature limit	Σ	Contains sufficient for <n> tests</n>
CONTROL	Control				

#### 5. MANUFACTURER AND TECHNICAL SUPPORT



Bioeksen AR GE Teknolojileri A.Ş

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Technical Support: <a href="mailto:support@bioeksen.com.tr">support@bioeksen.com.tr</a>

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

# Legionella pneumophila qPCR Kit



PIS.049

## Package Insert

•							
Component		Intende	d Use		25 Reactions 10	0 Reactions	
2X qPCR Mix	Optimized	ready-to-use	mix for RT-qPCR assa	y	1 x 125 μL	1 x 500 μL	
LP Oligo Mix	FA	AM: Legionella	lification and detectio <i>pneumophila</i> ternal Control)	n:	1 x 62.5 μL	1 x 250 μL	
NTC		Negative (	,		1 x 1000 μL	L x 1000 μL	
PC-LP		Positive Cor				1 x 1000 μL	
	torage Condition, and Shelf Life of t				1 × 100 με	1 Λ 100 με	
Component	Transport Conditio			Storage Condition	•	Shelf Life	
2X gPCR Mix				(-22) – (-18) °C			
Oligo Mix				(-22) – (-18) °C	12 Mont		
PC	(-22) - (+8) °C $(-22) °C - (-18) °C$ before opening, (+2) °C - (+8) °C after first thaw						
NTC					- (+8) °C after first thaw		
piration date of the reagents.	n reagent stored at storage temperatur Not Included in the Package Required		Not Included in the				
<ol> <li>A centrifuge or Mini-sp</li> <li>Vortex</li> <li>Reaction tubes, PCR stri</li> </ol>	patible filtered pipette tips (nuclease-fi in <u>ps, PCR plates and caps/films specific t</u> nciple, and Analytical Specifications	o qPCR instrum					
unction	Aid to diagnosis		Sample Type(s)		Table 5		
Analyte(s)	Table 1		Nucleic Acid Extrac	tion Method(s)	Bioeksen <b>vNAT® Transfer Tube</b> Zybio EXM3000 Nucleic Acid Iso Adaltis EXTRAlab and MDXIab		
Qualitative/Quantitative	alitative/Quantitative Qualitative		Validated qPCR Ins	trument(s)	Bio Molecular Systems: Magne Cycler (Mic)/Mic IVD Bio-Rad: CFX96 Touch/Dx, CFX CFX384 Touch, CFX Opus 384 Qiagen: Rotor-Gene Q 5-Plex/N Roche: LightCycler 96 Thermo Fisher Scientific: Quant Dx/6/7/12k Flex/Pro, StepOne 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	Dpus 96/Dx, IDx Studio 5/5	
Test Principle	Real-Time PCR (qPCR)			ucivity	Validated on the reference stra	ins and the fie	
Automated/Manual	Manual		Inclusivity and Excl	usivity	isolates		
ntended Users	Laboratory professionals trained in the of qPCR and in vitro diagnostic proceed	dures	Limit of Detection		Table 5		
Target Population	Individuals with the suspected infection		Sensitivity and Spe		%100.00 ve %100.00		
	d Transfer of Clinical Specimens / N		•				
Sample Type**	Sample Transfer		ple Storage		id Preparation Method	LoD (cp/n	
	✓NAT <sup>®</sup> Transfer Tube (Cat. No: BS-NA-513m)		at (+2) °C – (+8) °C ar at (-20) °C		preparation is not required. In be used directly in gPCR.	250	
mbined nasopharyngeal, and oropharyngeal swabs*** (Cat. No: BS-NA-513m) Viral Transport Medium (VTM) (CDC SOP#: DSR-052-05 (without antibiotic))		1 year at (-20) °C 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		lab 125	
				C Bio- Speedy <sup>®</sup> 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.

