REF 800501 NeuMoDx™ EBV Calibrators

℞ only

CAUTION: For US Export Only

IVD For *in vitro* diagnostic use with the NeuMoDx 288 and NeuMoDx 96 Molecular Systems

For insert updates, go to: www.qiagen.com/neumodx-ifu
For detailed instructions, refer to the NeuMoDx 288 Molecular System Operator's Manual; P/N 40600108 [REF 500100]
For detailed instructions, refer to the NeuMoDx 96 Molecular System Operator's Manual; P/N 40600317 [REF 500200] or P/N 40600655 [REF 500201]
See also the NeuMoDx EBV Quant Test Strip 2.0 Instructions For Use (package insert); P/N 40600562

INTENDED USE

The NeuMoDx EBV Calibrators are intended for use with the NeuMoDx EBV Quant Assay 2.0 to establish a calibration coefficient associated with a particular lot of the NeuMoDx EBV Quant Test Strip 2.0 and are used in conjunction with a standard curve to perform an accurate quantitative *in vitro* diagnostic test on the NeuMoDx 288 Molecular System or NeuMoDx 96 Molecular System (NeuMoDx System(s)) to quantify Epstein-Barr virus (EBV) DNA from human plasma specimens. The EBV target in these calibrators has been calibrated to the 1st WHO International Standard for Epstein-Barr Virus for Nucleic Acid Amplification Techniques (NIBSC code: 09/260).

SUMMARY AND EXPLANATION

The NeuMoDx EBV Calibrators are provided in a kit and comprised of a set of 3 low-positive and 3 High Positive External Calibrators. One low positive and one High Positive Calibrator (1 set) is processed every 90 days or with every new lot of NeuMoDx EBV Quant Test Strips 2.0 to establish a valid calibration of the NeuMoDx EBV Quant Assay 2.0. NeuMoDx EBV Calibrators contain encapsulated EBV target nucleic acid at 5 $\log_{10}$ IU/mL or 3 $\log_{10}$ IU/mL for the High and Low Calibrator, respectively. Both are diluted in Basematrix (Seracare® Life Sciences, Inc., Milford, MA).

The NeuMoDx EBV Quant Assay 2.0 combines automated DNA extraction, amplification, and detection by real-time PCR to enable the quantitative detection of EBV DNA in plasma specimens. The results attained from processing the NeuMoDx EBV Calibrators are applied to the stored standard curve and used to generate a calibration coefficient, which is used to automatically adjust the standard curve for slight variations across systems or test strip lots. Use of both the standard curve and the system/lot specific calibration coefficient allows for the accurate quantitation of EBV DNA in human clinical plasma samples.

Traceability of the calibrators to the WHO 1st International Standard enables laboratories to ensure that the testing results obtained using the NeuMoDx EBV Quant Test Strips 2.0 are consistent across reagent lots, systems, and operators.

PRINCIPLES OF THE PROCEDURE

The NeuMoDx EBV Calibrators have been formulated to mimic naturally occurring human plasma specimens containing EBV DNA. Additionally, the encapsulated material used in these calibrators allows for the verification of efficacious nucleic acid extraction as well as the real-time PCR amplification and detection process, thereby enabling calibration of the entire testing process. One set of these external calibrators – consisting of 1 High Calibrator and 1 Low Calibrator – is processed every 90 days, or with the change of a system, software, or test strip reagent lot; the system will automatically process each calibrator in triplicate. Such routine processing of the NeuMoDx EBV Calibrators enables the laboratories to ensure efficacy of the test results for human clinical specimens processed within the validity period. These calibrators are processed in a manner identical to the processing of the human clinical specimens intended for quantitative EBV testing.

The NeuMoDx System software automatically alerts the operator when a calibration is required. During processing, criteria for acceptance of the calibrator are automatically verified by the NeuMoDx System software. If less than two of the calibrator replicates are valid, the software automatically invalidates the calibration run. In the event of a calibration failure, the calibration must be retested using a new set of calibrators.

Upon successful processing of the NeuMoDx EBV Calibrators, the system software automatically records the validity of the processed calibrators for a period of 90 days unless there is a change to the system that causes the validity period to expire. The NeuMoDx System software will automatically notify the user to process these external calibrators when the previously processed external calibrator validity period has expired.

