2

2

January 10, 2002

To: Kathy Wright
Food and Drug Administration
Center for Devices and Radiological Health
Office of Device Evaluation
Division of Clinical Laboratory Devices
Microbiology Branch
Document Control Center (HFZ-440)
2098 Gaither Road.
Rockville, MD 20850

FR: Yvette Lloyd
Bio-Rad Laboratories
9500 Jeronimo Road
Irvine, CA 92618

Re: Meeting Minutes – FDA/Bio-Rad Laboratories Liquichek ToRCH Plus Control 510(k) submission teleconference.

This memorandum summarizes the discussions that transpired between the agency and Bio-Rad Laboratories with respect to the Bio-Rad Laboratories Liquichek ToRCH Plus Control 510(k) submission teleconference.

A teleconference was held on January 7, 2002, between Bio-Rad Laboratories and the FDA. The discussion served to discuss open issues identified by the FDA in relation to the Bio-Rad Laboratories Liquichek ToRCH Plus Control 510(k) Submission [K013716].

In attendance at the meeting were representatives from Bio-Rad Laboratories and the FDA. The meeting participants were as follows:

Food and Drug Administration:
Woody Dubois (DCLD/CDRH)
Kathy Wright (DCLD/CDRH)
Tom Simms (DLCD/CDRH)

Bio-Rad Laboratories:
Donna Chapman
Elizabeth Platt
Yvette Lloyd
Farrah Kamalian

I. Introduction:
The discussion commenced with an introduction and welcome from Bio-Rad Laboratories. All parties from the FDA were confirmed present by Bio-Rad Laboratories.

Bio-Rad Laboratories briefly discussed the nature of the product manufactured at QSD, and reiterated the scope and purpose of the conference call.

The groups referenced the proposed agenda, and both groups agreed to utilize the proposed agenda.

The FDA began with a brief introduction and reiterated that while global harmonization is rapidly transpiring, the FDA solely has jurisdiction over those products which are intended for the domestic market, regardless of whether they are to be sold internationally.

Bio-Rad Laboratories suggested that the discussion would commence with the parties from the FDA addressing each issue identified by the reviewer, and then proceeding with a discussion as to whether the issue has 1) been satisfied by the Bio-Rad Laboratories response, and if not, 2) indicate what is the fundamental nature of the issue that still requires resolution. All parties agreed to this.

II. List of issues:
The group agreed to begin discussing the list of issues identified by the agency. In order to provide the best summary of the discussion, each issue has been provided in ***bold, italicized print.*** The subsequent discussion and agreements (if assented) are provided in regular print.

Administrative Issues
The sponsor has provided examples how they derived an assigned value for each of the analytes of their control material. Discussion follows:

a) ***The First page discussion, section 6, states that the value assignment for the Abbott Tumor Marker is generated..... The sponsor should indicate how this is relevant to the device.***

   As per the FDA, the written response submitted by Bio-Rad Laboratories satisfies the issue.

   Status: **CLOSED**

b) ***On the first page of section 6 to the second the last paragraph has a disclaimer that the values are provided simply 'as a guide' and that 'each laboratory should establish [their] own specific means and acceptable ranges'. As an assayed control, this value should not be considered as a 'guide' but is considered a true value for a particular lot of material. Therefore, this we recommend a statement be presented in the PI but rewritten to reflect this concept.***

   The FDA articulated that CDRH does not like the idea of an 'assayed' quality control that has a corresponding disclaimer in the labeling discounting the representative ranges. The FDA considers this 'guide' disclaimer more appropriate for an unassayed control.

Bio-Rad Laboratories inquired as to what text the FDA would recommend to mitigate the issue.

The FDA suggested that changes to the intended use and indications for use to list only those approved assays which have been validated with the control be listed.

Status: **UNRESOLVED**. Bio-Rad Laboratories will discuss the issue and formulate a response to the Microbiology branch.

It should be noted that the groups digressed momentarily to discuss the concept of labeling. Bio-Rad Laboratories is currently undergoing a labeling review at the Office of Compliance. ODE in the past has performed labeling reviews for Bio-Rad Laboratories.

The FDA expressed a concern that labeling reviews for cleared 510(k)s need to transpire at ODE . Bio-Rad Laboratories reiterated that labeling reviews to the insert go through the Office of Compliance and that this has been done in the past to review global labeling changes which do not affect the 510(k) status.

Mr. Dubois indicated that he has spoken with Dr. Gutman regarding the listing of unapproved devices in this insert. He reiterated that the FDA's position for this product has not changed. In short, the FDA will not allow the listing of unapproved devices in this package insert.

In the interest of time, the groups agreed to table this discussion and take it offline, as it is something that affects not only the device which is the subject of the conference call, but potentially affects all Bio-Rad Laboratories devices.

c) ***There are provided protocols which contain two different sets of instructions for assay manufacturers and for reference laboratories. The sponsor recommends (first protocol) that assay manufacturer run this device for a minimum of 20 replicates whereas the reference laboratories' instructions (second protocol) are for a different function. The manufacturers are to test this device for reproducibility and establishing a mean and range. The reference labs are apparently to use this device as a specimen would be used. However, it is unclear why this investigator is requested to supply results of cutoff values, sample to cutoff ratios, clinical interpretation and quality control sample to cutoff ratio values (see comment #9). It is puzzling what sample(s) the sponsor wants this information for and how the data can be used for this device. Was the protocol(s) specifically followed?***

As per the FDA, the written response submitted by Bio-Rad Laboratories satisfies the issue.

Status: **CLOSED**

d) ***Because there is indication that 20 replicates were performed, we believe this constitutes reproducibility testing. We would welcome these results to be presented as standard deviation (SD) and percent coefficient of variation (%CV) in order to further evaluate its value as an assayed control material***

Bio-Rad Laboratories does not make any product claims in the labeling for reproducibility; furthermore, Bio-Rad Laboratories feels that this is not a claim that is supported by industry.

As per the FDA, the written response submitted by Bio-Rad Laboratories satisfies the issue.

Status: **CLOSED**

e) ***We recommend the sponsor provide a Financial Disclosure Form from each investigator participating in these studies.***

The FDA discussed that the Financial Disclosure requirements, which began to be enforced about 2 years ago, apply to IVDs, regardless of whether human subjects are involved.

Bio-Rad Laboratories agreed to provide one for this 510(k) submission and agreed to start providing one for each 510(k) submitted.

Status: **RESOLVED**

f) ***We suggest the sponsor provide the statistical format for calculating the acceptable range(s) of results for each analyte and for each instrument (if different) using their device.***

As per the FDA, the written response submitted by Bio-Rad Laboratories satisfies the issue.

Status: **CLOSED**

g) ***How is this device to be utilized if the user has plasma for specimen testing and it appears that performance data was obtained only from serum?***

The FDA reiterated the concern that the device, which is made from a serum-like matrix, is appropriate for use in assays cleared for use with plasma specimens.

Bio-Rad Laboratories suggested that the control has been validated with assays that have been cleared for both serum and plasma, thereby rendering it useable for all assays.

The FDA suggested that NCCLS guidelines on matrix studies and for IgM controls represent that the controls must be validated with each type of assay in order for it to be claimed. Further, there needs to be proof that the matrix is commutable for all assays.

Status: **UNRESOLVED**

Labeling

The groups commenced a generic discussion related to labeling.

Bio-Rad Laboratories had indicated that the Office of Compliance has approved the text templates via a labeling review.

The FDA is concerned that labeling reviews should go to ODE and not the Office of Compliance especially when it relates to cleared devices. The FDA believes that ODE should review for content labeling changes, and that the Office of Compliance is better suited to review format changes to labeling.

Bio-Rad Laboratories indicated that the company has a labeling review currently pending to address the text required for CE Marking. Bio-Rad Laboratories read those text changes to the FDA. The FDA agreed to follow up with Betty Collins the Office of Compliance for information related to the current labeling review.

The FDA agreed that the new text probably did not warrant ODE review.

Because this is a global issue that such reviews may pre-empt the need for a new 510(k) the groups agreed to table the discussion in order to address the labeling issues related to the current device 510(k).

The following dialogue involves both the existing draft PI and further suggestion(s) by FDA:

a) Intended use: Because the sponsor considers this an assayed device, we believe each legally marketed system for which the device's level should be indicated, e.g. Abbott AxSYM and Abbott ImX. In addition, each organism should be cited as well. This would also be the same for the Indications for Use statement.

The FDA indicated that if Bio-Rad Laboratories still wants to approach this as an 'assayed' control, that there should be express information in the 2nd paragraph of the intended use statement disclosing the information suggested by the FDA.

Bio-Rad Laboratories indicated that the data sheet in the draft package insert has been changed to incorporate the information requested. Bio-Rad Laboratories suggested that the new draft of the Package Insert be submitted to the FDA in the next response to determine if it satisfies the issues noted by the FDA.

The FDA agreed to this.

Status: **UNRESOLVED.** Bio-Rad Laboratories will submit a copy of new draft package insert and the FDA will review to see if it resolves issue.

It should be noted that at the end of the discussion the FDA appeared to suggest that the FDA would allow a reference to a list of assays in the data sheet as long as the sheet solely listed approved kits.

b) ***Reagents:***

i) Warnings: We believe that the sponsor should specify what their 'processed' plasma is and indicate that their device is not intended for use with assays which recommend using anticoagulated specimens.

This issues related back to the administrative issue identified previously.

Bio-Rad Laboratories agreed to take the discussion offline, and provide in the next FDA response what approach to take with the issue.

Status: **UNRESOLVED**

ii) Because the sponsor states (sect. 2, page 3 of 3) that stability studies have been performed with this device, 60 days opened and 3 years, 3 months for unopened (both at 2-8°C), we suggest they provide representative data to FDA. We suggest the sponsor also indicate whether the states unopened stability is from real-time or accelerated time determination.

As per the FDA, the written response submitted by Bio-Rad Laboratories satisfies the issue.

Status: **CLOSED**

c) Limitations

i) ***We recommend the sponsor state, "These ToRCH Controls are not considered calibrators and are not to be used for assay calibration."***

Bio-Rad Laboratories suggested that this current issue is already expressly stated in the draft insert, and it is further articulated in the draft text template which is currently undergoing a labeling review.

Bio-Rad Laboratories read to the FDA the proposed wording changes which incorporate the requested changes. The FDA agreed to take this discussion offline pending resolution of the labeling review issue with the Office of Compliance.

Status: **UNRESOLVED**

ii) We suggest, "These controls are not intended to replace the manufacturer's controls supplied with their kits."

Bio-Rad Laboratories agreed to insert this text on the labeling.

Status: **RESOLVED**

iii) We additionally recommend the following, "The ToRCH Controls are matrix specific and are intended for use only when testing serum specimens."

This is a labeling change request that is related to an administrative issue identified by the FDA.

The FDA strongly support the NCCLS guidelines which suggest that plasma assays utilize plasma specimens, and serum assays use serum specimens. As such, because this is essentially a serum sample, the FDA would like to have a matrix specific disclaimer.

Bio-Rad Laboratories suggested that if we were to place a matrix specific disclaimer in the insert, that it is already expressly specified in the intended use statement. The FDA indicated that the FDA would pursue this offline and get back to Bio-Rad Laboratories regarding this issue.

Bio-Rad Laboratories agreed to take this issue offline and address it in the next response to be submitted to the FDA.

