Genematrix

REF NR03A

NeoPlex™ RV-Panel A Detection kit

Multiplex Real-time PCR Reagents for Respiratory pathogens Detection
For professional *in vitro* diagnostic use only

[INTENDED USE]

The 'NeoPlex™ RV-Panel A Detection Kit' Assay is a qualitative *in vitro* test for the simultaneous detection and confirmation of respiratory infection-causing pathogens (Influenza A including Influenza virus A H3N2(Flu A/H3N2) and Influenza virus A H1N1pdm09(Flu A/H1N1pdm09), Influenza virus B(Flu B), Respiratory Syncytial Virus A (RSV A) and Respiratory Syncytial Virus B (RSV B), Parainfluenza 1, 2 and 3 (PIV1, PIV2 and PIV3) and Adenovirus(AdV)) from nasopharyngeal swab specimens. This test kit is intended for professional use.

[PRINCIPLE OF ASSAY]

'NeoPlex™ RV-Panel A Detection Kit' is based on two major processes, isolation of nucleic acid from specimens and multiplex real-time amplification. Respiratory disease infection-causing pathogen's nucleic acid is extracted from a specimen, amplified in multiplex One-step real-time RT-PCR and detected using fluorescent reporter dye probes specific for the pathogens nucleic acid and Internal Control.

[KIT CONTENTS] — 96 Tests /Kit

4X RV-Panel A PPM	Target[1] specific primer, probe set Tris-EDTA buffer	**500 µL x 1 Vial**
5X RV-Panel A Buffer		**400 µL x 1 Vial**
RV-Panel A Enzyme Mix		**100 µL x 1 Vial**
RV-Panel A PC	Target clone	**50 µL x 1 Vial**
RV-Panel A IC	IC clone	**1 mL x 1 Vial**
D·W(RNase/DNase-free Water)	Nuclease free Distilled Water	**1 mL x 1 Vial**

[Additional required equipment and materials]

- CFX96 real-time PCR detection system (BioRad, Inc., Cat No. 1845097-IVD) or equivalent
- 0.2 ml 8-Tube PCR Strips without Caps, low profile, white (BioRad, Inc., Cat No. TLS0851)
- Optical Flat 8-Cap Strips for PCR Tubes (BioRad, Inc., Cat No. TCS0803)
- QIAamp DSP Viral RNA Mini Kit (QIAGEN,Cat No.61904) or equivalent nucleic acid extraction kit
- Pipettes set
- Micro Centrifuge
- Disposable powder-free gloves

1 Target: Flu A, Flu A H3N2, Flu A H1N1pdm09, Flu B, RSV A, RSV B, PIV1, PIV2, PIV3, AdV, IC

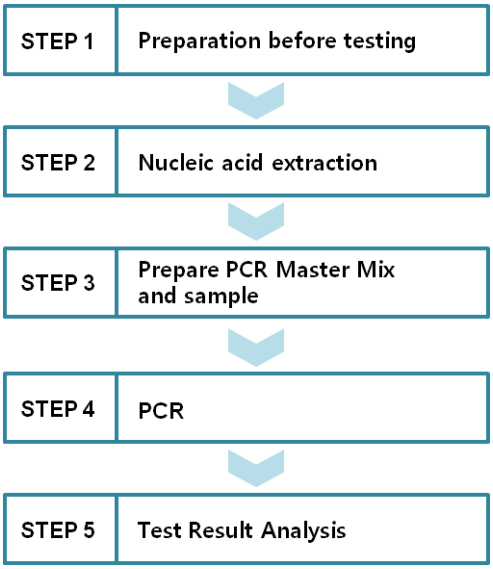
[KIT STORAGE AND STABILITY]

- Store the kit below -20℃(-4˚F).
- Kit materials are stable until the expiration date printed on the label under un-opened condition.
- Kit's shelf life is one **(1)** year.
- Please use the reagents within twelve **(12)** weeks after opening.

[WARNINGS AND PRECAUTIONS]

1. This device is intended for *in vitro* use only. Do not use the device for other purposes.
2. Wear personal protective equipments, such as gloves and lab coats when handling NeoPlex™ RV-Panel A Detection kit and/or specimens.
3. Do not smoke, drink or eat while handling NeoPlex™ RV-Panel A Detection kit and/or samples.
4. Please be careful when handling samples to prevent infections of user and/or indirect contact to a person. Sample contains a risk of infections and unknown diseases.
5. Do not use reagents from different lots or from different tubes of the same lot.
6. If you do not frequently inspect the product, keep a kit in a refrigerator for a certain amount of time. Do not freeze/thaw over four times. Repeated frozen/thawed product may result in false negative and false positive results.
7. Be careful not to contaminate the product when extracting nucleic acid, amplifying PCR product, using positive control (PC, Positive Control). The use of filter tips is recommended to prevent contamination of the product.
8. It is recommended that the sample or the positive control (PC, Positive Control) contained in the product to be frozen and stored separately from the freezer storing the product.
9. Use the sterilized consumable laboratory supplies. Do not reuse it.
10. Add the extracted nucleic acid sample and positive control (PC, Positive Control) into the reaction solution in a space separate from the PCR reaction solution preparation space.
11. Before using, read this instruction for use carefully.
12. Use calibrated measuring tools. (e.g. pipette)
13. Please check the expiration date before using the reagent.
14. Keep Positive Control separately when using to avoid contamination.
15. Before starting the PCR, make sure the lid is closed properly.
16. Dispose the product in accordance with local or national regulations.
17. Please consult with doctor about the test results.

[TEST PROCEDURE]



STEP 1. Preparation before testing

1) Preparation before testing

A. Prepare the all devices and reagent before use.

B. Place the kit under the room temperature at least 10 minutes before testing.

⚠ Do not freeze/thaw over four times.

2) Specimen Collection, Transportation and Storage

A. Specimens for use: Nasopharyngeal swab

B. It is recommended to process specimen within one (1) day after collection.

C. Store specimens at 2~8 °C (35.6~46.4˚F) for no longer than seventy two (72) hours. For pro-longed storage, Freeze under -20°C (-4˚F) condition.

