ZeptoMetrix®

USA FDA Registration Number 3000202849

IVD CE 2797 UKCA 0086

NATtrol™ CT/NG Negative Control Pack
Part Number: NATCT/NGNEG-6MC-IVD

INTENDED USE:

The NATtrol™ *Chlamydia trachomatis/Neisseria gonorrhoeae* (CT/NG) Negative Control is an unassayed *in vitro* diagnostic external run control intended to be used with qualitative molecular assays for detection of nucleic acids from these organisms. The control is intended to be used as an aid to diagnosis in that it is used to verify performance of the assays used to detect a physiological or pathological state. The routine and repetitive use of external run controls enables laboratories to monitor daily test variation, lot-to-lot test kit performance, individual operator variation, and can provide assistance in identifying increases in random or systemic errors. NATtrol™ CT/NG Negative Control contains intact organisms and should be run in a manner identical to that used for clinical specimens. This qualitative control is not automated and does not have an assigned value and it is the responsibility of the end user to establish their own target specifications for the control using their laboratory's molecular procedures.

PRODUCT SUMMARY AND EXPLANATION:

Each NATtrol™ CT/NG Negative Control Pack contains 6 x 1.25 mL vials of A-549 cells formulated in a Purified Protein Matrix.

Pat.: http://www.zeptometrix.com/patent-information/

PRINCIPLE:

NATtrol™ CT/NG Negative Controls contain A-549 cells formulated in a proprietary Purified Protein Matrix that mimics the composition of a true clinical specimen. These are full process controls designed to monitor the effectiveness of extraction, amplification, and detection in nucleic acid testing procedures. These controls are suitable for use in in-house molecular assays and commercially available platforms.

WARNINGS AND PRECAUTIONS:

Handling and disposal of NATtrol™ CT/NG Negative Controls should be conducted as if the material is potentially infectious.

This control contains material of human and animal origin and the user should observe Universal Precautions when handling and disposing of this product. Disposal must follow local regulations, if more stringent than regulations enforced by the CDC or the FDA.

Do not pipette by mouth.

To avoid cross-contamination, use separate transfer pipettes or tips for all materials.

Do not use beyond the expiration date shown on the label.

Usage beyond the expiration date shown on the label or after storage outside the recommended temperature may be detrimental to product performance or stability and lead to invalid or erroneous results.

If product is received damaged or leaking, contact ZeptoMetrix for instructions.

Changes in physical appearance of the product such as excessive turbidity, presence of precipitates, or discoloration may indicate degradation or contamination of the product. Discard the vial.

Failure to follow the assay or kit manufacturer's instructions explicitly for testing and analysis of results may lead to invalid or erroneous results.

If the expected result is not obtained, contact ZeptoMetrix for instructions.

NOT FOR USE IN HUMANS:

These products are NOT intended for use in the manufacture or processing of injectable products subject to licensure under the USA Food and Drug

Administration Section 351 of the Public Health Service Act or for any other product intended for administration to humans.

RECOMMENDED STORAGE:

NATtrol™ CT/NG Negative Controls should be stored at 2-8°C upon arrival.

When stored as directed, controls are suitable for use for up to 56 days (8 weeks) once opened.

INSTRUCTIONS FOR USE:

Vortex NATtrol™ CT/NG Negative Control vials for 10 seconds to mix.

Follow the manufacturer instructions for use as a clinical sample.

Any serious incident that has occurred in relation to the device shall be reported to ZeptoMetrix and the competent authority of the Member State in which the user and/or the patient is established.

LIMITATIONS:

NATtrol™ CT/NG Negative Controls are USA FDA Class 1 exempt, unassayed, *in vitro* diagnostic external run controls and are intended for professional use only.

NATtrol™ CT/NG Negative Controls are not intended for use as a substitute for the internal controls provided by *in vitro* diagnostic kit manufacturers.

NATtrol™ CT/NG Negative Controls are not intended for use as a primary reference standard or material for any assay or testing procedure.

Quality control materials should be used in accordance with local, state, federal and accreditation requirements.

EXPECTED RESULTS:

Qualitative results are shown in Table 1 below. This is provided for informational purposes only.

As stated in the intended use, this product does not have an assigned value. Each laboratory must evaluate each lot of controls and establish acceptance criteria with their own specific molecular assay procedure and according to their own established quality assurance requirements and guidelines.

Product homogeneity has been demonstrated by validation studies and quality control testing.

