REF 800500 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
For detailed instructions, refer to the NeuMoDx 96 Molecular System Operator's Manual; P/N 40600317
See also the NeuMoDx EBV Quant Test Strip Instructions For Use (package insert); P/N 40600294

INTENDED USE

The NeuMoDx EBV Calibrators are intended for use with the NeuMoDx EBV Quant Assay to establish a calibration coefficient associated with a particular lot of the NeuMoDx EBV Quant Test Strip and 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 fresh and frozen 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.

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 to establish a valid *calibration* of the NeuMoDx EBV Quant Assay. Both EBV calibrators contain encapsulated EBV target nucleic acid at 6 $\log_{10}$ IU/mL or 4 $\log_{10}$ IU/mL for the High and Low Calibrator respectively and both are diluted in Basematrix 53 Diluent (Basematrix) (Seracare Life Sciences, Inc., Milford, MA).

The NeuMoDx EBV Quant Assay combines automated DNA extraction, amplification and detection by real-time PCR to enable the quantitative detection of EBV DNA in plasma specimens.

The NeuMoDx EBV Calibrators will be 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. Accurate quantitation of the EBV DNA in the human clinical samples being tested can then be provided utilizing both the standard curve and the system/lot specific calibration coefficient.

In addition, the traceability of these calibrators to the WHO 1st International Standard enables the laboratories to ensure that the testing results obtained from use of the NeuMoDx EBV Quant Test Strips 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 to be 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.

Software on the NeuMoDx System 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 is valid, the software automatically invalidates the run. Samples in an invalidated run must be retested using a new set of calibrators and controls.

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 calibrator validity period has expired.

REAGENTS/CONSUMABLES

Material Provided

REF	Contents	Tests per unit	Total tests per kit
800500	**NeuMoDx EBV Calibrators** *Single use sets of EBV High and Low Calibrators to establish validity of standard curve* *(1 vial of 6 $\log_{10}$ IU/mL and 1 vial of 4 $\log_{10}$ IU/mL Basematrix = 1 set)*	1 set	3

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

REF	Contents
201500	**NeuMoDx EBV Quant Test Strip** *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*
900501	**NeuMoDx EBV External Controls** *Single use sets of Positive and Negative Controls to establish daily validity of NeuMoDx EBV Quant Assay*
400900	**NeuMoDx Lysis Buffer 5**
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]

WARNINGS & PRECAUTIONS

- The NeuMoDx EBV Calibrators are for *in vitro* diagnostic use only with the NeuMoDx EBV Quant Test Strip 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 test 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]
- 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 available upon request.

PRODUCT STORAGE, HANDLING & STABILITY

- The NeuMoDx EBV Calibrators are shipped with dry ice to maintain a frozen state; do not use if kit contents are not frozen upon receipt.
- It is recommended that the NeuMoDx EBV Calibrators be stored at ≤ -20 °C to ensure stability.
- Calibrator vials are intended for single use only. Thawed calibrators may be stored at 4 °C no more than for 7 days.
- Refreezing after a first thaw is not recommended.
- Discard any unused material after use in biohazard waste as the material contains non-infectious target DNA and could cause a contamination risk.
- Discard any calibrators that appear cloudy or contain large precipitates after thawing.

INSTRUCTIONS FOR USE

1. NeuMoDx Calibrators [REF 800500] 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
    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
High Calibrator (HC)	Green
Low Calibrator (LC)	Blue

4. Retrieve a set of NeuMoDx EBV Calibrators from freezer and allow the vials to set at room temperature (15-30 °C) until completely thawed. 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 32-Tube Carrier, and ensure caps are removed from all tubes.
7. Place the 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. To generate valid results, at least 2 out of the 3 replicates must yield results within predefined parameters. The low calibrator nominal target is 4.0 $\log_{10}$ IU/mL and the high calibrator nominal target is 6.0 $\log_{10}$ IU/mL.

NeuMoDx EBV Calibrator	EBV Result
High Calibrator (HC)	2/3 calibrators Valid
Low Calibrator (LC)	2/3 calibrators Valid

10. 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 only repeat the failed calibrator as system does not require the user to run both calibrators.
    b. If problem persists, contact NeuMoDx Molecular, Inc.
11. External Controls [REF 900501] 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 on the NeuMoDx System**.**
- A valid calibration of the NeuMoDx EBV Quant Test Strip using NeuMoDx EBV Calibrators [REF 800500] is required *before* the NeuMoDx EBV External Controls [REF 900501] 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. Biosafety in Microbiological and Biomedical Laboratories, 5th edition. HHS Publication No. (CDC) 21-1112, Revised December 2009
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

SYMBOLS

SYMBOL	MEANING
℞ only	**Prescription use only**
	**Manufacturer**
IVD	***In vitro* diagnostic medical device**
EC REP	**Authorized representative in the European Community**
REF	**Catalog number**
LOT	**Batch code**
	**Use-by date**
	**Temperature limit**
	**Humidity limitation**
	**Do not re-use**
	**Contains sufficient for <*n*> tests**
	**Consult instructions for use**
	**Caution**
	**Biological risks**
CE	**CE Mark**

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