D. Transportation of clinical specimens must comply with local regulations for the transport of etiologic agents.

⚠
- Use only the specimen type listed in the instruction manual.
- The specimen volume should be above 0.5ml.
- Wear eye protection, laboratory coats and disposable gloves when handling specimens.
- Specimens should be stored under the storage conditions above. Otherwise, the wrong test results can be obtained.
- Sample information should be recorded to avoid confusion.

STEP 2. Nucleic acid extraction

After pre-treatment, nucleic acid extraction can be done by automated purification system or using manual prep kits (QIAamp DSP Viral RNA Mini Kit or equivalent).

1) Pre-treatment of the Specimen

Nasopharyngeal swab
Place the specimen at room temperature to normal temperature.
Vortex the sample for 20 seconds or more before use.

***** The Internal Control (RV-Panel A IC) is included in the kit. This allows the user to monitor the nucleic acid isolation procedure and the possibility of PCR inhibition.

Add 10µL of RV-Panel A IC to the solution mixture or directly to the specimen if necessary.

2) For nucleic acid extraction, follow the manufacturer's protocol.

We recommend QIAamp DSP Viral RNA Mini Kit or equivalent nucleic acid extraction kit/automatic machine for nucleic acid extraction.

STEP 3. Prepare PCR Master Mix and sample

1) Prepare the PCR Master Mix

Contents	Volume per test
5X RV-Panel A Buffer	4ul
RV-Panel A Enzyme Mix	1ul
4X RV-Panel A PPM	5ul
D.W (RNase/DNase-free water)	5ul
Total Volume	15ul

Note : Calculate the required amount of each reagent based on the number of reactions (samples + controls).

2) Vortex and briefly centrifuge the PCR Master Mix.

3) Place 15µL aliquots of the PCR Master mix into 0.2ml PCR tubes, and close the lids.

4) Add 5µl of each nucleic acid sample to its respective tube.

Contents	1 test (Volume)
PCR Master Mix	15ul
Nucleic acid sample	5ul
Total Reaction Volume	20ul

⚠

- It is recommended that the PCR mixture to be prepared just before use.
- Aerosol-resistant filter tips and tight gloves should be used when preparing samples. Take great care to avoid cross contamination.
- Defrost the reagents completely
- Centrifuge the reagent tubes briefly to remove the drops from the inside of the lids.

5) Make the control amplification reactions

- Negative Control: Add 5μl of D.W (RNase/DNase-free water) instead of nucleic acid samples to the tube
- Positive Control: Add 5μl of RV-Panel A PC instead of nucleic acid samples to the tube

⚠
- Use a new pipette tip with each different sample.
- Avoid cross-contamination of PCR Master mix and samples with Positive Control.
- For CFX 96™, do not label on the cap of the reaction tubes as fluorescence is detected through the cap.
- Centrifuge the PCR tube thoroughly for 30 seconds

STEP 4. PCR

1) Setting the PCR protocol

PCR protocol should be set according to the table below.

Segment	Temperature (°C)	Time	Cycles
1	55	20 min	1
2	95	15 min	1
3	95	10 sec	40
4	65	90 sec	
5	73	10 min	1
6	55	30 sec	1
7*	Melting curve 55℃~90℃(5s/0.5℃)*		

* Segment 7: Melting curve measurement

⚠ For setting the PCR instrument, follow the Instruction for use from manufacturer of PCR instrument.

STEP 5. Test result analysis

Test results should be interpreted according to the ‘interpretation of test results’ presented as below.

[INTERPRETATION OF TEST RESULTS]

For the analysis of the test result after PCR amplification, take the melting peak result (For CFX96, check the 'Melt Peak' tab) and interpret the according to the following interpretation table.

1. Interpretation criteria for result analysis

Target	Dye	Melt Tm.	Cut-off Value (ΔRFU*)	Target	Dye	Melt Tm.	Cut-off Value (ΔRFU)
Flu A	Cal Red 610	77.5 ± 1℃	≥100	PIV1	Quasar 670	66.0 ± 1℃	≥100
Flu A/H3N2	FAM	76.5 ± 1℃	≥100	PIV2	Quasar 705	81.0 ± 1℃	≥100
Flu A/ H1N1pdm09	FAM	86.5 ± 1℃	≥100	PIV3	Quasar 670	85.5 ± 1℃	≥100
Flu B	HEX	85.5 ± 1℃	≥100	AdV	Cal Red 610	84.0 ± 1℃	≥100
RSV A	HEX	66.5 ± 1℃	≥100	IC	Cal Red 610	66.0 ± 1℃	≥100
RSV B	HEX	75.5 ± 1℃	≥100				

**RFU: Relative fluorescence units*

2. Interpretation of result

Target	IC	Interpretation*	
+	+	**Detected**	Target is detected.
-	+	**Not detected**	Target is not detected.
-	-	**Invalid**	The negative (-) result of IC is the result of inhibition of PCR reaction due to the presence of a PCR inhibitor contained in the sample, and the sample is not suitable for the test. It is recommended to remove the PCR inhibitor and perform the nucleic acid extraction again. RV-Panel A IC may be mixed with 10 µl during the extraction process.
+	-	**Detected**	If the nucleic acid concentration is high in the sample, IC signal may be attenuated. Dilute the template nucleic acid in distilled water and repeat the PCR with the diluted nucleic acid

* If only Influenza A (Flu A) virus is detected (and not the Flu A subtype such as H3N2 or H1N1pdm09), the subtype would be reported as unidentifiable and sequencing is recommended.

If only the Flu A subtype is detected the sample indicates a very low viral load of influenza virus, the result would be reported as Flu A "Positive".

3. Application examples of clinical samples

No	FAM		HEX			Quasar670		Quasar705	Cal Red 610			Interpretation
	H1N1 pdm09	H3N2	Flu B	RSV A	RSV B	PIV1	PIV3	PIV2	Flu A	AdV	IC	
Sample 1	-	+	-	-	-	-	-	-	+	-	+	Flu A, Flu A/H3N2 detected
Sample 2	-	-	-	+	-	-	-	-	-	-	+	RSV A detected
Sample 3	+	-	+	+	-	-	-	-	-	-	+	Flu A/H1N1pdm09, Flu B, RSV A detected
Sample 4	-	-	-	-	-	-	-	-	-	-	+	Not detected
Sample 5	-	-	-	-	-	-	-	-	-	-	-	Invalid

Positive control	+	+	+	+	+	+	+	+	+	+	+	Positive (Valid)
Negative control	-	-	-	-	-	-	-	-	-	-	-	Negative (Valid)

[Quality Control]

NeoPlex™ RV-Panel A Detection Kit includes RV-Panel A PC as positive control and D.W(RNase/DNase-free water) as negative control. For all runs, valid test results must be obtained for both Positive and Negative control. Positive Control result must be Positive (Valid). Negative Control result must be Negative (Valid). If the positive and negative control results are consistently invalid, contact us for technical assistance.