Table 1:

Assay	Site	Results n=2			
		CT		NG	
		Urine	Swab	Urine	Swab
Cepheid Xpert® CT/NG	1	Negative	Negative	Negative	Negative
	2	N/T*	N/T*	N/T*	N/T*
BD Probetec™ ET CT/NG	1	N/T*	N/T*	N/T*	N/T*
	2	Negative	Negative	Negative	Negative
Hologic APTIMA Combo 2® CT/NG	1	N/T*	N/T*	N/T*	N/T*
	2	Negative	Negative	Negative	Negative

*Not Tested

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Analytical Performance Characteristics:

Precision testing was performed in replicates of four per the final release assay in the QC SOP. Precision testing was performed on five different days for each of the three lots resulting in testing over 15 days. The testing was performed by three different technicians on two different instruments. The acceptance criteria for precision testing is a 25-27 result for SAC from each run and a %CV of ≤5% and negative or Not Detected for CT1, NG2, and NG4.

Intra-assay repeatability was measured by comparing the results of each day of testing for all lots (Table 1). Inter-assay reproducibility was measured by analyzing the results of testing of each lot across the five different days (Table 2), each technician (Table 3), and each instrument (Table 4).

Accuracy/Assay System Comparison testing was conducted on Multiple Platforms, (Table 1 on page 1). The final release QC testing data was generated on Cepheid® GeneXpert® using the Xpert® CT/NG Assay. Additional assays were performed on the BD ProbeTec™ and on the Hologic® Gen-Probe® APTIMA®. The data from testing on each platform was analyzed. The acceptance criteria for all accuracy testing were a result of negative or not detected on all assay systems/platforms.

For all data analyses, all acceptance criteria were met. *Chlamydia trachomatis*/*Neisseria gonorrhoeae* were not detected, and SAC was detected the %CV values were ≤5%. The control produces repeatable and reproducible results which are independent of the operator and instrument. All accuracy data was negative, for a 100% not detected rate. The control produces accurate results when tested using different assay systems/platforms.

Table 1 – Intra-Assay Repeatability

Lot Number	Day	CT1 Mean (Ct)	CT1 Std Dev (Ct)	CT1 %CV	NG2 Mean (Ct)	NG2 Std Dev (Ct)	NG2 %CV	NG4 Mean (Ct)	NG4 Std Dev (Ct)	NG4 %CV	SAC Mean (Ct)	SAC Std Dev (Ct)	SAC %CV
MD22-00027	1	0	0	0%	0	0	0%	0	0	0%	27.0	0.3	1.1%
	2	0	0	0%	0	0	0%	0	0	0%	26.4	0.5	1.9%
	3	0	0	0%	0	0	0%	0	0	0%	26.1	0.5	1.9%
	4	0	0	0%	0	0	0%	0	0	0%	26.1	0.4	1.5%
	5	0	0	0%	0	0	0%	0	0	0%	26.4	0.4	1.5%
MD22-00143	1	0	0	0%	0	0	0%	0	0	0%	25.7	0.5	1.9%
	2	0	0	0%	0	0	0%	0	0	0%	26.3	0.1	0.4%
	3	0	0	0%	0	0	0%	0	0	0%	26.2	0.4	1.5%
	4	0	0	0%	0	0	0%	0	0	0%	26.1	0.2	0.8%
	5	0	0	0%	0	0	0%	0	0	0%	25.6	0.2	0.8%
MD23-00066	1	0	0	0%	0	0	0%	0	0	0%	26.3	0.8	3.0%
	2	0	0	0%	0	0	0%	0	0	0%	25.8	0.7	2.7%
	3	0	0	0%	0	0	0%	0	0	0%	26.0	0.7	2.7%
	4	0	0	0%	0	0	0%	0	0	0%	25.8	0.5	1.9%
	5	0	0	0%	0	0	0%	0	0	0%	25.4	0.1	0.4%

Table 2 - Inter-Assay Precision - By Lot

Lot Number	Member	CT1 Mean (Ct)	CT1 Std Dev (Ct)	CT1 %CV	NG2 Mean (Ct)	NG2 Std Dev (Ct)	NG2 % CV	NG4 Mean (Ct)	NG4 Std Dev (Ct)	NG4 %CV	SAC Mean (Ct)	SAC Std Dev (Ct)	SAC %CV
MD22-00027	CT/NG Negative Control	0	0	0%	0	0	0%	0	0	0%	26.3	0.5	2.0%
MD22-00143	CT/NG Negative Control	0	0	0%	0	0	0%	0	0	0%	26.0	0.4	1.5%
MD23-00066	CT/NG Negative Control	0	0	0%	0	0	0%	0	0	0%	25.9	0.6	2.4%