REAGENTS/CONSUMABLES

Material Provided

REF	Contents	Tests per unit	Total tests per kit
800501	**NeuMoDx EBV Calibrators** *Single use sets of EBV High and Low Calibrators to establish validity of standard curve (1 vial of 5 $\log_{10}$ IU/mL and 1 vial of 3 $\log_{10}$ IU/mL Basematrix = 1 set)*	1 set	3

Reagents and Consumables Required but Not Provided (Available Separately from NeuMoDx)

REF	Contents
201501	**NeuMoDx EBV Quant Test Strip 2.0** *Dried PCR reagents containing EBV specific TaqMan® probes and primers, SPC1 specific TaqMan probe and primers.*
100200	**NeuMoDx Extraction Plate** *Dried paramagnetic particles, lytic enzyme, and sample process controls*
900502	**NeuMoDx EBV External Controls** *Single use sets of Low Positive, High Positive, and Negative Controls to establish daily validity of NeuMoDx EBV Quant Assay 2.0*
400400	**NeuMoDx Lysis Buffer 1**
400100	**NeuMoDx Wash Reagent**
400200	**NeuMoDx Release Reagent**
100100	**NeuMoDx Cartridge**
235903	**Hamilton CO-RE / CO-RE II Tips (300 µL) with Filters**
235905	**Hamilton CO-RE / CO-RE II Tips (1000 µL) with Filters**

Instrumentation Required

NeuMoDx 288 Molecular System [REF 500100] or **NeuMoDx 96 Molecular System** [REF 500200 or 500201]
NeuMoDx System Software version 1.9.2.6 or higher

WARNINGS & PRECAUTIONS

- The NeuMoDx EBV Calibrators are for *in vitro* diagnostic use only with the NeuMoDx EBV Quant Test Strip 2.0 as implemented on the NeuMoDx Systems.
- Do not use the NeuMoDx EBV Calibrators after the listed expiration date.
- Do not use the NeuMoDx EBV Calibrators if the packaging is damaged or kit is not frozen upon arrival.
- Because the external calibrators contain EBV target material, they should be handled carefully as cross-contamination with clinical samples could produce a false-positive result.
- Always handle specimens as if they are infectious and in accordance with safe laboratory procedures such as those described in Biosafety in Microbiological and Biomedical Laboratories[1] and in CLSI Document M29-A4.[2]
- When working with chemicals, always wear a suitable lab coat, disposable gloves, and protective goggles. For more information, please consult the appropriate safety data sheets (SDS).
- Do not pipette by mouth. Do not smoke, drink, or eat in areas where specimens or reagents are being handled.
- Dispose of unused reagents and waste in accordance with country, federal, provincial, state, and local regulations.
- Clean, powder-free, nitrile gloves should be worn when handling all NeuMoDx reagents and consumables.
- Wash hands thoroughly after performing the test.
- Safety Data Sheets (SDS) are provided for each reagent (as applicable) at www.qiagen.com/safety
- When working with chemicals, always wear a suitable lab coat, disposable gloves, and protective goggles. For more information, please consult the appropriate safety data sheets (SDS).

Emergency information

CHEMTREC
Outside USA & Canada +1 703-527-3887

Disposal

Dispose of as hazardous waste in compliance with local and national regulations. This also applies to unused products.

Follow recommendations in the Safety Data Sheet (SDS).

PRODUCT STORAGE, HANDLING & STABILITY

- The NeuMoDx EBV Calibrators are shipped with dry ice to maintain a frozen state; do not use if contents are not frozen upon receipt.
- It is recommended that the NeuMoDx EBV Calibrators be stored at -20 to -15°C to ensure stability.
- Calibrator vials are intended for single use only. Thawed calibrators may be stored at 4 °C for no more than for 7 days.
- Refreezing after a first thaw is not recommended.
- Although the NeuMoDx EBV Calibrators are non-infectious, any unused material should be discarded after use as biohazard waste to reduce risk of contamination by the target nucleic acid contained.
- Discard any calibrators that appear cloudy or contain large precipitates after thawing.