[Traceability of value assigned to calibrators and trueness-control materials]

RV-Panel A PC is confirmed by as following control material, which has a sequencing data confirmed with NCBI database.

Target	Product name	Manufacturer
Flu A/H3N2	Influenza A virus(H3N2)	Korea Bank for Pathogenic Viruses
Flu A/H1N1pdm09	Influenza A virus, A/Virginia/ATCC/2009	ATCC
Flu B	Influenza B virus, B/Hong Kong/5/72	ATCC
RSV A	Human respiratory syncytial virus A, Long	ATCC
RSV B	Human respiratory syncytial virus B, 9320	ATCC
PIV 1	Human parainfluenza virus 1 HPIV-1/C35	ATCC
PIV 2	Human parainfluenza virus 2 HPIV-2/Greer	ATCC
PIV 3	Human parainfluenza virus 3 HPIV-3/C243	ATCC
AdV	Human Adenovirus 2	Korea Bank for Pathogenic Viruses

[TROUBLE SHOOTING]

NeoPlex™ RV-Panel A Detection Kit includes RV-Panel A PC as positive control and D.W(RNase/DNase-free water) as negative control. For all runs, valid test results must be obtained for both Positive and Negative control. Positive Control result must be Positive (Valid). Negative Control result must be Negative (Valid). If the positive and negative control results are consistently invalid, contact us for technical assistance.

1. If the Internal control signal is not observed

Potential causes	Solution
Error in specimen collection	If the both target and IC signal were not observed, recollect the specimen
Nucleic acid extraction failure	Read carefully the instruction for use of nucleic acid extraction kit and extract the nucleic acid from specimen again. IC may be mixed with 10 µl during the extraction process.
Incorrect PCR setting	Repeat the detection procedure with a correct setting
Incorrect PCR cycle or machine temperature	Check the PCR conditions and repeat the PCR under the correct setting if necessary
The fluorescence for data analysis do not comply with the protocol	Select the correct fluorescence for each target listed in this Instruction guide for data analysis
Leaving reagents at room temperature for a long time or incorrect storage condition	Check the storage conditions and the expiration date of the reagents and use a new kit

Presence of inhibitor	Dilute the template nucleic acid in distilled water (10-100x) and repeat the PCR with the diluted nucleic acid (If specimen is still present, restart from nucleic acid extraction procedure)
High load of pathogen's nucleic acid	Dilute the template nucleic acid in distilled water (10-100x) and repeat the PCR with the diluted nucleic acid

2. If signals are observed at the negative control / false positive

Potential causes	Solution
Presence of cross contamination	Decontaminate all surfaces and instruments with sodium hypochlorite or ethanol. Use filter tips during the extraction procedure. Change tips among tubes. Repeat the nucleic acid extraction with the new set of reagents

3. If no signal is observed at the positive control / false negative

Potential causes	Solution
Error in specimen collection	Recollect the specimen
Incorrect storage of the specimen	Recollect the specimen and repeat the whole process. Make sure the product is stored in recommended conditions
Error in nucleic acid extraction	Re-extract the nucleic acid
Incorrect PCR setting	Repeat the PCR with corrected setting
Error in adding nucleic acid to corresponding PCR tubes	Check the sample numbers for nucleic acid containing tubes and make sure to add nucleic acid into correct PCR tubes during detection process.
Incorrect PCR mixture	Check whether all components are added or not (If you use to pre-composed premix, should be reduce sensitivity) Each reagents should be used after homogenization and spin down reagent tube before put the real-time PCR

[PERFORMANCE CHARACTERISTICS]

1 Analytical sensitivity

1.1 Cut-off value

For the cut-off establishment, ΔRFU value was set to be 100 for all targets.

1.2 Limit of Detection (LoD)

This study was conducted to determine the sensitivity by testing nasopharyngeal specimens.

The proportion of positive results obtained from each concentration was subjected to 95% hit rate by probit analysis, and LoD of each target were obtained by performing 24 times of the tests.

Target		LoD
Flu A	Flu A/H3N2	2.84 X 10^{-2} PFU/mL
	Flu A/H1N1pdm09	6.14 X 10^{-1} PFU/mL
Flu A/H3N2		4.65 X 10^{-3} PFU/mL
Flu A/H1N1pdm09		5.33 X 10^{-2} PFU/mL
Flu B		2.67 X 10^{2} CEID50/mL
RSV A		7.46 X 10^{1} PFU/mL
RSV B		3.15 X 10^{-2} TCID50/mL
PIV1		1.18 X 10^{2} TCID50/mL
PIV2		2.53 X 10^{3} TCID50/mL
PIV3		1.34 X 10^{2} TCID50/0.2mL
AdV		3.84 X 10^{3} PFU/mL

2 Analytical Specificity (Interference, Cross reactivity)

Total eleven (11) substances, endogenous and exogenous source, were studied to determine their interfering effect and no interference reactions was found with the concentration as below.

No.	Interfering substance	Concentration	Remark
1	Dexamethasone	1.53 µmol/L	Exogenous source
2	Zanamivir	3.3 mg/ml	
3	Oseltamivir	25 mg/ml	
4	Mupirocin	6.6 mg/ml	
5	Tobramycin	5 ug/ml	
6	Lidocaine	85.3 umol/L	
7	Guaifenesin	15.2 mmol/L	
8	L-Nicotine	6.1 umol/L	Endogenous source
9	mucin	50 ug/ml	
10	Blood	60 ug/ml	
11	Ethanol	7% v/v	

For analytical specificity, three (3) times of cross reactivity studies used fifty eight(58) different pathogens similar with RI-pathogens and other pathogens. As a result, PCR amplification and cross reactivity were not observed with all the pathogens as below.