Revision Date: 2024-11-19/Rev.03 Published Date: 2023-10-04 1

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For in vit For profe *** If dr 1. Al 1. 2. 3. 4. 5. 6. 7. 8. 9. 10 11 12 13	tro diagnostic use only. essional use only. ry swab samples are received <b>PPLICATION PROTOCOL</b> Program the qPCR device Take the PCR kit out of th Pipette (Sample Count + Add (Sample Count + 3) <sup>4</sup> Vortex the master mix to Pipette 7.5 µL of master Pipette 2.5 µL of pach iso Pipette 2.5 µL of NTC int Pipette 2.5 µL of PC-LP in Close the cap of the strip Spin-centrifuge the strip Open the lid of the instru	<ul> <li>a) *2.5 µL of LP Oligo Mix into an empty eppendorf tube. (i.e Sample Count = 5 µL of 2X qPCR Mix into the tube prepared in Step 3. (i.e Sample Count = 3, homogenize.</li> <li>mix into all PCR tubes, or wells to be used (including all samples, NTC and PC) lated/extracted sample into the relative PCR tube, or well.</li> <li>to the Negative Control PCR tube, or well.</li> <li>to the Positive Control PCR tubes, or wells.</li> <li>o, or PCR tubes or seal PCR plate. Label to avoid confusion during spin-centrif, or PCR tubes or PCR plates.</li> <li>ment. Place the strips, PCR tubes or PCR plate.</li> </ul>	pipette 5*(3+3) = 30 μL of 2X qPCR Mix)
Table 0	. Kear Time grok Flogram	qPCR Progr	am
		Protocol 1:	Protocol 2:
	Reaction Setup	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, Thermo Fisher Scie QuantStudio 5/5 Dx/6/7/12k Flex/Pro, StepOne Plus, A Biosystems 7500/7500 Fast, Adaltis: AmpliLab, MDXI

		qPCR Program										
			Protocol 1:				Protocol 2	-				
						Qiagen: Rotor-Gene Q 5-Plex/MDx, Thermo Fisher Scientific:						
Reaction Se	etup	Bio Molecular Systems: N	: IVD, Bio-	QuantStudio 5/5 Dx/6/	7/12k Flex/P	ro, StepOne Plu	s, Applied					
		Rad: CFX96 Touch/Dx, CF	X Opus 96/Dx, CFX	384 Touch, CFX (	Opus 384,	Biosystems 7500/75	00 Fast, Ada	ltis: AmpliLab, N	IDXlab,			
		Roche: LightCycle	HiMedia: InstaQ 9	6, Bioer: Line	gene 9600 Plus,	Atila						
			Biosystems: FujirebioTianlong: Gentier 96E, Sansure: SLAN-									
Reagent	Volume/Rxn	Step	Cycle No.	Temperature	Duration	Step	Cycle No.	Temperature	Duration			
		Enzyme Activation	1 Cycle	52 °C	3 min	Enzyme Activation	1 Cycle	52 °C	3 min			
2X qPCR Mix	5 μL	Pre-Incubation	1 Cycle	95 °C	10 sec	Pre-Incubation	1 Cycle	95 °C	10 sec			
	2.5 μL	Denaturation	12 Touchdown	95 °C	1 sec	Denaturation Annealing and		95 °C	1 sec			
Oligo Mix		Annealing and Extension	Cycles: 1 °C decrement in annealing	67 °C to 56 °C	15 sec		40 Cycles					
			temperature per cycle			Extension		55 °C	15 sec			
Template Nucleic	2 5	Denaturation		95 °C	1 sec							
Acid/NTC/PC	2.5 μL	Annealing and Extension	30 Cycles	55 °C	15 sec	Detection (Reading)		FAM/H				
Total Reaction Volume	10 µL	Detection (Reading)	SU CYCles	FAM/H	IEX	Detection (Reading)		FAIVI/F	EA			



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 <u>support@bioeksen.com.tr</u>.

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

		Real Time PCR Instrument													
Analyte	Bio-Rad CFX		Cielo		Ligh	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			
		Protoco				
Positive (+)	Positive (+) or Negative (-) Positive (+)	Results are valid Target is detected Protoco				
		If Cq<22 "High Positive" Results are valid				
Negative (-)		Target is not detected				

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#### For in vitro diagnostic use only. For professional use only. Table 9. Expected Performance of Kit Controls



		Expected Results and Cq Values							
Control Typ	e Purpose	Prot	ocol 1	Protocol 2					
		IC (HEX) Target		IC (HEX)	Target				
Negative Con	trol Contamination control during qPCR	Not Detected Not Detected		Not Detected	Not Detected				
Positive Cont	rol Reagent stability control	Detected (Cq≤30) Detected (Cq≤30)		Detected (Cq≤40)	Detected (Cq≤40)				
	. Nucleic acid extraction and	Detected	Detection insignificant	Detected	Detection insignificant				
Internal Cont	sampling control	If " <b>Not Detected</b> " check the target Cq	If "Detected" IC is valid	If " <b>Not Detected</b> " check the target Cq	If "Detected" IC is valid				

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

Contamination Problem: If a target in the Negative Control reaction is "Detected". 1.

Recommended action: Repeat the run, paying attention to the "Warnings and Limitations" section.

- Invalid Internal Control Problem: If the Internal Control (IC) and all other targets of a sample are "Not Detected". 2. 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.
- Reagent Problem: If all Internal Controls, Positive Controls and targets in the run are "Not Detected". 3.

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

- False-negative results may occur if inadequate number (below the LoD) of organisms are present in the specimen. 1.
  - 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.
  - 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
  - 7. Sample tubes should always be kept closed except for liquid transfers.
  - Filtered and nuclease-free pipette tips should be used for sample transfer. 8.
  - 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.
  - 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.
  - 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.

