



1

1

Dockets Management Branch
February 2, 2004
Page 1 of 12

February 2, 2004

Dockets Management Branch
Food and Drug Administration
Department of Health and Human Services, Room 1-23
12420 Parklawn Drive, Rockville, MD 20857

Citizen Petition

Dear Sir or Madam:

The undersigned submits this petition under section 10.30 of Title 21, Code of Federal Regulations, to request the Commissioner of Food and Drugs to issue a written opinion stating that Bio-Rad's longstanding practice, previously accepted by the agency, of developing unified, truthful labeling for domestic and international sales of its control products is lawful.

A. Action Requested

Specifically, we request that the Food and Drug Administration (FDA) issue an opinion containing the following statement:

Truthful references in labeling to test kits that are not legally available for use in the United States with Bio-Rad's control products do not adulterate or misbrand such control products, so long as a conspicuous disclaimer appears in adequate proximity to the unapproved test kit. Disclaimers that are noted and appear in the same type face as the test kit are adequate to satisfy the agency's concern that Bio-Rad's labeling not promote an unapproved use. Bio-Rad's labeling may refer to test kits that have not been approved or cleared for use domestically if the labeling includes such disclaimers. The agency has reviewed sample unified labeling submitted by Bio-Rad, and believes the form and content of the labeling, and particularly the disclaimers contained in the labeling, are sufficient and lawful.

B. Statement of Grounds

Bio-Rad markets several control products for use in laboratory procedures in the United States and the rest of the world. The products for sale in the domestic and foreign markets have unified labeling that lists analytes and test kits for which the Bio-Rad products can be used as controls, most of which have been cleared or approved by FDA, but some have not. The mention of uncleared/unapproved test kits is followed by a footnote that states their FDA status, e.g., "[t]est kit/instrument not available in the

USA.” Such footnotes have appeared in for Bio-Rad’s labeling for almost twenty years without FDA objection until recently, when FDA challenged the legality of such labeling.

We are writing to contest FDA’s assertion that labeling for Bio-Rad’s test kit controls is now illegal and to ask that the agency issue a statement similar to the one above expressly stating that references in labeling for Bio-Rad’s controls to test kits that cannot be legally marketed in the United States is legal so long as the company includes appropriate disclaimers in such labeling. FDA has objected to Bio-Rad’s practice of referring to test kits not legally available for diagnostic use with the Bio-Rad control in the labeling for these devices, even though a footnote identifies test kits that are not cleared for such use in the United States. We have discussed FDA’s objections with several agency officials, and reviewed the agency’s argument in light of First Amendment case law that limits government restrictions on commercial speech. We believe that FDA’s position that Bio-Rad may not refer in its labeling to test kits that are not approved or cleared for commercial distribution is illegal and not within the least burdensome spirit. Specifically, the First Amendment forbids FDA from regulating Bio-Rad’s labeling to indirectly encourage product submissions or prevent future, hypothetical off-label use, and requires that if FDA is to regulate commercial speech, the agency must do so by the least restrictive means. FDA’s attempted suppression of Bio-Rad’s labeling fails because the less restrictive option of requiring disclosure of the unapproved/uncleared status of the test kits adequately serves FDA’s and the public’s interest in regulating Bio-Rad’s labeling. Further, the Federal Food, Drug, and Cosmetic Act (the “Act”) expresses a preference for disclaimers over other means of regulating speech.

I. REFERENCES IN BIO-RAD’S LABELING TO UNAPPROVED TEST KITS HAVE APPEARED FOR MANY YEARS AND DO NOT GIVE RISE TO THE USUAL CONCERNS ABOUT UNAPPROVED USES.

A. FDA Has Historically Permitted Bio-Rad to Refer to Unapproved Test Kits in Its Labeling.

Bio-Rad markets several products that are intended as controls for laboratory procedures. Among the control products marketed by Bio-Rad are the Lyphochek Immunoassay Plus Control and the Lyphochek Tumor Marker Control, both of which have in their labeling lists of analytes and test kits for which the Bio-Rad products can be used as controls. Some of the test kits referred to in the labeling have not been cleared or approved by FDA.

In labeling for the Lyphochek Immunoassay Plus Control, the mention of such test kits is followed by a footnote that reads: “Test kit/instrument not available in the USA.”

In labeling for the Lyphochek Tumor Marker, the footnote reads: "Test kit/instrument has not been approved or cleared by the FDA for this analyte. Please refer to 21 C.F.R. § 809.30 for additional information regarding the regulation of analyte specific reagents".

Bio-Rad Laboratories has been using similar footnotes for control products since the early 1980's. Bio-Rad received 510(k) clearance to market for numerous products that have package inserts containing similar footnotes for analytes and test kits that are not recognized by the FDA. No issues were raised during the review process.