No.	Manufacturer	Pathogen	Result
1	Zeptometrix	Streptococcus pyogenes	No Cross-reactivity
2	Zeptometrix	Streptococcus oralis	No Cross-reactivity
3	Zeptometrix	Streptococcus mitis	No Cross-reactivity
4	Zeptometrix	Streptococcus bovis	No Cross-reactivity
5	Zeptometrix	Streptococcus anginosus	No Cross-reactivity
6	ATCC	Fluoribacter bozemanae (Legionella bozemanae)	No Cross-reactivity
7	ATCC	Legionella anisa	No Cross-reactivity
8	Zeptometrix	Legionella longbeachae	No Cross-reactivity
9	ATCC	Haemophilus parainfluenzae	No Cross-reactivity
10	ATCC	Aggregatibacter aphrophilus	No Cross-reactivity
11	ATCC	Haemophilus haemolyticus	No Cross-reactivity
12	Zeptometrix	Bordetella bronchiseptica	No Cross-reactivity
13	Zeptometrix	Bordetella holmesii	No Cross-reactivity
14	Zeptometrix	Pseudomonas aeruginosa	No Cross-reactivity
15	Zeptometrix	Klebsiella pneumoniae	No Cross-reactivity
16	Zeptometrix	Acinetobacter baumannii	No Cross-reactivity
17	ATCC	Haemophilus ducreyi	No Cross-reactivity
18	ATCC	Lactobacillus acidophilus	No Cross-reactivity
19	ATCC	Escherichia coli	No Cross-reactivity
20	ATCC	Bacteroides fragilis	No Cross-reactivity

21	ATCC	Enterobacter cloacae	No Cross-reactivity
22	ATCC	Proteus mirabilis	No Cross-reactivity
23	ATCC	Staphylococcus epidermidis	No Cross-reactivity
24	ATCC	Enterobacter faecalis	No Cross-reactivity
25	ATCC	Quantitative Synthetic Human bocavirus (HBoV) DNA	No Cross-reactivity
26	ZEPTOMETRIX	Human metapneumovirus (hMPV) 9 Type A1	No Cross-reactivity
27	ZEPTOMETRIX	Human metapneumovirus (hMPV) 3 Type B1	No Cross-reactivity
28	ZEPTOMETRIX	Human metapneumovirus (hMPV) 27 Type B2	No Cross-reactivity
29	ATCC	Human rhinovirus 1A	No Cross-reactivity
30	ATCC	Human rhinovirus 1B	No Cross-reactivity
31	ATCC	Human Rhinovirus 14	No Cross-reactivity
32	KBPV	Human Rhinovirus A, Human Rhinovirus 21	No Cross-reactivity
33	KBPV	Human Rhinovirus A, Human Rhinovirus 8	No Cross-reactivity
34	KBPV	Human Rhinovirus A, Human Rhinovirus 42	No Cross-reactivity
35	KBPV	Human Rhinovirus A, Human Rhinovirus 7	No Cross-reactivity
36	ATCC	Human Coxsackievirus A 10	No Cross-reactivity
37	ZEPTOMETRIX	Human Coxsackievirus A 16	No Cross-reactivity
38	ATCC	Human Coxsackievirus A 21	No Cross-reactivity
39	ATCC	Echovirus 4	No Cross-reactivity
40	ATCC	Echovirus 20	No Cross-reactivity
41	KBPV	Human Coxsackievirus B1	No Cross-reactivity
42	KBPV	Human Coxsackievirus B2	No Cross-reactivity
43	KBPV	Human Coxsackievirus B5	No Cross-reactivity
44	KBPV	Echovirus 6	No Cross-reactivity
45	KBPV	Echovirus 9	No Cross-reactivity
46	KBPV	Parainfluenza virus 4a	No Cross-reactivity
47	KBPV	Parainfluenza virus 4b	No Cross-reactivity
48	ATCC	Human coronavrius 229E	No Cross-reactivity
49	ZEPTOMETRIX	Human corona virus OC43	No Cross-reactivity
50	ZEPTOMETRIX	coronavirus culture fluid (NL63)	No Cross-reactivity
51	ATCC	Chlamydophila pneumoniae strain J-21	No Cross-reactivity
52	ATCC	Mycpoplasma pneumoniae	No Cross-reactivity
53	ATCC	Streptococcus pneumoniae	No Cross-reactivity
54	ATCC	Legionella pneumophila subsp pneumophila	No Cross-reactivity
55	ATCC	Heamophilus influenzae	No Cross-reactivity
56	ATCC	Bordetella pertussis	No Cross-reactivity
57	ATCC	Bordetella parapertussis	No Cross-reactivity
58	ATCC	Moraxella (Branhamella) catarrhalis	No Cross-reactivity

3 Carry over / Cross-Contamination

This study was performed to evaluate the carry-over and potential cross contamination effect. High concentrated positive sample and negative control sample were cross tested using same PCR instrument, and 100% negative results (72/72)(95% CI: 90.36%-100%) for each negative specimen were determined, respectively.

4 Precision

4.1 Repeatability

Repeatability was assessed by testing for twenty (20) different days, two (2) runs per day, three (3) cycles per run. Targets were set in three (3) levels of concentration, and 100% agreement was found determining the repeatability. The CV criteria, 10%, was met for all test results.