#### EXPLANATION OF SYMBOL Δ

Symbol	Title of Symbol	Symbol	Title of Symbol	Symbol	Title of Symbol
CE	European Conformity CE Mark	LOT	Batch code	漛	Keep away from sunlight
IVD	In vitro diagnostic medical device	REF	Catalogue number	澎	Protect from heat and radioactive sources
	Manufacturer		Non-sterile		Do not use if package is damaged and consult <i>Instructions for Use</i>
	Expiration Date YYYY-MM	<b>•m</b>	Consult Instructions for Use or consult electronic Instructions for Use	Ť	Keep dry
CONTROL -	ONTROL - Negative Control		Caution	<u>††</u>	Keep upright
CONTROL + Positive Control		X	Temperature limit	Σ	Contains sufficient for <i><n></n></i> 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 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-TF-T-25/BS-TF-T-100 Ordering Ref No: FEVER-T-25/FEVER-T-100

# **Tropical Fever RT-qPCR Panel**

## Package Insert

ble 1. Kit Content Component	Intende	ed Use	25 Reactions	100 Reactions	
2X Prime Script Mix	Optimized ready-to-use		2 x 1000 μL	7 x 1250 μL	
TF Oligo Mix 1	Specific nucleic acid amp FAM: Crimean-Congo Hemo HEX: Human (IC-	orrhagic Fever virus (CCHFV)	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: Eb ROX: Ha CY5: May	ntavirus	1 x 125 μL	1 x 500 μL	
TF Oligo Mix 4	FAM: Rift V ROX: Trypan CY5: Plasm	osoma cruzi	1 x 125 μL	1 x 500 μL	
TF Oligo Mix 5	FAM: Bru ROX: Coxie CY5: Burkholder	lla burnetii	1 x 125 μL	1 x 500 μL	
TF Oligo Mix 6	FAM: Salm HEX: Ricke ROX: Lepto CY5: Leishi	1 x 125 μL	1 x 500 μL		
TF Oligo Mix 7	FAM: West Nil HEX: Zika v CY5: Streptococo	1 x 125 μL	1 x 500 μL		
TF Oligo Mix 8	FAM: Yellow ROX: Chikungun CY5: Japanese Enc	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 Co	ontrol (PC)	1 x 100 μL	1 x 100 μL	
NTC	Negative	Control	1 x 1000 μL	1 x 1000 μL	
	e Condition, and Shelf Life of the Compo				
Component	Transport Condition	Storage Condition* (-22) °C – (-18) °C		Shelf Life	
2X Prime Script Mix Oligo Mix PC NTC	(-22) °C − (+8) °C	(-22) °C - (-18) °C (-22) °C - (-18) °C (-22) °C - (-18) °C before opening, (+2) °C - ( (-22) °C - (-18) °C before opening, (+2) °C - (	– (+8) °C after first thaw 12 Mor		
piration date of the reagents.		ed until the expiration date indicated on the	tube. The kit's expiration of	date is determined b	
ble 3. Required Components Not		nts Not Included in the Package			
<ol> <li>Micropipettes and compatib</li> <li>A centrifuge or Mini-spin</li> <li>Vortex</li> </ol>	ruments and nucleic acid preparation consu le filtered pipette tips (nuclease-free) suitab trips and caps or PCR plates and seals specif				
Function	Aid to diagnosis	Sample Type(s)	Table 5		
Analyte(s)	Table 1	Nucleic Acid Extraction Method(s)	Zybio EXM3000 Nucleic Adaltis EXTRAlab and M		
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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Bio-Speedy<sup>®</sup>

CE IVD

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or in vitro diagnostic use only. Tor professional use only.					b	iøeksen
					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 a (RT-qPCR)	nd Real-Time PCR	Inclusivity and Exclusivity		Validated on the reference strains and the field isolates	
Automated/Manual	Manual				isolates	
Intended Users		Laboratory professionals trained in the techniques of qPCR and in vitro diagnostic procedures		ection (LoD)	Table 5	
Target Population	Individuals with the sus	pected infection	Sensitivity a	and Specificity	98.55% and 99.21%	
able 5. Collection, Storage and Tr	ansfer of Clinical Specimens	s / Nucleic Acid Pr	eparation M	ethods		
Sample Type**	Sample Transfer	Sample St	orage	e Nucleic Acid Preparation Method		LoD (cp/mL)
Whole blood, serum and plasma	p blood, serum and blasma I FL) I A-treated blood tube		2) Adaltis EXTRA	nstruments: 1) Zybio EXM3000, lab, 3) Adaltis MDXlab	500-1000	
Urine	Preservative-free sterile tubes/containers	1 year at (	-20) °C		<b>n consumables:</b> Bio-Speedy® action Kit (Cat. No: ZFNAE01)	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).
- Pipette 15 µL of each master mix into all PCR tubes, or wells to be used (including all samples, NTC and PC). 7.
- 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.