Table 3 - Inter-Assay Precision - By User

User (number of tests)	Instrument	CT1 Mean (Ct)	CT1 Std Dev (Ct)	CT1 %CV	NG2 Mean (Ct)	NG2 Std Dev (Ct)	NG2 %CV	NG4 Mean (Ct)	NG4 Std Dev (Ct)	NG4 %CV	SAC Mean (Ct)	SAC Std Dev (Ct)	SAC %CV
MF (n=19)	Inst. 1 & 2	0	0	0%	0	0	0%	0	0	0%	26.2	0.6	2.2%
NG (n=20)	Inst. 1 & 2	0	0	0%	0	0	0%	0	0	0%	26.0	0.6	2.3%
ST (n=19)	Inst. 1 & 2	0	0	0%	0	0	0%	0	0	0%	26.0	0.5	1.8%

Table 4 - Inter-Assay Precision - By Instrument

Instrument	Number of tests	CT1 Mean (Ct)	CT1 Std Dev (Ct)	CT1 %CV	NG2 Mean (Ct)	NG2 Std Dev (Ct)	NG2 %CV	NG4 Mean (Ct)	NG4 Std Dev (Ct)	NG4 %CV	SAC Mean (Ct)	SAC Std Dev (Ct)	SAC %CV
Inst. 1	n=30	0	0	0%	0	0	0%	0	0	0%	26.1	0.5	2.0%
Inst. 2	n=28	0	0	0%	0	0	0%	0	0	0%	26.0	0.6	2.2%

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ETIOLOGIC STATUS/BIOHAZARD TESTING:

The Purified Protein Matrix used in the manufacture of this product is treated with 0.09% sodium azide. It was manufactured from materials that have been tested and found non-reactive at the donor level for HIV-1/HIV-2 Antibody, HBsAg and HCV Antibody by FDA licensed donor screening test methods. All materials are also tested for HIV-1 and HCV by FDA approved Nucleic Acid Test (NAT) methods. Heat inactivated bovine based source materials used in the manufacture of this product meet applicable USDA requirements for abattoir sourced animals, traceability and country of origin. The materials were collected at USDA licensed establishments or legally imported from countries recognized by the USDA as negligible or controlled for risk for Bovine Spongiform Encephalopathy (BSE) and other exotic disease agents. Donor animals were inspected ante and post mortem at the abattoir as required by the USDA.

PRODUCT WARRANTY:

ZeptoMetrix LLC's limited product warranty and other terms and conditions related to the purchase and use of ZeptoMetrix products are set forth in ZeptoMetrix's Terms and Conditions of sale found on ZeptoMetrix's website at Sales Terms and Conditions. If you have any questions, please contact ZeptoMetrix Customer Service at zepto.customerservice@antylia.com.

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LEGEND OF LABELING SYMBOLS:

	Manufacturer		**Temperature Limitation**
IVD	***In vitro* Diagnostic Use**		**Use-By Date**
CE	**European Mark of Conformity**		**Biological Risk**
REF	**Part / Catalogue Number**	EC REP	**Authorized Representative**
LOT	**Batch Code**		**Consult Instructions for Use**
BIO	**Contains biological material of animal origin**	BIO	**Contains biological material of human origin**
UDI	**Unique Device Identifier**	UKCA	**UKCA Mark of Conformity**

Manufacturer:
ZeptoMetrix LLC
25 Kenwood Circle
Franklin, MA 02038, USA

EC Representative:
EC REP
Emergo Europe
Westervoortsedijk 60
6827 AT, Amhem
The Netherlands

UK Responsible Person:
Emergo Consulting (UK) Limited
c/o Cr360 – UL International,
Compass House, Vision Park Histon,
Cambridge CB24 9BZ, United Kingdom

REVISION HISTORY.

Revision Level	Description of Revisions
11	Added additional statement to warning concerning usage beyond the expiration date shown on the label or after storage outside the recommended temperature, changes in physical appearance of the product, failure to follow the assay or kit manufacturer's instructions explicitly, and if the expected result is not obtained action. Added "NATtrol™ CT/NG Negative Control is not intended for use as a primary reference standard or material for any assay or testing procedure." to Limitations. Added "Any serious incident that has occurred in relation to the device shall be reported to ZeptoMetrix and the competent authority of the Member State in which the user and/or the patient is established." to Instructions for Use. Added verbiage to Intended Use to indicate it is a qualitative control that is not automated. The fundamental Intended Use has not changed. Added Revision History section. Changes in response to BSI Technical File review for IVDR compliance. Added biological and UDI symbols. Updated EC Representative Emergo Europe address to new location. Added UK Responsible Person contact details.
12	Added UKCA Mark of Conformity.
13	Added Precision and Accuracy/Assay System Comparison testing data.

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This product was manufactured in a facility which has a Quality Management System that is ISO 13485 certified.
For Customer Support, please visit www.zeptometrix.com or email zepto.customerservice@antylia.com