Target	Concentration	Within-run				Between-run				Between - Day			
		N	SD	CV(%)	Agreement(%)	N	SD	CV(%)	Agreement(%)	N	SD	CV(%)	Agreement(%)
Flu A	5x LoD	120	17.0	4.9	100%	40	9.1	2.6	100%	20	6.6	1.9	100%
	3x LoD	120	18.2	5.2	100%	40	9.4	2.7	100%	20	7.4	2.1	100%
	1X LoD	120	16.3	8.8	100%	40	9.2	4.9	100%	20	6.9	3.7	100%
Flu A/H3N2	5x LoD	120	8.1	3.2	100%	40	4.1	1.6	100%	20	2.6	1.0	100%
	3x LoD	120	8.1	3.2	100%	40	4.9	1.9	100%	20	3.2	1.2	100%
	1X LoD	120	15.9	8.3	100%	40	9.1	4.8	100%	20	6.8	3.6	100%
Flu A /H1N1pdm09	5x LoD	120	6.7	3.3	100%	40	3.9	1.9	100%	20	2.3	1.1	100%
	3x LoD	120	6.6	3.2	100%	40	3.9	1.9	100%	20	2.9	1.4	100%
	1X LoD	120	12.4	7.2	100%	40	8.6	5.0	100%	20	6.0	3.5	100%
Flu B	5x LoD	120	9.9	4.1	100%	40	5.5	2.3	100%	20	3.1	1.3	100%
	3x LoD	120	10.0	4.1	100%	40	5.8	2.4	100%	20	3.6	1.5	100%
	1X LoD	120	11.8	5.6	100%	40	6.8	3.2	100%	20	5.0	2.4	100%
RSV A	5x LoD	120	9.5	3.0	100%	40	5.3	1.7	100%	20	4.4	1.4	100%
	3x LoD	120	10.5	3.3	100%	40	5.5	1.7	100%	20	3.5	1.1	100%
	1X LoD	120	13.2	6.3	100%	40	7.4	3.5	100%	20	5.4	2.6	100%
RSV B	5x LoD	120	9.2	4.3	100%	40	4.4	2.1	100%	20	3.6	1.7	100%
	3x LoD	120	9.2	4.4	100%	40	5.1	2.4	100%	20	3.9	1.9	100%
	1X LoD	120	14.3	8.6	100%	40	7.4	4.4	100%	20	5.8	3.4	100%
PIV 1	5x LoD	120	20.2	7.1	100%	40	10.8	3.8	100%	20	6.8	2.4	100%
	3x LoD	120	19.3	6.8	100%	40	11.9	4.2	100%	20	7.2	2.5	100%
	1X LoD	120	14.0	6.6	100%	40	8.7	4.1	100%	20	7.0	3.3	100%
PIV 2	5x LoD	120	9.3	3.6	100%	40	6.0	2.3	100%	20	3.5	1.4	100%
	3x LoD	120	8.6	3.3	100%	40	4.5	1.7	100%	20	2.8	1.1	100%
	1X LoD	120	12.3	5.7	100%	40	7.6	3.5	100%	20	5.3	2.5	100%
PIV 3	5x LoD	120	17.4	7.5	100%	40	9.5	4.1	100%	20	6.0	2.6	100%
	3x LoD	120	16.9	7.2	100%	40	8.8	3.7	100%	20	6.0	2.6	100%
	1X LoD	120	12.8	7.1	100%	40	6.1	3.4	100%	20	5.0	2.8	100%
AdV	5x LoD	120	8.8	3.8	100%	40	5.0	2.2	100%	20	3.9	1.7	100%
	3x LoD	120	8.9	3.9	100%	40	5.7	2.5	100%	20	3.8	1.7	100%
	1X LoD	120	15.2	8.9	100%	40	8.9	5.2	100%	20	6.0	3.5	100%
NC (D.W)		120	-	-	0% (0/120)	40	-	-	0% (0/40)	20	-	-	0% (0/20)

4.2 Reproducibility

The reproducibility study was performed with four different conditions: for Between-lot (3 lots), Between-tester (3 testers), Between-instrument (3 instruments), and Between-site (3 sites). All results showed 100% agreements.

4.2.1 Between-Lot

Target	Titer	Lot 1 (n = 30)			Lot 2 (n = 30)			Lot 3 (n = 30)			Between - lot (n = 90)		
		SD	CV(%)	Agreement(%)	SD	CV(%)	Agreement(%)	SD	CV(%)	Agreement(%)	SD	CV(%)	Agreement(%)
Flu A	5x LoD	18.8	5.4	100%	17.8	5.1	100%	15.9	4.5	100%	17.5	5.0	100%
	3x LoD	18.3	5.2	100%	17.5	4.9	100%	18.1	5.2	100%	18.4	5.3	100%
	1X LoD	16.7	8.9	100%	17.1	9.2	100%	15.9	8.4	100%	16.4	8.8	100%
Flu A/H3N2	5x LoD	12.3	5.7	100%	10.2	4.5	100%	9.4	4.3	100%	11.5	5.2	100%
	3x LoD	11.3	5.1	100%	10.7	4.9	100%	11.3	5.1	100%	11.1	5.1	100%
	1X LoD	17.3	8.9	100%	15.0	7.9	100%	17.3	9.0	100%	16.5	8.6	100%
Flu A /H1N1pdm09	5x LoD	7.4	3.6	100%	6.2	3.0	100%	6.0	3.0	100%	6.6	3.3	100%
	3x LoD	7.1	3.5	100%	7.2	3.6	100%	7.3	3.6	100%	7.2	3.5	100%
	1X LoD	13.2	7.6	100%	13.4	7.8	100%	14.7	8.7	100%	13.8	8.0	100%
Flu B	5x LoD	9.9	4.1	100%	10.7	4.5	100%	11.8	4.9	100%	10.8	4.5	100%
	3x LoD	9.6	4.0	100%	9.1	3.8	100%	10.3	4.3	100%	9.7	4.0	100%
	1X LoD	11.9	5.7	100%	11.5	5.4	100%	11.2	5.3	100%	11.6	5.5	100%
RSV A	5x LoD	9.9	3.1	100%	8.9	2.8	100%	9.2	2.9	100%	9.4	3.0	100%
	3x LoD	10.2	3.2	100%	11.1	3.5	100%	9.1	2.9	100%	10.1	3.2	100%
	1X LoD	13.4	6.4	100%	13.5	6.7	100%	12.8	6.2	100%	13.5	6.5	100%
RSV B	5x LoD	10.4	4.9	100%	11.4	5.4	100%	9.9	4.7	100%	10.5	5.0	100%
	3x LoD	8.1	3.9	100%	9.6	4.5	100%	11.0	5.2	100%	9.6	4.5	100%
	1X LoD	14.3	8.5	100%	15.6	9.1	100%	14.6	8.5	100%	14.8	8.7	100%
PIV 1	5x LoD	21.0	7.4	100%	21.2	7.5	100%	18.8	6.8	100%	20.3	7.2	100%
	3x LoD	21.2	7.5	100%	22.6	7.8	100%	16.4	5.9	100%	20.4	7.2	100%
	1X LoD	13.6	6.5	100%	13.3	6.3	100%	13.6	6.4	100%	13.5	6.4	100%
PIV 2	5x LoD	9.8	3.8	100%	8.0	3.2	100%	9.3	3.6	100%	9.1	3.5	100%
	3x LoD	8.0	3.2	100%	9.1	3.5	100%	8.5	3.3	100%	8.7	3.4	100%
	1X LoD	11.8	5.5	100%	12.6	5.8	100%	12.2	5.8	100%	12.2	5.7	100%
PIV 3	5x LoD	19.7	8.3	100%	17.8	7.6	100%	18.5	7.8	100%	18.6	7.8	100%
	3x LoD	17.1	7.4	100%	18.7	8.0	100%	18.5	7.9	100%	18.0	7.7	100%
	1X LoD	11.8	6.5	100%	13.2	7.4	100%	13.0	7.1	100%	12.6	7.0	100%
AdV	5x LoD	9.5	4.2	100%	9.2	4.0	100%	9.7	4.2	100%	9.5	4.1	100%
	3x LoD	7.2	3.1	100%	9.1	4.0	100%	9.3	4.0	100%	8.7	3.7	100%
	1X LoD	15.3	8.9	100%	15.0	8.7	100%	14.4	8.5	100%	14.8	8.6	100%
NC (D.W)		-	100%		-	100%		-	100%		-	100%	