tubes/containers

- 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

					RT-qPCR P	rogram			
Reaction Setup		Bio Molecular Systems: Rad: CFX96 Touch/Dx, C Roche: LightCyc		384 Touch, CFX	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
	10.1	<b>Reverse Transcription</b>	1 Cycle	52 °C	3 min	<b>Reverse Transcription</b>	1 Cycle	52 °C	3 min
2X Prime Script Mix	10 µL	Pre-Incubation	1 Cycle	95 °C	10 sec	Pre-Incubation	1 Cycle	95 °C	10 sec
	5 μL	Denaturation	12 Touchdown Cycles:	95 °C	1 sec	Denaturation		95 °C	1 sec
Oligo Mix		5 μL	Annealing and Extension	1 °C decrement in annealing temperature per cycle	67 °C to 56 °C	15 sec	Annealing and Extension	40 Cycles	55 °C
Template Nucleic		Denaturation		95 °C	1 sec				
Acid/NTC/PC	5 μL	Annealing and Extension	30 Cycles	55 °C	15 sec	Detection (Reading)		FAM/HEX/R	OX/CY5
Total Reaction Volume	20 µL	Detection (Reading)		FAM/HEX/R	OX/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



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

#### 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 <u>support@bioeksen.com.tr</u>.

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

		Real Time PCR Instrument										
Analyte	Bio	Bio-Rad CFX		ielo	Light	tCycler 96		/lic IVD and -Dx Box	Rotor-	Gene Q****	-	studio 5/5 2k 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 In	terpretation			
				If 26 <cq "low="" positive"<="" th="" ≤30=""></cq>			
	Positive (+)	Positive (+) or Negative (-)	Protocol 1	If 16 <cq≤26 "positive"<="" td=""></cq≤26>			
			Results are valid	If Cq≤16 "High Positive"			
	Positive (+)		Target is detected	If 34 <cq "low="" positive"<="" td="" ≤40=""></cq>			
			Protocol 2	If 22 <cq≤34 "positive"<="" td=""></cq≤34>			
				If Cq≤22 "High Positive"			
	Negative ( )			s are valid			
	Negative (-)	Positive (+)	Target is not detected				

#### Table 9. Expected Performance of Kit Controls

		Expected Results and Cq Values								
Control Type	Purpose	Prot	ocol 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	Reagent stability control <b>Detected</b> (Cq≤30) <b>Detected</b> (Cq≤30)		Detected (Cq≤40)	Detected (Cq≤40)					
	Nucleic acid extraction and	Detected	Detection insignificant	Detected	Detection insignificant					
Internal Control	sampling control	If " <b>Not Detected</b> " check the target Cq	If "Detected" IC is valid	If " <b>Not Detected</b> " 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.

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



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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	淡	Protect from heat and radioactive sources
***	Manufacturer	NON	Non-sterile	8	Do not use if package is damaged and consult <i>Instructions for Use</i>
$\square$	Expiration Date YYYY-MM	i	Consult Instructions for Use or consult electronic Instructions for Use	ا	Keep dry
CONTROL -	Negative Control	$\triangle$	Caution	<u> </u>	Keep upright
CONTROL +	Positive Control	X	Temperature limit	Σ	Contains sufficient for <n> tests</n>
CONTROL	Control				

#### 5. MANUFACTURER AND TECHNICAL SUPPORT Bioeksen AR GE Teknolojileri A.Ş



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

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**

# bi eksen Bio-Speedy®

#### 1. Product Content

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

Component	Component Amount				<b>Transport Conditions</b>	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<sup>®</sup> Viral Nucleic Acid Buffer is a <u>10x concentrated</u> 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<sup>®</sup> 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: <a href="https://www.cdc.gov/coronavirus/2019-ncov/lab/guidelines-clinical-specimens.html">https://www.cdc.gov/coronavirus/2019-ncov/lab/guidelines-clinical-specimens.html</a>.

#### 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<sup>®</sup> 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<sup>®</sup> 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 *νNAT® 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	·淡·	Protect from heat and radioactive sources
••••	Manufacturer	NON	Non-sterile	Ť	Keep dry
	Use-by date		Consult instructions for use or consult electronic instructions for use	<u>tt</u>	Keep it upright
	Temperature limit	Σ	Contains sufficient for <n> tests</n>	$\triangle$	Caution

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#### 7. Manufacturer and Technical Support



Bioeksen R&D Technologies Incorporated Company

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