Status: **UNRESOLVED**

iv) ***Because this device has been established with specified assays, a statement is advised for limiting this device to those systems listed in the Intended Use and Indications for Use. Alternatively, the sponsor could say that the performance characteristics have not been established for assays other than those listed in the Intended Use section.***

This is the same issue that arose at the beginning of the discussion.

Both groups feel strongly about each of their respective positions.

Bio-Rad Laboratories further recognized that if the inserts were restricted to those assays which are cleared for the domestic market, that it would essentially pre-empt the need for a new 510(k) every time a new assay became cleared for the domestic market, since this would be considered a change in the intended use. Bio-Rad Laboratories is willing to comply with this requirement for this particular 510(k) submission, although it is feasible that with over 100 cleared 510(k)s it would place a substantial burden on DCLD in the future when new assays would become available.

Bio-Rad Laboratories also brought up the issue that assays manufacturers are continuously removing their assays from the market. The FDA discussed that no new 510(k) is required when assays are removed from the intended use.

Both groups agreed that this is really a global issue related not only to the current device. Both groups agreed to table the discussion discuss it after Bio-Rad Laboratories has submitted the second response.

Status: **UNRESOLVED**

d) ***Expected values: We recommend a brief statement about the method(s) used to verify the expected results for this control.***

As per the FDA, the written response submitted by Bio-Rad Laboratories satisfies the issue.

Status: **CLOSED**

e) ***Quality Control: We suggest the sponsor include a quality control section recommending that each laboratory validates each lot of control with each specific assay system prior to its routing use in their laboratory.***

The FDA indicated that this request is understood through the CLIA regulations, and that an additional express statement is needed on the insert.

Bio-Rad Laboratories agreed to discuss this offline and address the issue in the next response to the FDA.

Status: **UNRESOLVED.**

III. Conclusion

The meeting terminated with a summation of the items that are still unresolved at the current time and a summation of the items that had been resolved during the conference call.

Bio-Rad Laboratories agreed to send a new draft package insert in the next response as well as a sample of a labeling review performed by the Office of Compliance.

Both groups articulated that each group's arguments had merits and that each group could respect and understand the other group's logic behind the arguments.

The FDA is cognizant that the issues that are transpiring with this submission are not new and that they are an oversight on the part of the FDA. The FDA articulated that they are making good faith effort to try and rectify these issues for the future.

Bio-Rad Laboratories expressed concerns that some of the issues identified in this product submission are truly global and may potentially affect other product manufactured by Bio-Rad Laboratories. Additionally, Bio-Rad Laboratories suggested that the company might wish to escalate some of these issues directly to Dr. Gutman, especially issues such as listing of unapproved kits, which has been allowed by the FDA for quite some time.

In addition, the FDA suggested that Bio-Rad Laboratories provide DCLD with a paper detailing all the 'global' issues that affect Bio-Rad Laboratories product and DCLD will address these issues after receiving the labeling review.

Lastly, Bio-Rad Laboratories agreed to provide meeting minutes to summarize issues and ensure that all parties comprehend the issues in the same manner.

Bio-Rad Laboratories

Diagnostics Group
9500 Jeronimo Road
Irvine, California 92618-2017
Telephone (949) 598-1200

Bio-Rad 510(k) Response to FDA for Liquichek ToRCH Plus Control

January 28, 2002

Kathy Wright
Food and Drug Administration
Center for Devices and Radiological Health
Office of Device Evaluation
Division of Clinical Laboratory Devices
Microbiology Branch
Document Control Center (HFZ-440)
2098 Gaither Road.
Rockville, MD 20850

Re. K013716

Dear Ms. Wright:

Pursuant to our conversation on January 23, 2002, I am submitting a response to the FDA regarding the change in the intended use for the ToRCH Plus Control. Positive.

Bio-Rad Laboratories has chosen to modify the intended use from an ASSAYED control to an UNASSAYED control. As such, this relegates the control from the premarket notification requirements of 21 CFR §862.1660, since unassayed products are exempted by statute.

Although the product is exempted by regulation, Bio-Rad Laboratories would like to partner with the FDA to create labeling that is suitable for the domestic market. A draft copy of the proposed labeling changes has been provided in Attachment A; because some of the FDA requested changes were not incorporated, a justification for non-incorporation has been provided in Attachment B. Bio-Rad Laboratories welcomes your feedback.

Bio-Rad Laboratories urges the agency to reasonably consider the proposed justification. Because Bio-Rad Laboratories is a global company with approximately 70 products sold worldwide, Bio-Rad Laboratories has a valid concern that the changes requested for the Liquichek ToRCH Control, Positive will impact other product labeling by setting a precedent. Furthermore, as there may be differences among reviewers within the departments the Division of Clinical Laboratory Devices, Bio-Rad Laboratories has a concern that these changes may not be harmonized and may be dynamic with respect to each individual 510(k) premarket notification review. Therefore, Bio-Rad Laboratories agrees to work with the agency on the requested labeling changes, and asks that only those changes which are integral to ensuring compliance with the federal statues be implemented.

In addition, Bio-Rad Laboratories would like to partner with the FDA long term and keep the Liquichek ToRCH Plus Control, Positive 510(k) open in order to enable the company to market an assayed serology control. Because that is beyond the scope of the current response, issues related to this request will not be articulated *herein*. Nonetheless, Bio-Rad Laboratories would like to work the FDA long-term to determine what requirements may be necessary to support a substantial equivalence decision for an assayed serology control.

As discussed in phone conversations with you, Bio-Rad Laboratories understands the sense of urgency in working to resolve the issues with the current premarket notification submission. We appreciate your earliest attention to this matter, and thank you in advance for resolving these issues in an expeditious manner.

Should you require additional information please contact me directly at (949) 598-1465, via facsimile at (949) 598-1555, or via the Internet at yvette_lloyd@bio-rad.com.

Thank you.

With best regards,

Yvette Lloyd
Senior Regulatory Affairs Specialist
Bio-Rad Laboratories

Attachment A:

Proposed Domestic Labeling

Bio-Rad Laboratories

Liquichek™ ToRCH Plus Control, Positive

INTENDED USE

Liquichek ToRCH Plus Control, Positive is intended for use as an unassayed quality control serum to monitor the precision of laboratory testing procedures for the analytes listed in this package insert.

SUMMARY AND PRINCIPLE

The use of quality control materials is indicated as an objective assessment of the precision of methods and techniques in use and is an integral part of good laboratory practices.

REAGENT

Liquichek ToRCH Plus Control, Positive is prepared from human serum and preservatives. The control is provided in liquid form for convenience.

STORAGE AND STABILITY

Liquichek ToRCH Plus Control, Positive will be stable until the expiration date when stored unopened at 2-8°C. Once opened, all constituents will be stable for 60 days when stored tightly capped at 2-8°C. The vials should be stored upright to prevent leakage.

PROCEDURE

Liquichek ToRCH Plus Control, Positive should be treated and analyzed the same as patient specimens and run in accordance with the instructions accompanying the instrument, kit or reagent being used. Before sampling, allow the control to reach room temperature then gently swirl the contents to ensure homogeneity. Do not mix vial contents by inversion or by vigorous agitation.

LIMITATIONS

Liquichek ToRCH Plus Control, Positive should not be used past the expiration date. If there is evidence of microbial contamination or excessive turbidity in the control, discard the vial.

Liquichek ToRCH Plus Control, Positive is not intended for use as a standard nor to verify trueness of measurement and is not traceable to internationally recognized standards.

Liquichek ToRCH Plus Control, Positive is independent from the positive and negative controls provided with the manufacturer test kits.

ASSIGNMENT OF VALUES

The results printed in this insert were derived from replicate analyses and are specific for this lot of Liquichek ToRCH Plus Control, Positive. The tests listed were performed by the reagent manufacturer and/or independent laboratories using manufacturer supported reagents and a representative sampling of this lot of control. Variations over time and between laboratories may be caused by differences in laboratory technique, instrumentation and reagents, or by manufacturer test method modifications. Representative results are provided for informational purposes only. Each laboratory should establish its own parameters of precision.

SPECIFIC PERFORMANCE CHARACTERISTICS

Liquichek ToRCH Plus Control, Positive is a stabilized liquid product manufactured under rigid quality control standards. To obtain consistent vial to vial assay values, the control requires proper storage and handling as described.

DISPOSAL

Dispose of control material in accordance with the requirements of local waste management authorities.

DAMAGE TO PACKAGING

In the event of damage to the packaging contact the local Bio-Rad Laboratories distributor or Bio-Rad Laboratories Technical Services.

WARNING

Human source material. Treat as potentially infectious.
Each serum/plasma donor unit used to manufacture this control was tested by FDA accepted methods and found non-reactive for Hepatitis B Surface Antigen (HBsAg), antibody to hepatitis C (HCV) and antibody to HIV-1/HIV-2. No test method can offer complete assurance that products containing human source materials will be absent of these and other infectious agents. This product may also contain other human source material for which there are no approved tests. In accordance with good laboratory practice, all human source material should be considered potentially infectious for Hepatitis B (HBV), Hepatitis C (HCV), HIV-1, HIV-2, HTLV-I, HTLV-II, and all other infectious agents; therefore, handle Liquichek ToRCH Plus Control, Positive with the same precautions used with patient specimens.

FOR IN VITRO DIAGNOSTIC USE

Analyte Manufacturer/Method	Lot 18601 Results
Toxoplasma gondii IgG	
Abbott AxSYM TOXO IgG	Weakly reactive
Abbott IMx TOXO IgG	Weakly reactive
Beckman ACCESS Toxo IgG	Weakly reactive
bioMérieux VIDAS TOXOGII IgG	Weakly reactive
Diagnostic Products Immulite Toxoplasma IgG	Weakly reactive
Diagnostic Products Immulite 2000 Toxoplasma IgG	Weakly reactive
DiaSorin ETI-TOXO-G Plus	Reactive
SeraQuest TOXOPLASMA IgG	Reactive
Wampole Laboratories/Trinity TOXO IgG ELISA	Weakly reactive
Rubella Virus IgG	
Abbott AxSYM Rubella IgG	Weakly reactive
Abbott IMx Rubella IgG	Weakly reactive
Beckman ACCESS Rubella IgG	Weakly reactive
bioMérieux VIDAS RUBGII IgG	Weakly reactive
Diagnostic Products Immulite Rubella IgG	Weakly reactive
Diagnostic Products Immulite 2000 Rubella IgG	Weakly reactive
DiaSorin ETI-RUBEK-G-Plus	Weakly reactive
SeraQuest RUBELLA IgG	Weakly reactive
Wampole Laboratories/Trinity Rubella IgG ELISA	Weakly reactive
Cytomegalovirus (CMV) IgG	
Abbott AxSYM	Reactive
bioMérieux VIDAS CMVG IgG	Reactive
Diagnostic Products Immulite CMV IgG	Weakly reactive
Diagnostic Products Immulite 2000 CMV IgG	Weakly reactive
DiaSorin ETI-CYTOK-G Plus	Weakly reactive
SeraQuest CMV IgG (1)	Weakly reactive
Wampole Laboratories/Trinity CMV IgG ELISA	Weakly reactive
Herpes Simplex Virus Type 1 (HSV-1) IgG	
Wampole Laboratories/Trinity HSV 1 IgG ELISA	Weakly reactive
Herpes Simplex Virus Type 2 (HSV-2) IgG	
Wampole Laboratories/Trinity HSV 2 IgG ELISA	Weakly reactive
Herpes Simplex Virus Type 1 / 2 (HSV-1/2) IgG	
Diagnostic Products Immulite HSV IgG	Reactive
DiaSorin ETI-HSVK I/II IgG	Weakly reactive
SeraQuest HSV IgG (2)	Weakly reactive

