



NATtrol™ *Clostridium difficile* Negative Control
Part Number: NATCSO-6MC-IVD

INTENDED USE:

The NATtrol™ *Clostridium difficile* 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 this organism. 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™ *Clostridium difficile* 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:

NATtrol™ *Clostridium difficile* Negative Control is formulated with purified, intact *Clostridium sordellii* bacterium that have been chemically modified to render them non-infectious and refrigerator stable*.

Each NATtrol™ *Clostridium difficile* Negative Control contains 6 x 0.5 mL vials of NATtrol™ *Clostridium sordellii* formulated in a Purified Protein Matrix.

*Pat.: <http://www.zeptometrix.com/patent-information/>

PRINCIPLE:

The NATtrol™ *Clostridium difficile* Negative Control contains *Clostridium sordellii* cells inactivated by ZeptoMetrix's patented NATtrol™ process 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:

Although NATtrol™ *Clostridium difficile* Negative Control contains inactivated microorganisms, handling and disposal should be conducted as if materials are 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 section 351 of the Public Health Service Act or for any other product intended for administration to humans.

RECOMMENDED STORAGE:

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

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

NATtrol™ *Clostridium difficile* Negative Control is 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:

Part Number	Organism/ Strain	Expected Results
NATCSO-6MC-IVD	<i>Clostridium sordellii</i> (Z077)	Toxigenic <i>C. difficile</i> not detected 027 Presumptive not detected

Table 2:

Assay	Toxin B Result
Cepheid® Xpert® <i>C. difficile</i> /Epi	Not Detected
BIOFIRE® FilmArray® GI Panel	Not Detected



NATtrol™ *Clostridium difficile* Negative Control
Part Number: NATCSO-6MC-IVD

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 four lots resulting in testing over 20 days. The testing was performed by three different technicians on two different instruments. The acceptance criteria for precision testing is a negative result for Toxin B from each run and a %CV of ≤5%.

Intra-assay repeatability was measured by comparing the results of each day of testing for four lots (Table 3). Inter-assay reproducibility was measured by analyzing the results of testing of each lot across the five different days (Table 4), each technician (Table 5), and each instrument (Table 6).

Accuracy/Assay System Comparison testing was conducted on Multiple Platforms, (Table 2 on page 1). The final release QC testing data was generated on Cepheid® GeneXpert® using the Xpert® *C. difficile*/Epi Assay. Additional assays were performed on the BIOFIRE® FilmArray® GI Panel. The data from testing on each platform was analyzed. The acceptance criteria for all accuracy testing were a result of Toxin B not detected for each lot on both assay systems/platforms.

For all data analyses, all acceptance criteria were met. *Clostridium difficile* was not detected and the %CV values were considered ≤5%. The control produces repeatable and reproducible results which are independent of the operator and instrument. All accuracy data was negative for Toxin B, for a 100% non-detection rate. The control produces accurate results when tested using two different assay systems/platforms.

Table 3 – Intra-Assay Repeatability

Lot	Day	Toxin B Mean (Ct)	Toxin B Std Dev (Ct)	Toxin B %CV
Validation Lot 2	1	0.0	0.0	0.0%
	2	0.0	0.0	0.0%
	3	0.0	0.0	0.0%
	4	0.0	0.0	0.0%
	5	0.0	0.0	0.0%
Validation Lot 3	1	0.0	0.0	0.0%
	2	0.0	0.0	0.0%
	3	0.0	0.0	0.0%
	4	0.0	0.0	0.0%
	5	0.0	0.0	0.0%
Validation Lot 4	1	0.0	0.0	0.0%
	2	0.0	0.0	0.0%
	3	0.0	0.0	0.0%
	4	0.0	0.0	0.0%
	5	0.0	0.0	0.0%
Lot 5	1	0.0	0.0	0.0%
	2	0.0	0.0	0.0%
	3	0.0	0.0	0.0%
	4	0.0	0.0	0.0%
	5	0.0	0.0	0.0%

Table 4 - Inter-Assay Precision - By Lot

Lot	Member	Instrument	Toxin B Mean (Ct)	Toxin B Std Dev (Ct)	Toxin B %CV
Validation Lot 2	NATtrol™ <i>C. difficile</i> Negative Control	1	0.0	0.0	0.0%
Validation Lot 3	NATtrol™ <i>C. difficile</i> Negative Control	1	0.0	0.0	0.0%
Validation Lot 4	NATtrol™ <i>C. difficile</i> Negative Control	1	0.0	0.0	0.0%
Lot 5	NATtrol™ <i>C. difficile</i> Negative Control	2	0.0	0.0	0.0%

Table 5 - Inter-Assay Precision - By User

User (number of tests)	Instrument	Toxin B Mean (Ct)	Toxin B Std Dev (Ct)	Toxin B %CV
EF (n=10)	2	0.0	0.0	0.0%
DB (n=5)	2	0.0	0.0	0.0%
ST (n=5)	1	0.0	0.0	0.0%

Table 6 - Inter-Assay Precision - By Instrument

Instrument	Number of tests	Toxin B Mean (Ct)	Toxin B Std Dev (Ct)	Toxin B %CV
Inst. 1	n=15	0.0	0.0	0.0%
Inst. 2	n=5	0.0	0.0	0.0%



NATtrol™ *Clostridium difficile* Negative Control
Part Number: NATCSO-6MC-IVD

ETIOLOGIC STATUS/BIOHAZARD TESTING:

NATtrol™ inactivation was completed on the stocks used to formulate each control and further verified by the absence of bacterial growth in a validated growth protocol.

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 diagnostic.cs@zeptometrix.com.

DISCLAIMER AND LIMITATION OF LIABILITY:

ZeptoMetrix LLC disclaims all warranties with respect to this document and the information contained herein, expressed or implied, including but not limited to those of merchantability, fitness for a particular purpose, or non-infringement. To the extent allowed by law, in no event shall ZeptoMetrix LLC be liable, whether in contract, tort, warranty, or consequential damages or lost profits in connection with or arising from this document and the information contained herein, including but not limited to the use thereof even if ZeptoMetrix is advised of the possibility of such damages.

LEGEND OF LABELING SYMBOLS:

	Manufacturer		Temperature Limitation
	<i>In vitro</i> Diagnostic Use		Use-By Date
	European Mark of Conformity		Biological Risk
	Catalogue Number		Authorized Representative
	Batch Code		Consult Instructions for Use
	Contains biological material of animal origin		Contains biological material of human origin
	Unique Device Identifier		UKCA Mark of Conformity

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

EC Representative:



Emergo Europe
 Westervoortsewijk 60
 6827 AT, Arnhem
 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
06	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™ <i>Clostridium difficile</i> 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.
07	Adding UKCA Mark of Conformity.
08	Updated Customer Service email. Added analytical performance characteristics per DC-23-0005.
09	Adding CE2797 Mark of Conformity per DC-24-004.