4.2.2 Between-Tester

Target	Titer	Tester 1 (n = 30)			Tester 2 (n = 30)			Tester 3 (n = 30)			Between - Tester (n = 90)		
		SD	CV(%)	Agreement(%)	SD	CV(%)	Agreement(%)	SD	CV(%)	Agreement(%)	SD	CV(%)	Agreement(%)
Flu A	5x LoD	20.3	5.9	100%	18.4	5.2	100%	19.3	5.5	100%	19.4	5.5	100%
	3x LoD	20.2	5.7	100%	18.8	5.3	100%	18.7	5.4	100%	19.1	5.4	100%
	1X LoD	15.4	8.3.	100%	15.7	8.4	100%	16.5	8.9	100%	15.7	8.4	100%
Flu A/H3N2	5x LoD	10.9	5.0	100%	11.9	5.5	100%	11.8	5.3	100%	11.5	5.3	100%
	3x LoD	12.4	5.6	100%	10.3	4.6	100%	12.7	5.8	100%	11.9	5.3	100%
	1X LoD	13.9	7.3	100%	13.8	7.2	100%	17.6	9.1	100%	15.1	7.9	100%
Flu A /H1N1pdm09	5x LoD	7.7	3.8	100%	6.5	3.2	100%	7.5	3.7	100%	7.2	3.5	100%
	3x LoD	7.7	3.8	100%	7.3	3.6	100%	6.0	3.0	100%	7.0	3.4	100%
	1X LoD	12.9	7.4	100%	12.5	7.3	100%	14.4	8.5	100%	13.3	7.8	100%
Flu B	5x LoD	11.1	4.6	100%	10.9	4.5	100%	10.2	4.2	100%	10.6	4.4	100%
	3x LoD	11.1	4.6	100%	9.9	4.1	100%	12.1	5.0	100%	11.0	4.5	100%
	1X LoD	8.4	4.0	100%	13.6	6.3	100%	10.7	5.1	100%	11.3	5.3	100%
RSV A	5x LoD	9.1	2.9	100%	9.8	3.1	100%	10.7	3.4	100%	9.9	3.1	100%
	3x LoD	8.2	2.6	100%	10.3	3.2	100%	10.8	3.4	100%	9.8	3.1	100%
	1X LoD	13.0	6.3	100%	12.3	5.9	100%	13.2	6.4	100%	12.7	6.1	100%
RSV B	5x LoD	9.9	4.7	100%	8.4	4.0	100%	10.9	5.1	100%	9.8	4.6	100%
	3x LoD	11.3	5.3	100%	9.3	4.4	100%	8.6	4.0	100%	9.7	4.6	100%

	1X LoD	15.6	8.8	100%	14.3	8.4	100%	15.2	8.9	100%	15.2	8.8	100%
PIV 1	5x LoD	20.3	7.1	100%	23.9	8.5	100%	21.8	7.6	100%	22.0	7.7	100%
	3x LoD	21.9	7.6	100%	23.1	8.0	100%	19.2	6.7	100%	21.2	7.4	100%
	1X LoD	13.6	6.4	100%	15.4	7.3	100%	13.3	6.4	100%	14.1	6.7	100%
PIV 2	5x LoD	9.4	3.7	100%	8.1	3.2	100%	8.5	3.3	100%	8.6	3.4	100%
	3x LoD	8.6	3.4	100%	8.1	3.2	100%	8.8	3.4	100%	8.5	3.3	100%
	1X LoD	11.9	5.5	100%	14.8	6.7	100%	13.4	6.2	100%	13.3	6.1	100%
PIV 3	5x LoD	18.2	7.7	100%	17.2	7.6	100%	18.6	8.0	100%	18.2	7.8	100%
	3x LoD	16.6	7.0	100%	17.4	7.4	100%	17.0	7.2	100%	16.8	7.1	100%
	1X LoD	10.4	5.6	100%	15.1	8.3	100%	12.7	7.0	100%	13.0	7.1	100%
AdV	5x LoD	9.0	3.9	100%	8.6	3.7	100%	9.3	4.0	100%	9.0	3.9	100%
	3x LoD	8.2	3.6	100%	8.5	3.7	100%	9.5	4.1	100%	8.7	3.8	100%
	1X LoD	14.9	8.7	100%	14.0	8.1	100%	13.3	7.6	100%	14.0	8.1	100%
NC (D.W)		-	100%		-	100%		-	100%		-	100%	