Helicobacter pylori IgG	
Bio-Rad /Helix Enzyme Immunoassay Anti-Helicobacter pylori IgG Test	Weakly reactive
Diagnostic Products Immulite H.pylori IgG	Weakly reactive
Diagnostic Products Immulite 2000 H.pylori IgG	Weakly reactive
Wampole Laboratories/Trinity H. pylori IgG ELISA	Weakly reactive
Varicella Zoster Virus (VZV) IgG	
bioMérieux VIDAS VZG	Weakly reactive
SeraQuest VZV IgG (3)	Weakly reactive
Wampole Laboratories/Trinity VZV IgG ELISA	Weakly reactive
Epstein Barr Virus (VCA) EBV (VCA) IgG	
DiaSorin ETI-VCA G	Reactive
SeraQuest EB VCA IgG	Weakly reactive
Trinity Captia EBV VCA (P-18) - IgG	Weakly reactive
Treponema pallidum (Syphilis) IgG	
Fujirebio Lumipulse TP-N	Reactive
SciMedix FTA-Abs *Treponema pallidum* test	Reactive
Syphilis Rapid Plasma Reagin (RPR)	
AMPCOR Syphilis RPR	Reactive
Becton Dickinson Macro-Vue RPR Card Tests	Reactive

Footnotes:
(1) A 1:5 dilution should be made prior to running those tests where the value listed exceeds the highest standard
(2) A 1:3 dilution should be made prior to running those tests where the value listed exceeds the highest standard
(3) A 1:2 dilution should be made prior to running those tests where the value listed exceeds the highest standard

Attachment B:

Justification for non-incorporation of FDA requested labeling changes

The foregoing justification is based on Bio-Rad Laboratories' response to the FDA's concerns regarding the Premarket Notification [510(k)] submission of the Liquichek ToRCH Plus Control, Positive.

In order to facilitate the analysis, the original opinion from the agency has been set in bold, italic print, while the Bio-Rad Laboratories response has been set in normal type.

Labeling

The following dialogue involves both the existing draft PI and further suggestion(s) by FDA:

a) ***Intended use: Because the sponsor considers this an assayed device, we believe each legally marketed system for which the device's level should be indicated, e.g. Abbott AxSYM and Abbott ImX. In addition, each organism should be cited as well. This would also be the same for the Indications for Use statement.***

   Pursuant to the teleconference held between the agency and Bio-Rad Laboratories, it was agreed that the new draft of the insert be submitted to the agency for review.

   The new draft insert has incorporated the full manufacturer's name as well as the full name for the organism in the data sheet.

   Furthermore, Bio-Rad Laboratories has removed all references to uncleared reagent kits as agreed during the teleconference.

   Bio-Rad Laboratories reasonably believes that the modification to the data sheet should take care of the issue noted.

   The proposed draft of the data sheet incorporating the changes may be found in the draft package insert in Attachment A.

b) ***Reagents:***

   i) ***Warnings: We believe that the sponsor should specify what their 'processed' plasma is and indicate that their device is not intended for use with assays which recommend using anticoagulated specimens.***

      The term 'processed plasma' has been removed from the reagent section of the package insert, as it may be confusing to the customer.

      Therefore, Bio-Rad Laboratories reasonably believes that this should dissuade the concern noted.

ii) ***Because the sponsor states (sect. 2, page 3 of 3) that stability studies have been performed with this device, 60 days opened and 3 years, 3 months for unopened (both at 2-8°C), we suggest they provide representative data to FDA. We suggest the sponsor also indicate whether the states unopened stability is from real-time or accelerated time determination.***

Pursuant to the teleconference, this issue has been resolved by the Bio-Rad Laboratories written response from December 2001. Therefore, no further labeling changes are necessary.

c) ***Limitations***

i) ***We recommend the sponsor state, "These ToRCH Controls are not considered calibrators and are not to be used for assay calibration."***

The new draft insert in Attachment A contains a number of limitations. In particular, Limitation #3 states:

"This product is not intended for use as a standard nor to verify trueness of measurement and is not traceable to internationally recognized standards."

The company believes that the term 'standard' may be equated with 'calibrator'. As such, the express disclaimer intimates that the control is not a calibrator, and may not be used for assay calibration.

While these limitations do not expressly state the requested verbiage, Bio-Rad Laboratories reasonably believes that the statement implies that the control may not be considered a calibrator nor may be it used for assay calibration. As such the company requests an exemption from this requirement.

ii) ***We suggest, "These controls are not intended to replace the manufacturer's controls supplied with their kits."***

Pursuant to the discussions during the teleconference, Bio-Rad Laboratories agreed to implement this type of verbiage in the insert.

While this exact disclaimer has not been implemented in the package insert, verbiage that is quite similar to the above suggested text has been placed in the Limitations section and may be viewed in the new draft insert provided in Attachment A.

iii) ***We additionally recommend the following, "The ToRCH Controls are matrix specific and are intended for use only when testing serum specimens."***

Pursuant to the teleconference, it was discussed between the two groups that the intended use might serve as an effective disclaimer.

The current intended use states: "Liquichek ToRCH Plus Control, Positive is intended for use as an unassayed quality control serum to monitor the precision of laboratory testing procedures for analytes listed in the package insert."

Because the intended use expressly provides that the product is made from serum, this implies that the control may only be used for assessing the precision of assays testing serum specimens.

Therefore, Bio-Rad Laboratories requests an exemption from this labeling requirement.

iv) ***Because this device has been established with specified assays, a statement is advised for limiting this device to those systems listed in the Intended Use and Indications for Use. Alternatively, the sponsor could say that the performance characteristics have not been established for assays other than those listed in the Intended Use section.***

As specified in Section A, *supra*, Bio-Rad Laboratories has deleted reference to all known uncleared reagent kits from the data sheet in the Package Insert.

Additionally, the Assignment of Values clearly states that the values printed in the insert may only be used as a guide, and the end-user must validate the control appropriately. This is a requirement promulgated by CLIA and specified in 42 CFR §493.

Because the data sheet does not reference uncleared kits and since the end user may only use the information as a guide, Bio-Rad Laboratories reasonably believes that the current package insert is self-limiting to those reagent methods shown in the package insert.

d) ***Expected values: We recommend a brief statement about the method(s) used to verify the expected results for this control.***

Pursuant to the teleconference, this issue has been resolved by the Bio-Rad Laboratories written response from December 2001. Therefore, no further labeling changes are necessary.

e) ***Quality Control: We suggest the sponsor include a quality control section recommending that each laboratory validates each lot of control with each specific assay system prior to its routing use in their laboratory.***

As stated in Section c.iv, *supra*, the Assignment of Values section expressly provides that the control must be validated by the end-user. The information provided may only be used as a guide when self-validating the control.

Because of this self-limiting feature of the control, Bio-Rad Laboratories reasonably believes that there is no need to place additional verbiage in the insert and requests an exemption from this requirement.

Attachment A:

Liquichek ToRCH Plus Control (K013716)
510(k) Documents

- Proposed Package Insert Originally Submitted with the 510(k)
- Summary from FDA of Issues in the 510(k) review
- Meeting Minutes from the Bio-Rad/FDA Conference Call on the 510(k)
- Bio-Rad 510(k) Response to FDA for Liquichek ToRCH Plus Control

Proposed Package Insert Originally Submitted with the 510(k) for Liquichek ToRCH Plus Control

[redacted]

Liquichek™ ToRCH Plus Control, Positive

LOT : XXXX0
XXXX1- Level 1
XXXX2- Level 2

EXP : YYYY MM DD

3577

INTENDED USE

Liquichek ToRCH Plus Control, Positive is intended for use as an assayed quality control serum to monitor the precision of laboratory testing procedures for the analytes listed in this package insert.

SUMMARY AND PRINCIPLE

The use of quality control materials is indicated as an objective assessment of the precision of methods and techniques in use and is an integral part of good laboratory practices.

REAGENT

Liquichek ToRCH Plus Control, Positive is prepared from human serum or processed plasma and preservatives. The control is provided in liquid form for convenience.

STORAGE AND STABILITY

Liquichek ToRCH Plus Control, Positive will be stable until the expiration date when stored unopened at 2-8°C. Once opened, all constituents will be stable for 60 days when stored tightly capped at 2-8°C. The vials should be stored upright to prevent leakage.

PROCEDURE

Liquichek ToRCH Plus Control, Positive should be treated and analyzed the same as patient specimens and run in accordance with the instructions accompanying the instrument, kit or reagent being used. Before sampling, allow the control to reach room temperature then gently swirl the contents to ensure homogeneity. Do not mix vial contents by inversion or by vigorous agitation.

LIMITATIONS

Liquichek ToRCH Plus Control, Positive should not be used past the expiration date.

If there is evidence of microbial contamination or excessive turbidity in the control, discard the vial.

Liquichek ToRCH Plus Control, Positive is not intended for use as a standard.

Liquichek ToRCH Plus Control, Positive is not an accuracy control and is not intended to have traceability to internationally recognized standards.

ASSIGNMENT OF VALUES

The mean values printed in this insert were derived from replicate analyses and are specific for this lot of Liquichek ToRCH Plus Control, Positive. The tests listed were performed by the reagent manufacturer and/or independent laboratories using manufacturer supported reagents and a representative sampling of this lot of control. Individual laboratory means should fall within the corresponding acceptable range; however, the values listed may vary during the life of this control. Variations over time and between laboratories may be caused by differences in laboratory technique, instrumentation and reagents, or by manufacturer test method modifications. It is recommended that each laboratory establish its own means and acceptable ranges and use those provided only as guides.

SPECIFIC PERFORMANCE CHARACTERISTICS

Liquichek ToRCH Plus Control, Positive is a stabilized liquid product manufactured under rigid quality control standards. To obtain consistent vial to vial assay values, the control requires proper storage and handling as described.

DISPOSAL

Dispose of control material in accordance with the requirements of local waste management authorities.

DAMAGE TO PACKAGING

In the event of damage to the packaging contact the local Bio-Rad Laboratories distributor or Bio-Rad Laboratories Technical Services.

WARNING

Human source material. Treat as potentially infectious.

Each serum/plasma donor unit used to manufacture this control was tested by FDA accepted methods and found non-reactive for Hepatitis B Surface Antigen (HBsAg), antibody to hepatitis C (HCV) and antibody to HIV-1/HIV-2. No test method can offer complete assurance that products containing human source materials will be absent of these and other infectious agents. This product may also contain other human source material for which there are no approved tests. In accordance with good laboratory practice, all human source material should be considered potentially infectious for Hepatitis B (HBV), Hepatitis C (HCV), HIV-1, HIV-2, HTLV-I, HTLV-II, and all other infectious agents; therefore, handle Liquichek ToRCH Plus Control, Positive with the same precautions used with patient specimens.

FOR IN VITRO DIAGNOSTIC USE

ANWENDUNG

Die Liquichek ToRCH Plus Control, Positive ist ein Kontrollserum, das dem Laborpersonal dient die Präzision der verwendeten Analyseverfahren, für die Analyte, die in dieser Packungsbeilage angegeben sind, beurteilen zu können.