INSTRUCTIONS FOR USE

1. NeuMoDx EBV Calibrators [REF 800501] must be processed under the following scenarios:
    a. Validity of previously established calibration has expired (past 90 days)
    b. Calibration validity has not been established on the NeuMoDx System(s)
    c. Calibration validity has not been established with a new lot of NeuMoDx EBV Quant Test Strips 2.0
    d. The NeuMoDx System software has been modified
2. If a valid calibration does not exist, the NeuMoDx System will prompt the user to process external calibrators (and external controls) before sample results can be reported.
3. If calibrators are required, process the NeuMoDx EBV Calibrators (1 High Calibrator and 1 Low Calibrator per reagent lot):

NeuMoDx EBV Calibrator	Label Color Scheme
NeuMoDx EBV High Calibrator (EBVHC)	Green
NeuMoDx EBV Low Calibrator (EBVLC)	Blue

4. Remove a set of NeuMoDx EBV Calibrators from freezer and thaw completely at room temperature (15-30 °C). The calibrators must be completely thawed and equilibrated to room temperature prior to use. If using an already thawed set of calibrators, ensure that the thawed calibrators were stored at 4 °C and are not more than 7 days old.
5. Vortex gently to ensure homogeneity.
6. Load the calibrator vials into a standard Sample Tube Carrier (32 Tube), and ensure caps are removed from all tubes.
7. Place the Sample Tube Carrier on the Autoloader shelf and use the touchscreen to load carrier into the NeuMoDx System.
8. The NeuMoDx System will recognize the barcode and start processing the specimen tubes unless reagents or consumables required for testing are not available.
9. Three replicates of each calibrator are performed.
10. Calibration is considered valid if at least two out of the three replicates yield results within predefined parameters. The low calibrator nominal target is 3.0 $\log_{10}$ IU/mL, and the High Calibrator nominal target is 5.0 $\log_{10}$ IU/mL.

NeuMoDx EBV Calibrator	EBV Result
NeuMoDx EBV High Calibrator (EBVHC)	2/3 Calibrators Valid
NeuMoDx EBV Low Calibrator (EBVLC)	2/3 Calibrators Valid

11. Discrepant result handling for calibrators should be performed as follows:
    a. If one or both the calibrators fails the validity check, repeat processing of the failed calibrator(s) using a new vial. In the event one calibrator fails validity, it is possible to repeat only the failed calibrator as the system does not require the user to run both calibrators.
    b. If the problem persists, contact QIAGEN technical support.
12. EBV External Controls [REF 900502] must be processed *after* calibrator validity has been established, prior to obtaining test results from human clinical samples.

LIMITATIONS

- The NeuMoDx EBV Calibrators can only be used in conjunction with the NeuMoDx EBV Quant Test Strips 2.0 on the NeuMoDx System**.**
- A valid calibration of the NeuMoDx EBV Quant Test Strip 2.0 using NeuMoDx EBV Calibrators [REF 800501] is required *before* the NeuMoDx EBV External Controls [REF 900502] can be processed.
- Erroneous results could occur from improper handling, storage, or other technical error.
- Operation of the NeuMoDx System is limited to use by personnel trained on the use of the NeuMoDx System**.**

REFERENCES

1. Centers for Disease Control and Prevention. Biosafety in Microbiological and Biomedical Laboratories, 6th edition. HHS Publication HHS Publication No. (CDC) 300859, Revised June 2020

2. Clinical and Laboratory Standards Institute (CLSI). Protection of Laboratory Workers from Occupationally Acquired Infections; Approved Guideline – Fourth Edition. CLSI document M29-A4; May 2014

TRADEMARKS

SYMBOL KEY

The following symbols may appear in the instructions for use or on the packaging and labeling:

℞ only	Prescription use only		Do not re-use
	Manufacturer	Σ	Contains sufficient for *<n>* tests
IVD	*In vitro* diagnostic medical device		Consult instructions for use
EC REP	Authorized representative in the European Community		Caution
REF	Catalog number	CE	CE Mark
LOT	Batch code	CONT	Contains
	Use-by date	BIO	Contains biological material of human origin
	Temperature limit		

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Technical support/Vigilance reporting: support.qiagen.com

Patent: www.neumodx.com/patents

EC REP Emergo Europe B.V.
Westervoortsedijk 60
6827 AT Arnhem
The Netherlands

CE