4.2.3 Between-Instrument

Target	Titer	Instrument 1 (n = 30)			Instrument 2 (n = 30)			Instrument 3 (n = 30)			Between - Instrument (n = 90)		
		SD	CV(%)	Agreement(%)	SD	CV(%)	Agreement(%)	SD	CV(%)	Agreement(%)	SD	CV(%)	Agreement(%)
Flu A	5x LoD	18.2	5.3	100%	20.1	5.8	100%	16.9	4.9	100%	18.3	5.3	100%
	3x LoD	16.2	4.7	100%	19.2	5.6	100%	18.6	5.4	100%	18.0	5.2	100%
	1X LoD	15.8	8.4	100%	16.6	8.9	100%	15.1	8.1	100%	15.8	8.4	100%
Flu A/H3N2	5x LoD	10.6	4.8	100%	10.5	4.7	100%	10.5	4.7	100%	10.5	4.7	100%
	3x LoD	12.0	5.5	100%	11.6	5.3	100%	10.0	4.5	100%	11.2	5.1	100%
	1X LoD	13.4	6.9	100%	16.8	8.9	100%	14.8	7.7	100%	15.1	7.8	100%
Flu A /H1N1pdm09	5x LoD	6.6	3.3	100%	7.2	3.5	100%	7.6	3.7	100%	7.1	3.5	100%
	3x LoD	8.1	4.0	100%	7.0	3.4	100%	6.0	3.0	100%	7.0	3.4	100%
	1X LoD	11.5	6.5	100%	13.5	7.8	100%	12.8	7.5	100%	12.8	7.4	100%
Flu B	5x LoD	9.6	4.0	100%	12.0	4.9	100%	11.2	4.6	100%	10.9	4.5	100%
	3x LoD	11.4	4.7	100%	11.6	4.7	100%	9.5	3.9	100%	11.0	4.5	100%
	1X LoD	10.7	5.0	100%	11.1	5.3	100%	10.9	5.2	100%	10.9	5.2	100%
RSV A	5x LoD	9.1	2.9	100%	10.0	3.1	100%	10.1	3.2	100%	10.0	3.2	100%
	3x LoD	9.6	3.0	100%	9.9	3.2	100%	8.9	2.8	100%	9.7	3.1	100%
	1X LoD	12.8	6.2	100%	12.4	5.9	100%	12.9	6.1	100%	12.7	6.1	100%
RSV B	5x LoD	9.2	4.4	100%	9.8	4.7	100%	11.0	5.2	100%	10.1	4.8	100%
	3x LoD	10.8	5.2	100%	8.8	4.1	100%	10.3	4.8	100%	10.2	4.8	100%
	1X LoD	14.8	8.7	100%	15.3	8.8	100%	15.1	8.9	100%	15.0	8.7	100%
PIV 1	5x LoD	22.5	7.8	100%	19.9	7.1	100%	20.8	7.3	100%	21.2	7.4	100%
	3x LoD	19.8	7.0	100%	19.2	6.8	100%	21.4	7.5	100%	19.9	7.0	100%
	1X LoD	14.6	7.0	100%	14.0	6.7	100%	14.4	6.9	100%	14.2	6.8	100%
PIV 2	5x LoD	8.7	3.4	100%	9.1	3.5	100%	8.7	3.4	100%	8.9	3.5	100%
	3x LoD	9.3	3.7	100%	9.4	3.6	100%	8.1	3.1	100%	9.4	3.7	100%
	1X LoD	13.2	6.1	100%	11.6	5.4	100%	12.9	6.0	100%	12.6	5.8	100%
PIV 3	5x LoD	17.5	7.4	100%	18.4	7.8	100%	16.3	7.0	100%	17.4	7.4	100%
	3x LoD	18.9	8.0	100%	18.4	7.9	100%	16.0	6.9	100%	17.7	7.6	100%
	1X LoD	12.0	6.6	100%	13.0	7.2	100%	11.8	6.6	100%	12.1	6.7	100%
AdV	5x LoD	7.8	3.4	100%	8.0	3.5	100%	9.0	3.9	100%	8.3	3.6	100%
	3x LoD	9.3	4.1	100%	8.3	3.6	100%	8.2	3.6	100%	8.7	3.8	100%
	1X LoD	14.7	8.6	100%	15.3	8.9	100%	14.5	8.3	100%	14.7	8.6	100%
NC (D.W)		-	100%		-	100%		-	100%		-	100%	

4.2.4 Between-site

Target	Titer	Site 1 (n = 30)			Site 2 (n = 30)			Site 3 (n = 30)			Between - Site (n = 90)		
		SD	CV(%)	Agreement(%)	SD	CV(%)	Agreement(%)	SD	CV(%)	Agreement(%)	SD	CV(%)	Agreement(%)
Flu A	5x LoD	19.1	5.6	100%	16.5	4.8	100%	17.8	5.1	100%	17.9	5.2	100%
	3x LoD	16.8	4.9	100%	17.4	5.1	100%	17.2	4.9	100%	17.3	5.0	100%