EINLEITUNG

Die Anwendung entsprechender Qualitätskontrollmaterialien ermöglicht eine objektive Beurteilung der Qualität der im Labor angewendeten Methoden und Techniken als wesentlicher Bestandteil der Guten Laborpraxis (GLP).

REAGENZ

Liquichek ToRCH Plus Control, Positive wurde aus humanem Serum bzw. prozessiertem Plasma unter Verwendung von Konservierungsstoffen hergestellt. Die Kontrolle ist flüssig, gebrauchsfertig und dadurch sehr komfortabel in der Anwendung.

AUFBEWAHRUNG UND HALTBARKEIT

Ungeöffnet ist die Liquichek ToRCH Plus Control, Positive bei Aufbewahrung im Kühlschrank bei 2-8°C bis zum angegebenen Verfallsdatum haltbar. Nach dem Öffnen sind sämtliche Bestandteile 60 Tage stabil, wenn das Produkt gut verschlossen bei 2-8°C aufbewahrt wird. Die Fläschchen aufrecht lagern, um ein Auslaufen des Kontrollserums zu vermeiden.

GEBRAUCHSANWEISUNG

Die Liquichek ToRCH Plus Control, Positive ist genau wie eine Patientenproben in Übereinstimmung mit den Vorschriften, für das verwendete Gerät, den Kit oder das Reagenz, einzusetzen. Vor der Probennahme sollte die Kontrolle auf Raumtemperatur gebracht werden, danach vorsichtig durchmischen um die Homogenität für die entnommene Probe zu gewährleisten. - Nicht mit einer Wärmequelle auf Raumtemperatur bringen und nicht schütteln!

EINSCHRÄNKUNGEN

Die Liquichek ToRCH Plus Control, Positive soll nicht über das angegebene Verfallsdatum hinaus angewendet werden.

Bei Anzeichen von mikrobieller Kontamination oder einer starken Trübung ist das Fläschchen zu verwerfen.

Die Liquichek ToRCH Plus Control, Positive ist nicht geeignet für den Einsatz als Standard.

Die Liquichek ToRCH Plus Control, Positive ist nicht geeignet zur Überprüfung der Richtigkeit der Messung und auch nicht rückführbar auf international bekannte Standards.

WERTEERMITTLUNG

Die in diesem Datenblatt angegebenen Ergebnisse wurden von Reagenzienherstellern und/oder unabhängigen Referenzlaboratonen mit derzeit verfügbaren Reagenziensätzen und einer repräsentativen Anzahl an Kontrollfläschchen ermittelt. Jedes Labor sollte seine eigenen Kontrollgrenzen ermitteln und die angegebenen Werte als Orientierungshilfe betrachten. Die resultierenden Ergebnisse hängen von Variationen der verwendeten Instrumente, Reagenzien sowie der angewandten Techniken und Methoden ab. Daher sollte jedes Labor seine eigenen Präzisionsparameter erstellen und die angegebenen Bereiche lediglich als Orientierungshilfe ansehen.

SPEZIFISCHE EIGENSCHAFTEN DES PRÄPARATES

Die Liquichek ToRCH Plus Control, Positive ist ein flüssiges, stabilisiertes Produkt, das bei der Herstellung strengen Qualitätsnormen unterliegt. Richtige und präzise Ergebnisse erfordern sachgerechte Lagerung und Handhabung wie angegeben.

ENTSORGUNG

Das Material sollte den vorort geltenden Richtlinien entsprechend entsorgt werden.

BESCHÄDIGUNG DER PACKUNG

Falls die Packung beschädigt ist, ist die zuständige Bio-Rad Niederlassung zu kontaktieren.

WARNUNG

Alle Materialien humanen Ursprungs sollten als potentiell infektiös angesehen werden.

Jede, für die Herstellung dieser Kontrolle verwendete Serum-/Plasma-Spendereinheit wurde mit von FDA (Food and Drug Administration, USA) zugelassenen Methoden auf Hepatitis-B-Oberflächenantigen (HBsAg), Antikörper gegen Hepatitis C (HCV) und Antikörper gegen HIV-1/HIV-2 untersucht und für negativ befunden. Für den Nachweis von Infektionserregern gibt es jedoch keine absoluten Testmethoden. Demzufolge ist nicht auszuschließen, daß Materialien humanen Ursprungs Infektionserreger enthalten können. Dieses Produkt kann weitere, zusätzliche Bestandteile enthalten, für die es derzeit keine erprobten Methoden gibt. In Übereinstimmung mit den GLP Richtlinien (Gute Labor Praxis) sollten aus diesen Gründen alle Produkte die Humanmaterialien enthalten als potentiell infektiös für Hepatitis B (HBV), Hepatitis C (HCV), HIV-1, HIV-2, HTLV-I, HTLV-II und alle anderen Infektionskrankheiten betrachtet werden. Die Liquichek ToRCH Plus Control, Positive ist aus diesen Gründen mit den gleichen Vorsichtsmaßnahmen wie eine Patientenprobe zu handhaben.

IN VITRO-DIAGNOSTICUM

LEGEND

Temperature Limit // GERMAN // FRENCH // ITALIAN // SPANISH // PORTUGUESE // DANISH // SWEDISH // DUTCH // NORWEIGIAN	Use by // GERMAN // FRENCH // ITALIAN // SPANISH // PORTUGUESE // DANISH // SWEDISH // DUTCH // NORWEIGIAN
REF Catalog Number // GERMAN // FRENCH // ITALIAN // SPANISH // PORTUGUESE // DANISH // SWEDISH // DUTCH // NORWEIGIAN	EC REP Authorized representative // GERMAN // FRENCH // ITALIAN // SPANISH // PORTUGUESE // DANISH // SWEDISH // DUTCH // NORWEIGIAN
LOT Lot Number // GERMAN // FRENCH // ITALIAN // SPANISH // PORTUGUESE // DANISH // SWEDISH // DUTCH // NORWEIGIAN	CE Conformity Europe // GERMAN // FRENCH // ITALIAN // SPANISH // PORTUGUESE // DANISH // SWEDISH // DUTCH // NORWEIGIAN
Manufactured for // GERMAN // FRENCH // ITALIAN // SPANISH // PORTUGUESE // DANISH // SWEDISH // DUTCH // NORWEIGIAN	

BIO-RAD

Liquichek™ ToRCH Plus Control, Positive

LOT : XXXX0
XXXX1- Level 1
XXXX2- Level 2

EXP : YYYY MM DD

3577

UTILISATION

Liquichek ToRCH Plus Control, Positive est conçu pour l'utilisation au laboratoire comme sérum de contrôle de qualité dosé pour le suivi de la précision des méthodes de dosage ou de détection des paramètres répertoriés dans cette notice.

INTRODUCTION ET PRINCIPE

L'utilisation de matériel de contrôle de qualité est indiquée en tant qu'évaluation objective de l'exactitude et de la précision des méthodes et des techniques, et fait partie intégrante des Bonnes Pratiques de Laboratoire.

RÉACTIF

Liquichek ToRCH Plus Control, Positive est préparé à partir de sérum ou de plasma humain traité additionné de conservateurs. Pour plus de praticabilité, le contrôle se présente sous forme liquide.

CONSERVATION ET STABILITÉ

Liquichek ToRCH Plus Control, Positive est stable jusqu'à la date de péremption en flacon non ouvert et conservé à 2-8°C. Après ouverture du flacon, tous les composants restent stables pendant 60 jours s'ils sont conservés correctement bouchés à 2-8°C. Les flacons doivent être conservés en position verticale pour éviter les fuites.

MODE OPÉRATOIRE

Liquichek ToRCH Plus Control, Positive doit être traité et analysé dans les mêmes conditions que les échantillons de patients en suivant les instructions accompagnant l'instrument, la trousse utilisés. Avant utilisation, laisser le contrôle revenir à la température ambiante, puis agiter délicatement le contenu par rotation pour assurer une bonne homogénéisation. Ne pas mélanger le contenu du flacon par inversion ou agitation vigoureuse.

LIMITES

Ne pas utiliser Liquichek ToRCH Plus Control, Positive ne doit pas être utilisé après la date de péremption.

Tout flacon de contrôle présentant un signe de contamination microbienne ou de trouble excessif doit être éliminé.

Liquichek ToRCH Plus Control, Positive ne doit pas être utilisé comme un calibrant.

Liquichek ToRCH Plus Control, Positive n'est pas conçu pour vérifier l'exactitude dune mesure et il n'est pas comparable à des calibrants reconnus au niveau international

DÉTERMINATION DES VALEURS

Les valeurs moyennes imprimées sur la notice on été obtenues à partir d'analyses répétées plusieurs fois et sont spécifiques à ce n° de lot de Liquichek ToRCH Plus Control. Les paramètres indiqués ont été réalisés par les fournisseurs eux-mêmes ou par des laboratoires indépendants en utilisant les réactifs des fabricants sur un nombre de valeurs représentatif de ce lot de contrôle. Les moyennes d'un laboratoire doivent être comprises dans les intervalles acceptables correspondants; toutefois, les valeurs indiquées peuvent varier au cours de la vie du contrôle. Les variations dans le temps et les variations inter-laboratoires peuvent être dues aux différences de manipulations, aux instruments, aux réactifs, ou des modifications de réactif par le fournisseur. Il est recommandé à chaque laboratoires d'établir ses propres moyennes et intervalles acceptables et de n'utiliser celles fournies dans la notice qu'à titre indicatif.

CARACTÉRISTIQUES

Liquichek ToRCH Plus Control, Positive est un produit liquide stabilisé, fabriqué selon des normes de contrôle de qualité rigoureuses. Pour obtenir des valeurs de dosage stables d'un flacon à l'autre, le témoin doit être soumis aux conditions de conservation et de manipulation décrites dans cette notice.

ELIMINATION

Eliminer les matériaux de contrôle selon les procédures locales des autorités officielles.

Conditionnement endommagé

En cas de dommage du conditionnement, veuillez contacter votre filiale Bio-Rad locale.

ATTENTION

Matériel d'origine humaine. A considérer comme une source potentiellement infectieux.

Toutes les unités provenant de donneurs de sérum/plasma utilisées pour fabriquer ce témoin ont été testées par des méthodes approuvées par la FDA et ont été déterminées négatives pour l'antigène de surface de l'hépatite B (HBsAg), pour les anticorps dirigés contre l'hépatite C (HCV) et les anticorps dirigés contre HIV-1/HIV-2. Aucune méthode ne peut garantir l'assurance totale que des produits contenant une substance d'origine humaine sont exempts d'agents infectieux. Ce produit peut également contenir d'autres substances d'origine humaine pour lesquelles il n'existe pas encore de tests approuvés. Conformément aux bonnes pratiques de laboratoire, toute substance d'origine humaine doit être considérée comme une source de contamination possible par le virus de l'hépatite B (HBV), de l'hépatite C (HCV), du HIV-1, du HIV-2, du HTLV-I, du HTLV-II, et tous autres agents infectieux; il convient donc de manipuler Liquichek ToRCH Plus Control avec les mêmes précautions que les échantillons de patients.

USAGE DIAGNOSTIC IN VITRO

USO PREVISTO

Il Liquichek ToRCH Plus Control, Positive è un siero di controllo, dosato, formulato per il monitoraggio della precisione delle procedure di dosaggio del laboratorio per gli analiti elencati in questo inserto.

SOMMARIO E PRINCIPIO

L'uso di materiali di controllo è raccomandato per una valutazione obiettiva dell'accuratezza e precisione delle metodologie e tecniche in uso ed è parte integrante delle buone pratiche di laboratorio.

REATTIVO

Il Liquichek ToRCH Plus Control, Positive è preparato da siero umano o plasma processato e conservanti. Il controllo è in forma liquida per maggiore praticità.

CONSERVAZIONE E STABILITA'

Il Liquichek ToRCH Plus Control, Positive nella confezione originale, rimane stabile fino alla data di scadenza, se conservato a 2-8°C. Una volta aperto, tutti gli analiti sono stabili 60 giorni se il controllo è conservato, ben chiuso, a 2-8°C. I flaconi devono essere conservati verticali per prevenire perdite di liquido.

PROCEDURE

Il Liquichek ToRCH Plus Control, Positive deve essere trattato ed analizzato come i campioni dei pazienti, secondo le istruzioni che accompagnano lo strumento, il kit, o i reagenti in uso. Prima di utilizzarlo, lasciare il controllo a temperatura ambiente, quindi agitare delicatamente per assicurare l'omogeneità. Non miscelare il prodotto per inversione o con agitatori meccanici.

LIMITI

Il Liquichek ToRCH Plus Control, Positive non deve essere utilizzato oltre la data di scadenza.

In caso di evidente contaminazione microbica o di eccessiva torbidità del controllo scartare il flacone.
Il Liquichek Urine Toxicology Control, Positive non deve essere utilizzato come standard.

Il Liquichek ToRCH, Control Positive non è formulato per verificare l'esattezza della misura e non è equiparabile ai riconosciuti standard internazionali

ASSEGNAZIONE VALORI

Le medie riportate sull'inserto sono il risultato di analisi in replicato e sono specifiche per questo lotto di Liquichek ToRCH Contro, Positive. I valori riportati sono stati ottenuti dalle case produttrici dei kit e/o da laboratori di riferimento utilizzando i reattivi in commercio ed un campione rappresentativo di questo lotto di controllo. La media di ogni laboratorio dovrebbe cadere entro i limiti di accettabilità indicati, comunque i valori possono variare durante il periodo di validità del lotto del controllo; modifiche procedurali o dei reagenti tra laboratori differenti o modifiche da parte dei produttori dei kit, possono alterare il valore medio. Ogni laboratorio dovrebbe stabilire i propri parametri di precisione ed utilizzare i valori riportati sull'inserto solo come guida.

CARATTERISTICHE

Il Liquichek ToRCH Plus Control, Positive è un prodotto stabilizzato, preparato sotto un rigido controllo standard di qualità. Per ottenere una consistente uniformità di risultati da flacone a flacone, il controllo richiede una corretta conservazione ed un corretto uso come descritto.

SMALTIMENTO

Smaltire il materiale di controllo in accordo alle regolamentazioni in vigore.

CONFEZIONE DANNEGGIATA

In caso di danno alla confezione del prodotto contattare la Bio-Rad Laboratories.

ATTENZIONE

Materiale di origine umana.Trattare come potenzialmente infettivo.

Ogni unità donatore di siero o plasma utilizzata per preparare questo prodotto, è stata testata con metodi approvati dalla FDA ed è risultata negativa alla ricerca dell'antigene di superficie dell'epatite B (HBsAg) e negativa alla ricerca di anticorpi anti Epatite C (HCV) e anti HIV-1/HIV-2. Nessun metodo può garantire che prodotti contenenti materiali di origine umana siano privi di questi o di altri agenti infettivi. Questo prodotto potrebbe contenere anche altro materiale di origine umana per il quale non esistono metodi di analisi approvati. In accordo con le buone pratiche di laboratorio, tutti i materiali di origine umana devono essere considerati potenzialmente infettivi per Epatite B (HBV), Epatite C (HCV), HIV-1, HIV-2, HTLV-I, HTLV-II ed altri agenti infettivi; perciò si raccomanda di trattare il Liquichek ToRCH Plus Control, Positive con la stessa precauzione che si presta ai campioni dei pazienti.

PER USO DIAGNOSTICO IN VITRO

REF 227 227X 3 x 3 mL CE 0197

Printed: MMM. YY

BIO-RAD

Liquichek™ ToRCH Plus Control, Positive

3577

LOT : XXXX0
XXXX1- Level 1
XXXX2- Level 2

EXP : YYYY MM DD

USO INTENCIONADO

Liquichek ToRCH Plus Control, Positive tiene un uso intencionado como suero ensayado para el control de la calidad, con el fin de monitorizar la precisión de procedimientos de análisis del laboratorio para los analitos listados en este folleto.

RESUMEN Y PRINCIPIO

El uso de materiales de control de la calidad está indicado como una evaluación objetiva de la precisión de métodos y técnicas en uso y es una parte integral de las buenas prácticas de laboratorio.

REACTIVOS

Liquichek ToRCH Plus Control, Positive está preparado a partir de suero humano o plasma procesado y preservantes. El control se proporciona en forma líquida por conveniencia.

ALMACENAMIENTO Y ESTABILIDAD

Liquichek ToRCH Plus Control, Positive permanecerá estable hasta la fecha de caducidad si se almacena sin abrir entre 2-8ºC. Una vez abierto, todos los constituyentes permanecerán estables durante 60 días cuando se almacene bien tapado entre 2-8ºC. Los viales deben almacenarse en posición vertical para evitar pérdidas.

PROCEDIMIENTO

Liquichek ToRCH Plus Control, Positive debe tratarse y analizarse de igual modo que los especímenes de los pacientes y procesado de acuerdo con las instrucciones que acompañan al instrumento, equipo o reactivo a utilizarse. Antes del muestreo, permita que el control alcance la temperatura ambiental, luego agite suavemente el contenido para asegurar la homogeneidad. No mezcle el contenido del vial por inversión o por agitación enérgica.

LIMITACIONES

Liquichek ToRCH Plus Control, Positive no debe usarse después de la fecha de caducidad.

Si existiera evidencia de contaminación microbiana o excesiva turbidez en el control, desechar el vial.

Liquichek ToRCH Plus Control, Positive no tiene un uso intencionado como estandar.

Liquichek ToRCH Plus Control, Positive no está previsto para verificar la veracidad de medida y no es trazable a los estándares reconocidos internacionalmente.

ASIGNACIÓN DE VALORES

Los valores medios incluidos en este folleto son derivados de análisis repetidos y son específicos para este lote de Liquichek ToRCH Plus Control, Positive. Los tests listados fueron analizados por el fabricante de los reactivos y/o laboratorios independientes usando reactivos soportados por el fabricante y una muestra representativa de este lote del control. Los valores medios obtenidos por cada laboratorio individualmente deberían estar comprendidos dentro del rango aceptable correspondiente; sin embargo, los valores listados pueden variar durante la vida del control. Variaciones en el tiempo y entre laboratorios pueden ser debidas a diferencias entre la técnicas de cada laboratorio, instrumentos y reactivos o por modificaciones del fabricante en el método. Se recomienda que cada laboratorio establezca sus propias medias y rangos aceptables y utilicen los valores proporcionados en este folleto sólo como guía.

CARACTERÍSTICAS ESPECÍFICAS DE FUNCIONAMIENTO

Liquichek ToRCH Plus Control, Positive es un producto líquido estabilizado, fabricado bajo rigurosos estandares de control de calidad. Para obtener valores de ensayo consistentes de vial a vial, el control requiere almacenamiento y manipulación adecuada según lo descrito.

DESHECHAR

El deshecho de material de control debe realizarse de acuerdo con los requerimientos de las autoridades locales.

DAÑOS EN EL EMPAQUETAMIENTO

Si se observan daños en el empaquetamiento, contactar con el distribuidor local de Bio-Rad Laboratories o con atención al cliente.

PRECAUCIÓN

Material de origen humano. Trátelo como si fuera potencialmente infeccioso.

El suero/plasma de cada donante utilizado para la preparación de este control ha sido ensayado por métodos aceptados por la FDA y encontrado no reactivo frente al antígeno de superficie de la Hepatitis B (HBsAg), anticuerpos anti-hepatitis C (HCV) y anticuerpos frente a HIV-1/HIV-2. Ningún método puede ofrecer una seguridad completa de que los productos que contienen material de origen humano estén ausentes de éstos y otros agentes infecciosos. Este producto también podría contener otros materiales de origen humano para los que no existen ensayos aprobados. De acuerdo con las buenas prácticas del laboratorio, todo material de origen humano debe ser considerado potencialmente infeccioso para hepatitis B (HBV), hepatitis C (HCV), HIV-1, HIV-2, HTLV-I, HTLV-II, así como otros agentes infecciosos; en consecuencia, Liquichek ToRCH Plus Control, Positive debería ser tratado con las mismas precauciones utilizadas con las muestras de pacientes.

PARA USO DIAGNÓSTICO IN VITRO

UTILIZAÇÃO

Liquichek ToRCH Plus Control, Positive deve ser utilizado como um soro de controlo da qualidade não ensaiado para controlar a precisão dos procedimentos laboratoriais de análise para os analitos listados neste folheto informativo.

SUMÁRIO E PRINCÍPIO

A utilização de materiais de controlo da qualidade está indicada para a acessora dos objectivos de precisão das técnicas e métodos correntes e é parte integral das boas práticas laboratoriais.

REAGENTE

Liquichek ToRCH Plus Control, Positive é preparado a partir de soro humano ou plasma processado e preservativos. O controlo é fornecido na apresentação líquida para maior conveniência de utilização.

ARMAZENAMENTO E ESTABILIDADE

Liquichek ToRCH Plus Control, Positive é estável até ao fim da data de validade quando armazenado, por abrir, a 2-8ºC. Depois de aberto, todos os constituintes são estáveis por 60 dias, desde que armazenado fechado e selado a 2-8ºC. Os frascos devem ser guardados na vertical para evitar derrame de líquido.

PROCEDIMENTO

Liquichek ToRCH Plus Control, Positive deve ser tratado e analizado da mesma forma que as amostras de pacientes e utilizado de acordo com as instruções que acompanham o equipamento, dispositivo ou reagente em uso. Antes de colocar o controlo a uso permita que este equilibre à temperatura ambiente e de seguida agite-o suavemente para garantir homogeneidade. Não agite vigorosamente nem inverta o frasco como forma de garantir a homogeneização.

LIMITAÇÕES

Liquichek ToRCH Plus Control, Positive não deve ser utilizado como um calibrador.

Liquichek ToRCH Plus Control, Positive não dever utilizado para verificar a veracidade de resultados e não tem traçabilidade com relação a calibradores internacionalmente reconhecidos.

VALORIZAÇÕES

Os valores médios impressos neste folheto informativo foram obtidos a partir de análises repetidas e são específicos para este lote de Liquichek ToRCH Plus Control, Positive. Os testes listados foram executados pelo fabricante do reagente e/ou por laboratónos independentes que utilizam os reagentes de acordo com as especificações do fabricante e uma amostra significativa deste lote de controlo. Os valores obtidos no laboratóno deverão encontrar-se dentro da gama aceitável de valores apresentada; no entanto, os valores listados podem variar ao longo da existência deste controlo. Variações ao longo do tempo e entre laboratónos podem ser devidos a diferenças de técnicas, instrumentos ou reagentes, ou por modificações nas técnicas de teste pelo fabricante. É recomendado que cada laboratório estabeleça o seu valor médio e intervalo aceitável de valores e utilize estes apenas como guia.