	1X LoD	15.0	8.0	100%	15.3	8.2	100%	16.9	9.1	100%	15.7	8.4	100%
Flu A/H3N2	5x LoD	12.2	5.6	100%	10.6	4.8	100%	11.1	5.0	100%	11.5	5.2	100%
	3x LoD	12.4	5.7	100%	11.2	5.1	100%	11.7	5.3	100%	11.7	5.3	100%
	1X LoD	16.9	8.9	100%	15.2	7.9	100%	15.6	8.2	100%	15.8	8.3	100%
Flu A /H1N1pdm09	5x LoD	7.5	3.7	100%	6.1	3.0	100%	6.2	3.0	100%	6.6	3.2	100%
	3x LoD	7.6	3.7	100%	6.9	3.4	100%	6.0	3.0	100%	6.8	3.3	100%
	1X LoD	12.9	7.6	100%	14.2	8.3	100%	11.7	6.8	100%	12.9	7.5	100%
Flu B	5x LoD	10.9	4.6	100%	10.6	4.4	100%	10.0	4.1	100%	10.5	4.4	100%
	3x LoD	10.1	4.1	100%	10.8	4.5	100%	10.9	4.5	100%	10.6	4.4	100%
	1X LoD	10.7	5.0	100%	9.3	4.4	100%	11.4	5.4	100%	10.4	4.9	100%
RSV A	5x LoD	10.6	3.3	100%	10.9	3.4	100%	10.3	3.3	100%	10.6	3.4	100%
	3x LoD	9.9	3.1	100%	10.6	3.3	100%	10.0	3.2	100%	10.3	3.3	100%
	1X LoD	12.6	6.1	100%	13.9	6.7	100%	12.5	6.0	100%	12.8	6.2	100%
RSV B	5x LoD	9.5	4.4	100%	10.1	4.8	100%	9.0	4.2	100%	9.6	4.5	100%
	3x LoD	10.3	4.8	100%	9.7	4.6	100%	10.9	5.2	100%	10.4	4.9	100%
	1X LoD	13.9	8.0	100%	14.7	8.6	100%	15.5	9.0	100%	14.6	8.5	100%
PIV 1	5x LoD	18.4	6.7	100%	20.8	7.5	100%	19.0	6.7	100%	19.4	7.0	100%
	3x LoD	19.6	6.8	100%	19.5	6.9	100%	21.0	7.4	100%	20.0	7.0	100%
	1X LoD	13.6	6.6	100%	13.8	6.7	100%	15.0	7.3	100%	14.0	6.8	100%
PIV 2	5x LoD	9.4	3.7	100%	7.8	3.1	100%	9.4	3.7	100%	8.8	3.4	100%
	3x LoD	7.3	2.9	100%	8.6	3.4	100%	9.2	3.6	100%	8.3	3.3	100%
	1X LoD	11.3	5.2	100%	12.4	5.7	100%	12.0	5.5	100%	11.8	5.4	100%
PIV 3	5x LoD	16.9	7.1	100%	17.8	7.8	100%	19.3	8.3	100%	18.2	7.8	100%
	3x LoD	20.3	8.5	100%	13.8	6.0	100%	17.6	7.6	100%	17.6	7.6	100%
	1X LoD	10.4	5.9	100%	12.5	7.0	100%	13.3	7.2	100%	12.4	6.9	100%
AdV	5x LoD	9.0	3.9	100%	9.9	4.3	100%	9.7	4.2	100%	9.5	4.1	100%
	3x LoD	8.8	3.8	100%	9.4	4.1	100%	7.7	3.3	100%	8.6	3.7	100%
	1X LoD	15.1	8.8	100%	15.2	8.8	100%	15.1	8.9	100%	15.0	8.8	100%
NC (D.W)		-	100%		-	100%		-	100%		-	100%	

5 Inclusivity test

The inclusivity of NeoPlex™ RV-Panel A Detection Kit, were determined based on –in silico and wet test results. In the wet test, the subtypes for each targets were used in three (3) repeated tests, and the results showed 100% detection rate.

Subtype
Influenza A virus (H3N2)
Influenza A virus (H3N2), A/Hong Kong/8/68
Influenza A virus (H1N1), A/Virginia/ATCC1/2009
Influenza B virus, B/Maryland/1/59
Influenza B virus, B/Taiwan/2/62
Influenza B virus, B/Hong Kong/5/72
Influenza B virus, B/Allen/45
Influenza B virus, B/GL/1739/54
Human Respiratory syncytial Virus, A2001/3-12
Human respiratory syncytial virus A, Long
Human Respiratory syncytial virus 9320, complete genome
Human parainfluenza virus 1 HPIV-1, C35
Human parainfluenza virus 2 (HPIV-2), Greer
Human parainfluenza virus 3 NIH 47885

Human parainfluenza virus 3 HPIV-1, C243
Human adenovirus 1
Human adenovirus B Adenovirus type 3
Human adenovirus C Adenovirus type 2
Human adenovirus E Adenovirus type 4
Human adenovirus B Adenovirus type 11
Mastadenovirus, Human Adenovirus D type 8
Adenovirus Type 41 Culture Fluid
DNA from Human adenovirus 31 strain 1315

6 Clinical evaluation

The clinical performance study was performed in the clinical laboratory with the specimen collected from various sources, such a hospitals or clinics. The comparable CE-marked product already available on EU market was used as reference test.

For clinical sensitivity and specificity, the test results were analyzed with 2x2 table, and summarized as below:

Target	Specimen type	Clinical sensitivity	Clinical specificity
Flu A	NPS	100%(148/148) [95% CI 97.47-100]	100%(495/495) [95% CI 99.23-100]
Flu A/H1N1pdm09	NPS	100%(63/63) [95% CI 94.25-100]	100%(580/580) [95% CI 99.34-100]
Flu A/H3N2	NPS	100%(83/83) [95% CI 95.58-100]	100%(560/560) [95% CI 99.32-100]
Flu B	NPS	98.67%(74/75) [95% CI 92.83-99.76]	100%(568/568) [95% CI 99.33-100]
RSV A	NPS	100%(73/73) [95% CI 95.00-100]	100%(570/570) [95% CI 99.33-100]
RSV B	NPS	100%(109/109) [95% CI 96.60-100]	100%(534/534) [95% CI 99.29-100]
PIV1	NPS	100%(66/66) [95% CI 94.50-100]	100%(577/577) [95% CI 99.34-100]
PIV2	NPS	100%(53/53) [95% CI 93.24-100]	100%(590/590) [95% CI 99.35-100]
PIV3	NPS	100%(71/71) [95% CI 94.87-100]	100%(572/572) [95% CI 99.33-100]
AdV	NPS	97.58%(121/124) [95% CI 93.13-99.17]	100%(519/519) [95% CI 99.27-100]

[LIMITATION OF TEST]

1. Results from this test must be correlated with the clinical history, epidemiological data, and other data of the patient available to the clinician.
2. If you do not use the samples and other specimens described in this manual, you may get inaccurate results.
3. Although the results of this test are negative, it is not advisable to exclude the possibility that the infection is actually present.
4. It is not excluded that this kit shows false positive results due to the presence of cross-contamination.
5. False negative results may occur due to polymerase inhibition. RV-Panel A IC may help to identify any substance existing in the specimens interfering with nucleic acid isolation and PCR amplification.

6. This kit is for professional use only. Only trained healthcare provider can use this kit.

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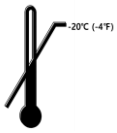
NeoPlex™ RV-Panel A Detection kit

Multiplex Real-time PCR Reagents for Respiratory pathogens Detection
For professional *in vitro* diagnostic use only

[SYMBOLS]

			
Catalogue number	Batch code	Date of manufacture	Use-by date
			
In vitro diagnostic medical device	Upper limit of temperature	Caution	Consult instruction for use
			
Manufacturer	Contains sufficient for <n> tests	Authorized representative in the European Community	Conformity to European Directive 98/79/EC

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