CARACTERÍSTICAS ESPECÍFICAS DE DESEMPENHO

Liquichek ToRCH Plus Control, Positive é um produto líquido estabilizado fabricado sob os mais rígidos padrões de controlo da qualidade. Para obter valorizações consistentes de frasco para frasco o controlo deve ser manuseado e armazenado de acordo com o descrito.

ELIMINAÇÃO

Elimine o material de controlo da qualidade de acordo com as disposições locais em vigor para a eliminação de detritos biológicos.

ESTRAGOS NA EMBALAGEM

Na eventualidade de observar estragos na embalagem contacte a Bio-Rad Laboratories.

AVISO

Material de origem humana. Tratar como potencialmente infeccioso.

Cada unidade de soro/plasma doada e utilizada no fabrico deste controlo for testado com métodos aceitáveis pela FDA e determinada não reativa para o Antigénio de Superfície da Hepatite B (HbsAg), para o anticorpo contra o vírus da Hepatite C (HCV) e para o anticorpo contra o vírus HIV-1/HIV-2. Nenhum método de teste pode garantir a completa certeza de que produtos de origem humana não contenham estes ou outros agentes infecciosos. Este produto também pode conter outro material de origem humana para os quais não existem testes aprovados. De acordo com as boas práticas laboratoriais, todo o material de ongem humana deve ser considerado potencialmente infeccioso para a Hepatite B (HBV), Hepatite C (HCV), HIV-1, HIV-2, HTLV-I, HTLV-II e todos os outros agentes infecciosos; assim, manuseie o Liquichek ToRCH Plus Control, Positive com as mesmas precauções que utiliza para o manuseamento de amostras.

UTILIZAR APENAS EM DIAGNÓSTICO IN VITRO

REF 227
227X

3 x 3 mL

CE 0197

Printed: MMM. YY

BIO-RAD

Liquichek™ ToRCH Plus Control, Positive

3577

LOT : XXXX0
XXXX1- Level 1
XXXX2- Level 2

EXP : YYYY MM DD

使用目的

Liquichek ToRCH Plus Control, Positive は、表示値のない管理血清として、本説明書にリストされた対象物を分析する際、臨床試験室での検査の精度をモニターするために使用されます。

概要と基本理念

コントロールの使用は、方法や技術の精度を客観的に評価することを目的とします。

試薬

Liquichek ToRCH Plus Control, Positive はヒト血清あるいは血漿と保存剤から調製されています。

保存法と安定性

Liquichek ToRCH Plus Control, Positive は2~8°Cで未開封の状態で保存すれば使用期限まで安定です。一旦開封した後は、2~8°Cでフタをしっかり閉めておけば60日間はすべての成分が安定に保たれます。バイアルは漏れないように立てて保存してください。

操作上の注意

Liquichek ToRCH Plus Control, Positive を患者の検体と同様に使用中の機器、キット、試薬の取り扱い説明書にしたがって測定を行ってください。本コントロールを室温に戻し、ゆっくり回して内容物が均一であることを確かめてから、サンプリングを行います。逆さまにしたり、激しく振ったりしないでください。

使用上の注意

ラベルに記載された使用期限を過ぎた Liquichek ToRCH Plus Control, Positive は使用しないでください。バイアルを開けたり液を分けたりする時は微生物の混入を避けてください。コントロールに明らかに微生物が混入していたり、濁度の濁りがある場合は、破棄してください。

Liquichek ToRCH Plus Control, Positive は標準液としては使用できません。

性能特性

Liquichek ToRCH Plus Control, Positive は厳格な精度管理基準の下で調製された安定な液体です。バイアル間で一定の結果を得るためには、本コントロールを上述したように適切に保存し、取り扱うことが必要です。

注意

ヒトから採取して調整された材料ですので、感染の恐れがあります。十分に注意して取り扱ってください。

本製品の調製に使用している血清・血漿の各ドナーユニットは、FDAの認可を得た方法で検査されており、B型肝炎抗原(HBsAg)、C型肝炎抗体(HBC)およびHIV-1/HIV-2抗体に対して陰性反応であることが示されています。ヒトの試料を含むこのような製品に対する、感染物質の混入がないことを保証する検査法は、いまだに開発されていません。ヒトから採取されたすべての試料が、B型肝炎(HBV)、C型肝炎(HCV)、HIV-1、HIV-2、HTLV-I、HTLV-IIおよび他のすべての感染物質に感染されている恐れがあることを考慮する必要があります。したがって Liquichek ToRCH Plus Control, Positive を、患者の検体と同じように注意を払って取り扱ってください。

精度管理用

REF 227
227X

3 x 3 mL

CE 0197

Printed: MMM. YY

BIO-RAD

Liquichek™ ToRCH Plus Control, Positive

3577

LOT : XXXX0
XXXX1- Level 1
XXXX2- Level 2

EXP : YYYY MM DD

VARNING

Detta material är av humant ursprung och skall behandlas som potentiellt smittfarligt.

Varje givarenhet av serum/plasma som har använts till produktion av detta kontrollmaterial har blivit testade med FDA-godkända metoder och funnits icke-reaktiva för Hepatit C (HCV) och för antikroppar mot HIV-1/HIV-2. Inga testmetoder kan erbjuda fullständig säkerhet för att produkter innehållande material av humant ursprung inte innehåller dessa eller andra smittfarliga ämnen. Denna produkt kan också innehålla annat material av humant ursprung för vilka det ej finns någon godkänd test. I överensstämmelse med god laboratoriepraxis skall allt material av humant ursprung betraktas som potentiellt smittfarligt för Hepatit B (HBV), Hepatit C (HCV), HIV-1, HIV-2, HTLV-I, HTLV-II, och alla övriga infektiösa ämnen.

Hantera därför Liquicheck ToRCH Plus kontroll som positiv med samma försiktighetsåtgärder som för patientprov.

ADVARELSE

Humant materiale. Bør behandles som potentiel smittede materiale.

Alt donor materialet som indgår i denne kontrol er testede med FDA godkendte metoder og fundet negativ for Hepatitis B Surface Antigen (HBsAg), antistof overfor hepatitis C (HCV) og antistof overfor HIV-1/HIV-2. Men da ingen in vitro test garantere 100% sensitivtet mod disse eller andre infektioner og da der kan være en risiko for dette produkt indeholder andre smittekilder, anbefales det, at produktet behandles efter gældende GLP regleme, nemlig at alt humant materiale skal behandles som en potentiel smittekilde overfor Hepatitis B (HBV), Hepatitis C (HCV), HIV-1, HIV-2, HTLV-I, HTLV-II, og alle andre infektion sygdomme;

Derfor anbefaldelse det, at Liquichek ToRCH Plus Control Positive, behandles med same forsigtighed som en potentiel smittede patient prøve.

WAARSCHUWING:

Materiaal van humane oorsprong. Behandel materiaal als potentieel

infectieus. Iedere serum/plasma donor unit, gebruikt om deze controle te produceren, is getest door middel van door de FDA geaccepteerde methoden en is niet reactief met Hepatitis B Surface antigen (hBsAg), antilichamen tegen Hepatitis C (HCV) en antilichamen tegen HIV-1/HIV-2. Geen enkele testmethode kan complete zekerheid bieden, dat humaan materiaal bevattende producten vrij zijn van deze en andere infectieuze componenten. Dit product kan ook andere humane componenten bevatten, waarvoor nog geen gevalideerde testen bestaan. Volgens GLP normen moet al het materiaal van humane oorsprong behandeld worden als potentieel infectieus voor Hepatitis B (HBV), Hepatitis C (HCV), HIV-1, HIV-2, HTLV-1, HTLV-2 en alle andere infectieuze componenten.

Daarom dient men voor de Liquichek Torch Plus Control Positive, dezelfde voorzorgsmaatregelen te nemen zoals bij patientenmateriaal gebeurt.

ADVARSEL

Inneholder humant materiale. Behandles som potensielt smittestoff.

Alle donorenheter av serum/plasma som er benyttet i fremstillingen av dette produktet, er testet med FDA godkjente metoder, og funnet negative på hepatitt B overflateantigen (HBsAg), antistoff mot hepatitt C (HCV) og antistoff mot HIV-1 / HIV-2. Ingen godkjente testmetoder kan garantere at produkter som inneholder humant materiale ikke inneholder nevnte eller andre smittestoff. Dette produktet kan inneholde smittestoff det ikke finnes godkjente tester for. I samsvar med god laboratoriepraksis behandles alle produkter fra human kilde som potensielt smittestoff for hapatitt B (HBV), hepatitt C (HCV), HIV-1, HIV-2, HTLV-I, HTLV-II og andre infeksiöse smittestoff.

Liquichek ToRCH Plus Control behandles derfor på samme måte som pasientprøver.

REF 227
227X

3 x 3 mL

CE 0197

Printed: MMM. YY

ANALYTE / MANUFACTURER/ METHOD	UNITS	LOT XXXX0 MEAN	ACCEPTABLE RANGE
TOXOPLASMA GONDII IgG			
Abbott AxSYM	IU/mL	7.0	5.6 – 8.4
Abbott IMx	IU/mL	6.8	5.5 – 8.2
Beckman ACCESS	IU/mL	12.9	10.3 – 15.4
Bio-Rad EIA (1)	IU/mL	15.9	12.7 – 19.0
Diagnostic Products Immulite	IU/mL	18.1	14.5 – 21.7
Diagnostic Products Immulite 2000	IU/mL	19.2	15.4 – 23.1
DiaSorin EIA (1)	IU/mL	58.6	46.9 – 70.3
Radim EIA (1)	IU/mL	n/a	15.0 – 44.0
Roche COBAS Core EIA II (1)	IU/mL	14.7	6.0 – 24.9
SeraQuest ELISA	IU/mL	n/a	33.0 – 71.0
Wampole EIA	ISR	1.63	1.3 – 2.0
RUBELLA VIRUS IgG			
Abbott AxSYM	IU/mL	24.9	19.9 – 29.8
Abbott IMx	IU/mL	26.0	20.8 – 31.2
Beckman ACCESS	IU/mL	24.2	19.4 – 29.1
Bio-Rad EIA (1)	IU/mL	35.7	28.6 – 42.8
Diagnostic Products Immulite	IU/mL	19.6	15.7 – 23.6
Diagnostic Products Immulite 2000	IU/mL	22.5	18.0 – 27.0
DiaSorin EIA (1)	IU/mL	20.1	16.1 – 24.1
Radim EIA (1)	IU/mL	n/a	22.0 – 45.0
Roche COBAS Core EIA II (1)	IU/mL	21.5	13.6 – 29.3
SeraQuest (Measles IgG)	ISR	n/a	1.1 – 3.2
SeraQuest (Rubella IgG)	IU/mL	n/a	10.0 – 28.0
Wampole EIA	ISR	1.6	1.2 – 1.9
CYTOMEGALOVIRUS (CMV) IgG			
Abbott AxSYM	AU/mL	143.1	114.5 – 171.7
Diagnostic Products Immulite	ISR	8.0	6.4 – 9.6
Diagnostic Products Immulite 2000	ISR	8.8	7.1 – 10.6
DiaSorin EIA (1)	IU/mL	3.7	2.9 – 4.4
Radim EIA (1)	UR/mL	n/a	42.0 – 98.0
Roche COBAS Core EIA II (1)	IU/mL	8.7	6.5 – 10.9
SeraQuest (3)	ISR	n/a	1.8 – 5.4
Wampole EIA	ISR	1.9	6.5 – 10.9
HERPES SIMPLEX VIRUS TYPE 1 (HSV-1) IgG			
Radim EIA (1)		Positive	
Wampole ELISA	ISR	2.8	2.2 – 3.3
HERPES SIMPLEX VIRUS TYPE 2 (HSV-2) IgG			
Diagnostic Products Immulite	ISR	3.0	2.4 – 3.6
Roche COBAS Core EIA II (1)	ISR	0.9	0.5 - 1.3
Wampole EIA	ISR	1.3	1.0 – 1.5
HERPES SIMPLEX VIRUS TYPE 1 / 2 (HSV-1/2) IgG			
DiaSorin EIA (1)	ISR	6.9	5.6 – 8.3
Diagnostic Products Immulite	ISR	18.4	14.7 – 22.0
Roche COBAS Core EIA II (1)	ISR	3.2	2.7 – 3.7
SeraQuest (1)	ISR	n/a	2.4 – 7.4
VARICELLA-ZOSTER VIRUS (VZV)			
Radim EIA (1)		Positive	
SeraQuest (VZV IgG) (4)	ISR	n/a	1.3 – 3.3
SeraQuest (Mumps IgG)	ISR	n/a	1.1 – 3.3
Wampole EIA	ISR	3.3	2.6 – 3.9
HELICOBACTER PYLORI IGG			
Bio-Rad EIA (Helix)	ISR	1.1	1.0 – 1.7
Bio-Rad EIA (1)	ISR	2.1	1.7 – 2.5
Diagnostic Products Immulite	U/mL	1.1	0.9 – 1.3
Diagnostic Products Immulite 2000	U/mL	1.3	1.1 – 1.6
Roche COBAS Core EIA II (1)	U/mL	34.4	14.7 – 54.7
Wampole EIA	ISR	2.0	1.6 – 2.3
EPSTEIN BARR VIRUS VCA (EBV-VCA)			
DiaSorin EIA (1)	AU/mL	170.0	136.0 – 204.0
SeraQuest (EB VCA IgG)	ISR	n/a	1.8 – 5.4
SeraQuest (EBNA IgG) (2)	ISR	n/a	1.1 – 2.6
Trinity ELISA	ISR	4.7	3.8 – 5.6
***TREPONEMA PALLIDUM* (SYPHILIS) IgG**			
Diesse (Syphilis Screen Recombinant)	ISR	7.5	6.0 – 9.0
Diesse (Treponema IgG)	ISR	3.4	2.7 – 4.1
NEW Market Laboratories (TPHA) (1)		Positive	
NEW Market Laboratories (Total Antibody EIA) (1)		Positive	
SYPHILIS RAPID PLASMA REAGIN (RPR)			
Becton Dickinson		Reactive	
NEW Market Laboratories (1)		Reactive	
SciMedix		Reactive	

FOOTNOTES

(1) Test/kit not available in the U.S.

(2) A 1:5 dilution should be made prior to running those tests where the value listed exceeds the highest standard

(3) A 1:3 dilution should be made prior to running those tests where the value listed exceeds the highest standard

(4) A 1:2 dilution should be made prior to running those tests where the value listed exceeds the highest standard

NOTE

(1) FRENCH TRANSLATION
(2) FRENCH TRANSLATION
(3) FRENCH TRANSLATION
(4) FRENCH TRANSLATION

FUSSNOTEN

(1) GERMAN TRANSLATION
(2) GERMAN TRANSLATION
(3) GERMAN TRANSLATION
(4) GERMAN TRANSLATION

NOTE A PIE' PAGINA

(1) ITALIAN TRANSLATION
(2) ITALIAN TRANSLATION
(3) ITALIAN TRANSLATION
(4) ITALIAN TRANSLATION

NOTAS A PIÉ DE PÁGINA

(1) SPANISH TRANSLATION
(2) SPANISH TRANSLATION
(3) SPANISH TRANSLATION
(4) SPANISH TRANSLATION

control Try other products from Bio-Rad's comprehensive line of Liquichek™ and Lyphochek® controls and data management programs.

Testez les autres produits des gammes Liquichek™ et Lyphochek® et les programmes de Contrôle de Qualité.

• • •

Testen Sie auch weitere Produkte aus der umfassenden Produktlinie der Bio-Rad Liquichek™ und Lyphochek® Kontrollen und der Datenmanagement-Programme.

• • •

Prova altri prodotti dalla completa linea di controlli Bio-Rad Liquichek™ e Lyphochek® e i programmi per la gestione dei dati.

• • •

Pruebe otros productos de la línea de controles de Bio-Rad, Liquichek™ y Lyphochek®, así como de los programas para la gestión de los datos de Control de la calidad.

Autoimmune
ANA Control, Centromere Pattern
ANA Control, Homogeneous Pattern
ANA Control, Nucleolar Pattern
ANA Control, Speckled Pattern
ANA Control, EIA Screen
Anti-dsDNA Control, EIA
Anti-Jo-1 Control, EIA
Anti-RNP Control, EIA
Anti-Scl-70 Control, EIA
Anti-Sm Control, EIA
Anti-SS-A Control, EIA
Anti-SS-B Control, EIA
ENA Control, EIA Screen

Blood Gas
Blood Gas Control
Blood Gas Plus CO-Oximeter Control (Bayer 800 Series)
Blood Gas Plus CO-Oximeter Control (IL)
Blood Gas Plus CO-Oximeter Control (Radiometer)
Blood Gas Plus E Control
Blood Gas Plus EGL

Cardiac
Cardiac Markers Control
Cardiac Markers Control LT
CK/LD Isoenzyme Control
Homocysteine Control

Chemistry
Assayed Chemistry Control
Assayed & Unassayed Multiqual®
Assayed QCS®
Lipids Control
Pediatric Control
Quantitative Urine Control
Unassayed Chemistry Control (Human)
Urinalysis Control
Urine Chemistry Control

Drugs of Abuse
Blind Performance Specimens
DAU 3, 4 Controls
REMEDI™ Control
Urine Toxicology Control
Urine Toxicology Negative Control
Urine Toxicology Control Level C1, C2, C3 & C4
Urine Toxicology Control Level C2 & C3 Low Opiate
Urine Toxicology Control Level S1, S2 & S3
Urine Toxicology Control Level S1 & S2 Low Opiate
Qualitative Urine Toxicology Control

Hemoglobin
Diabetes Control
Hemoglobin A_2 Control
Hemoglobin A_{1c} Linearity Set

Hematology & Coagulation
Coagulation Control
Hematology-16 Control
Hematology Control (A)
Hematology Control (C)
Reticulocyte Control
Reticulocyte Stain
Sedimentation Rate Control

Immunoassay
Anemia Control
Fertility Control
Hypertension Markers Control
Immunoassay Plus Controls
Maternal Serum Control
Tumor Marker Control

Immunology/Protein
Immunology Control
Immunology Plus Control
Rheumatoid Factor Control
Spinal Fluid Control

Molecular Biology
Amplichek™ BCR/ABL Control

Seroconversion & Antigen Panels
HIV-1 HAV Rubeola
HCV CMV
HBV Rubella

* For research use only. Not for use in diagnostic procedures.

Specialty
Endocrine Control
Ethanol/Ammonia Control
Serum Alcohol Control
Serum Volatiles Control
Urine Bone Markers Control
Urine Metals Control
Whole Blood Control
Whole Blood Metals Control
Whole Blood Tox Control

Therapeutic Drug Monitoring
Benzo/TCA Control-Set A
Benzo/TCA Control-Set B
Drug Free Serum
Therapeutic Drug Monitoring Controls

External Quality Assurance Services (EQAS)
Clinical Chemistry
Immunoassay
Therapeutic Drug Monitoring

Data Management Solutions
Hands-Free QC™
• UNITY Pro/Plus™
• QCNet™

BIO-RAD
Bio-Rad Laboratories

For complete product information contact your local Bio-Rad office or sales representative. In the United States, call 1-800-2-BIO-RAD. Or visit our website at www.bio-rad.com.

5/01

Level 1 - Lot XXXX1

Level 2 - Lot XXXX2

Exp. Date: YYYY MM DD

MANUFACTURERS LISTED / AUFGELISTETE HERSTELLER
LISTE DES FABRICANTS / ELENCO DEI PRODUTTORI

ANALYTE LIST

Toxoplasma gondii IgG
Rubella Virus IgG
Cytomegalovirus (CMV) IgG
Herpes Simplex Virus Type 1 (HSV-1) IgG
Herpes Simplex Virus Type 2 (HSV-2) IgG
Varicella-Zoster Virus (VZV) IgG
Helicobacter pylori IgG
Epstein-Barr Virus (EBV) VCA IgG
Treponema pallidum (Syphilis) IgG
Syphilis Rapid Plasma Reagin (RPR)

Authorized Representative
Bio-Rad Laboratories S.A.
3 boulevard Raymond Poincaré
92430 Marnes-la-Coquette
Phone: (33) 1-4795-6000 / Fax: (33) 1-4741-9133

BIO-RAD

Bio-Rad Laboratories
Diagnostics Group

9500 Jeronimo Road
Irvine, California 92618
(800) 854-6737
(949) 598-1200
Telefax (949) 598-1550

Technical Service:
(800) 854-6737

***UNITED STATES CUSTOMER SERVICE:** 4000 Alfred Nobel Drive • Hercules, California 94547 • Phone (800) 2-BIO-RAD • Telefax (510) 741-6373*

***AUSTRALIA,** Bio-Rad Laboratories Pty. Ltd. Unit 1 Block Y, 391 Park Road, Regents Park NSW 2143 • Phone 61-2-9914-2800 • Telefax 61-2-9914-2888*
***AUSTRIA,** Bio-Rad Laboratories Ges.m.b.H., Auhofstrasse 78D, A-1130 Vienna • Phone 43-1-877-6901 • Telefax 43-1-876-5629*
***BELGIUM,** Bio-Rad S.A.-N.V. Begoniastraat 5, B-9810 Nazareth Eke • Phone 32-9-385-5511 • Telefax 32-9-385-6554*
***BRAZIL,** Bio-Rad do Brasil, Rua dos Invalidos 212, 5 Andar, Lapa CEP 20231-020, Rio de Janeiro • Phone 5521-2507-6191 • Telefax 5521-2224-6524*
***CANADA,** Bio-Rad Laboratories, Ltd., 2403 Guénette Montreal, Québec H4R2E9 • Phone 1-514-334-4372 • Telefax 1-514-334-4415*
***CZECH REPUBLIC,** Bio-Rad spol. s.r.o., Ned ostrovem 1119/7, 147 00 Prague 4 • Phone 420-2-41430532 • Telefax 420-2-41431642*
***CHINA,** Bio-Rad China Limited, 18F/D Hai Li Building, No. 88 Da Pu Road, Shanghai 200023 • Phone 86-21-63052255 • Telefax 86-21-53964775*
***DENMARK,** Bio-Rad Laboratories, Generatorvej 8 C, 2730 Herlev • Phone 45-4452-1000 • Telefax 45-4452-1001*
***FINLAND,** Bio-Rad Laboratories, Pihatorma 1 A, FIN-02240 Espoo • Phone 358-9-804-22-00 • Telefax 358-9-804-11-10*
***FRANCE,** Bio-Rad S.A., 3 boulevard Raymond Poincaré 92430 Marnes-la-Coquette • Phone 33-1-4795-6000 • Telefax 33-1-4741-9133*
***GERMANY,** Bio-Rad Laboratories GmbH, Heidemannstrasse 164, D-80939 Munich • Phone 49-89-318840 • Telefax 49-89-318-84100*
***HONG KONG,** Bio-Rad Pacific Ltd., Unit 1111, 11F, New Kowloon Plaza 38, Tai Kok Tsui Rd., Tai Kok Tsui, Kowloon • Phone 852-2789-3300 • Telefax 852-2789-1257*
***INDIA,** Bio-Rad Laboratories (India) Pte. Ltd., B&B1, Enkay Towers, Vanijya Nikunj, Udhyog Vihar, Phase-V, Gurgaon, 122016 Haryana • Phone 91-124-6398112 • Telefax 91-124-6398115*
***ISRAEL,** Bio-Rad Laboratories Ltd., 14 Homa Street, New Industrial Area, Rishon Le Zion 75655 • Phone 972-3-9514127 • Telefax 972-3-9514129*
***ITALY,** Bio-Rad Laboratories S.r.l., Via Cellini 18/A, 20090 Segrate, Milan • Phone 39-02-216091 • Telefax 39-02-21609-396*
***JAPAN,** Nippon Bio-Rad Laboratories, 7-18, Higashi-Nippori 5-chome, Arakawa-ku, Tokyo 116-0014 • Phone 81-3-5811-6290 • Telefax 81-3-5811-6282*
***KOREA,** Bio-Rad Korea Ltd., B1, Cambridge Building, 1461-15, Seocho-Dong, Seocho-Gu, Seoul, 137-070 • Phone 82-2-3473-4460 • Telefax 82-2-3472-7003*
***LATIN AMERICA,** Bio-Rad Latin America, 14100 Palmetto Frontage Road, Suite 101, Miami Lakes, Florida 33016 • Phone 305-894-5950 • Telefax 305-894-5960*
***MEXICO,** Bio-Rad Laboratorios Mexico, S.A. de C.V., Adolfo Prieto No 1653, Colonia Del Valle, 03100 Mexico, D.F. • Phone 525-534-2552 • Telefax 525-524-5555*
***THE NETHERLANDS,** Bio-Rad Laboratories BV, Fokkerstraat 10, 3905 KV Veenendaal • Phone 31-318-540666 • Telefax 31-318-542216*
***NEW ZEALAND,** Bio-Rad New Zealand, Unit B 156 Bush Road, Albany, Auckland • Phone 64-9-415-2280 • Telefax 64-9-415-2284*
***NORWAY,** Bio-Rad Laboratories, Johan Scharffenbergs vei 91, N-0694, Oslo • Phone 47-23-38-41-30 • Telefax 47-23-38-41-39*
***POLAND,** Bio-Rad Laboratories, ul Barburki 8, 04511 Warsaw • Phone 48-22-815-39-51 • Telefax 48-22-812-66-82*
***PORTUGAL,** Bio-Rad Laboratories, Rua do Entreposto Industrial, 3-1° Esq., 2724 - 513, Amadora • Phone 351-21-472-7700 • Telefax 351-21-472-7777*
***RUSSIA,** Bio-Rad Laboratories Ltd., 37A/14 Leningradsky Pr., 125167 Moscow • Phone 7-095-721-14-00 • Telefax 7-095-721-14-12*
***SINGAPORE,** Bio-Rad Laboratories (Singapore) Pte. Ltd., 211 Henderson Road #03-02, Henderson Industrial Park, 159552 • Phone 65-272-9677 • Telefax 65-273-4835*
***SOUTH AFRICA,** Bio-Rad Laboratories (Pty) Ltd., 34 Bolton Road, Parkwood, Johannesburg 2193 • Phone 27-11-442-85-08 • Telefax 27-11-442-85-25*
***SPAIN,** Bio-Rad Laboratories S.A., Lopez de Hoyos 245-247, 28043 Madrid • Phone 34-91-590-5200 • Telefax 34-91-590-5211*
***SWEDEN,** Bio-Rad Laboratories A.B., Vintergatan 1, Box 1097, S-172 22, Sundbyberg • Phone 46-8-555-127-00 • Telefax 46-8-555-127-60*
***SWITZERLAND,** Bio-Rad Laboratories, Nenzlingerweg 2, CH-4153 Reinach BL • Phone 41-61-717-95-55 • Telefax 41-61-717-95-50*
***THAILAND,** Bio-Rad Laboratories Ltd., 1st & 2nd Floor, Lumpini I Bldg., 239/2 Rajdamri Rd., Lumpini, Pathumwan, Bangkok 10330 • Phone 662-651-8311 • Telefax 662-651-8312*
***UNITED KINGDOM,** Bio-Rad Laboratories Ltd., Bio-Rad House, Maylands Ave., Hemel Hempstead, Herts HP2 7TD • Phone 44-208-328-2000 • Telefax 44-208-328-2550*

©2001 ALL RIGHTS RESERVED. PRINTED IN U.S.A.

10/01

Manufactured for / Hergestellt für / Fabriqué pour / Prodotto per / Fabricado para / Manufaturado para Bio-Rad Laboratories

Summary from FDA of Issues in the 510(k) Review for Liquichek ToRCH Plus Control

FDA'S OFFICE OF DEVICE EVALUATION
DIVISION OF CLINICAL LABORATORY DEVICES
MICROBIOLOGY BRANCH
FAXING

2098 Gaither Road, HFZ-440
Rockville, Maryland 20850

Phone No.: (301) 594-2096
Fax No.: (301) 594-5940 or (301) 594-5941

"THIS DOCUMENT IS INTENDED ONLY FOR THE USE OF THE PARTY TO WHOM IT IS ADDRESSED AND MAY CONTAIN INFORMATION THAT IS PRIVILEGED, CONFIDENTIAL, AND PROTECTED FROM DISCLOSURE UNDER APPLICABLE LAW. If you are not the addressee, or a person authorized to deliver the document to the addressee, you are hereby notified that any review, disclosure, dissemination, copying, or other action based on the content of this communication is not authorized. If you have received this document in error, please immediately notify us by telephone and return it to us at the above address by mail. Thank you."

DATE: 12/6/01 Fax No.: 949-598-1555

TO: Yvette Lloyd

FROM: Kathy Wright

No. of pages (including cover sheet): 4

COMMENTS: Enclosed are our issues. We may discuss this further if you like.
Again, be advised your submission will be placed on phone hold.

NOTE: Please advise if transmission is illegible.

Thanks

Kathy

The issues which suggest a response from the sponsor are indicated as ***bolded italics.***

REVIEW:

Administrative The sponsor has provided a 510(k) summary, labeling which consists of package labels and a draft package insert (PI), a "value assignment protocol," a Summary of Safety and Effectiveness, a PI to the predicate, a Truthful and Accurate statement, and an Indications for Use statement. The administrative aspect of the submission is well organized and each indicated aspect is separated numerically and appears to be adequate. ***In the future it would be helpful if the sponsor also numbered each page within sections in order to facilitate communication with the sponsor.***

The sponsor has provided examples how they derived an assigned value for each of the analytes of their control material. Discussion follows:

a) ***The first page discussion, section 6, states that the value assignment for the Abbott Tumor Marker is generated..... The sponsor should indicate how this is relevant to this device.***

b) On the first page of section 6 the second to last paragraph has a disclaimer that values are provided simply "as a guide" and that "each laboratory should establish [their] own means and acceptable range(s)." ***As an assayed control, this value should not be considered a 'guide' but is considered a true value for a particular lot of material. Therefore, this we recommend a statement be presented in the PI but rewritten to reflect this concept.***

c) There are provided protocols which contain two different sets of instructions for assay manufacturers and for reference laboratories. The sponsor recommends (first protocol) that assay manufacturers run this device for a minimum of 20 replicates whereas the reference laboratories' instructions (second protocol) are for a different function. The manufacturers are to test this device for reproducibility and establishing a mean and range. The reference labs are apparently to use this device as a specimen would be used. ***However, it is unclear why this investigator is requested to supply results of cutoff values, sample to cutoff ratios, clinical interpretation and quality control sample to cutoff ration values (see comment #9). It is puzzling what sample(s) the sponsor wants this information for and how the data can be used for this device. Was the protocol(s) specifically followed?***

d) ***Because there is indication that 20 replicates were performed, we believe this constitutes reproducibility testing. We would welcome these results to be presented as standard deviation (SD) and percent coefficient of variation (%CV) in order to further evaluate its value as a assayed control material.***

e) ***We recommend the sponsor provide a Financial Disclosure Form from each investigator participating in these studies.***

f) ***We suggest the sponsor provide the statistical format for calculating the acceptable range(s) of results for each analyte and for each instrument (if different) using their device.***

g) ***How is this device to be utilized if a user has plasma for specimen testing and it appears that performance data was obtained only from serum?***

Labeling

The following dialogue involves both the existing draft PI and further suggestion(s) by FDA:

a) Intended Use: ***Because the sponsor considers this an assayed device, we believe each legally marketed system for which the device's levels determined should be indicated, e.g., Abbott's AxSYM and Abbott's Imx. In addition, each organism should be cited as well.***

This would also be the same for their Indications for Use statement.

b) Reagents:

i) Warnings: ***We believe the sponsor should specify what their 'processed' plasma is and indicate that their device is not intended for use with assays which recommend using anticoagulated specimens.***

ii) ***Because the sponsor states (sect 2, page 3 of 3) that stability studies have been performed with this device, 60 days opened and 3 years, 3 months for unopened (both at 2-8°C), we suggest they provide representative data to FDA. We suggest the sponsor also indicate whether the stated unopened stability is from real time or accelerated time determination.***

c) Limitations

i) ***We recommend the sponsor state, "These ToRCH Controls are not considered calibrators and are not to be used for assay calibration."***

ii) ***We suggest, "These controls are not intended to replace the manufacturer's controls supplied with their kits."***

iii) ***We additionally recommend the following, "The ToRCH Controls are matrix specific and are intended for use only when testing serum specimens."***

iv) ***Because this device has been established with specified assays, a statement is advised for limiting this device to those systems listed in the Intended Use and Indications for Use. Alternatively, the sponsor could say that performance characteristics have not been established for assays other than those listed in the Intended Use section.***

d) Expected Values: ***We recommend a brief statement about the method(s) used to verify the expected results for this control.***

e) Quality Control: ***We suggest the sponsor include a quality control section recommending that each laboratory validate each lot of control with each specific assay system prior to its routing use in their laboratory.***

BIO-RAD

Bio-Rad Laboratories

Diagnostics Group
9500 Jeronimo Road
Irvine, California 92618-2017
Telephone: (949) 598-1200

FACSIMILE

Meeting Minutes from the Bio-Rad/FDA Conference Call on the 510(k) for Liquichek ToRCH Plus Control

Date: January 16, 2002

To: Kathy Wright
Food and Drug Administration
Center for Devices and Radiological Health
Office of Device Evaluation
Division of Clinical Laboratory Devices
Microbiology Branch
Document Control Center (HFZ-440)
2098 Gaither Road.
Rockville, MD 20850

Fax: (301) 594-5940

Phone: (301) 594-2096

From: Yvette Lloyd
Bio-Rad Laboratories, Irvine
(949) 598-1465 – phone
(949) 598-1555 - fax

Subject: K013716 Conference Call

Pages: 10 (including Cover Sheet)

Original copies will be sent via regular mail.