Historically, there were actually two of Bio-Rad products that DCLD requested regional labeling during the 510(k) review processes in 1989 that contained analytes that the FDA did not recognize and therefore did not have any cleared testing method. [Lyphochek Urine Metals Control (K891691), Lyphochek Tumor Marker Control (K8916080)]. Bio-Rad was informed during another 510(k) review in 1998 that FDA had changed their position and would allow the analytes without any cleared testing methods to be listed in the package inserts for third party control products with a footnote indicating clearance status. Through work with DCLD to consolidate regional labeling for these products, new 510(k)s were submitted that received premarket clearance for both products [Lyphochek Urine Metals Control (K990928), Lyphochek Tumor Marker Control (K983807)]. Bio-Rad has not had any further comments occur during the 510(k) process regarding footnotes for uncleared kits until the Liquichek ToRCH Plus Control 510(k) in 2001 (K013716).

In 2001, Bio-Rad submitted a premarket notification to FDA for the Liquichek ToRCH Plus Control. Certain test kits listed in the labeling were followed by the footnote "Test/kit not available in the U.S." In discussions with Bio-Rad, FDA reviewers expressed the opinion that listing unapproved/uncleared reagent kits was illegal. The Office of Device Evaluation had apparently determined that the previous practice of allowing truthful statements about uncleared in vitro products rendered the devices adulterated and misbranded, and directed the Division of Clinical Laboratory Devices to disallow such statements. See Attachment A.

Unless Bio-Rad can make such statements, the company will be required to develop, at great expense, unique labeling for marketing for most of its control products in the United States. Bio-Rad is sincerely interested in responding to the agency's concerns. To this end, the Company has unified labeling with conspicuous disclaimers placed in proximity to the test kits that are unavailable for use domestically. Enclosed with this petition is a sample of Bio-Rad's unified labeling. See Attachment B. We request that the agency make a finding that this labeling is lawful.

B. FDA Must Align its Position on Unapproved Uses With First Amendment Law.

ODE officials take the position that references in labeling to use of Bio-Rad controls for test kits that are not legally marketed in the United States adulterates and misbrands the Bio-Rad products because they are labeled for uses that have not been approved in an application for premarket approval or cleared in a 510(k).¹ See 21 CFR § 801.4. Bio-Rad believes that CDRH is concerned about the promotion of off-label use and may not consistently view a disclaimer as an adequate means of addressing such abuses.

As discussed below, the Center's position is at odds with several recent court decisions that have found specific FDA restrictions on labeling and promotional materials to violate the First Amendment. In response to these decisions, FDA has published a notice and request for comments in the *Federal Register*, seeking public input on the agency's approach to regulating these materials. See 67 *Federal Register* 34,942 (May 16, 2002). In this Notice, the agency acknowledged "there may be some tension between some aspects of FDA's authority and judicial developments." *Id.* At 34,943. We believe the Center's determination concerning Bio-Rad's labeling is an example of such tension. In keeping with the agency's interest in aligning its regulation of commercial speech with First Amendment requirements, FDA must permit Bio-Rad to market its product with unified labeling, provided the labeling includes appropriate disclaimers, and is truthful and not misleading.

C. Labeling For Bio-Rad's Controls Does Not Raise the Usual Concerns Associated with Labeling for Unapproved Uses.

The agency's concern that a general rule permitting reference to unapproved use, even with a disclaimer, could undermine FDA's premarket review authority rests on the assumption that users view labeling that refers to a use with a disclaimer concerning FDA review as no different than similar labeling without the disclaimer. In other words, the agency assumes the disclosure is, by definition, ineffective. Bio-Rad disagrees with this assumption, because we believe device users value FDA review as an assurance that a device is safe and effective for a particular use. Further, the users of Bio-Rad's controls are sophisticated professionals, e.g., clinical laboratory technicians, who understand that controls must be validated for use with an assay to provide reliable results, and that without FDA oversight, the safety and effectiveness of such products may not be assured. More importantly, however, three factors distinguish Bio-Rad's controls and

¹ Section 501(f)(1)(B) of the Federal Food, Drug, and Cosmetic Act provides that a device is adulterated if it is classified under the Act's automatic classification provisions, not exempt from premarket approval, and not approved. Section 502(o) of the Act provides that a device is misbranded if "a notice or other information respecting it was not provided as required by ...section 510(k)."

labeling from the usual situation in which FDA objects to an unapproved use. These factors make the agency's general concern inapplicable to Bio-Rad's labeling.

Unapproved Test Kits Identified In Labeling for Bio-Rad's Controls Are Not Available in the U.S. First, Bio-Rad's labeling for its control kits creates no threat of unapproved use of the company's 510(k) cleared controls because unapproved/uncleared products listed in its labeling cannot be obtained in the United States for diagnostic use. Thus, the agency can permit Bio-Rad's unified labeling without upsetting FDA's usual policy of not allowing unapproved uses to appear on device labeling because the concern addressed by this policy – that devices will be used in ways that the agency has not reviewed and cleared or approved – cannot occur if the test kit required for the use is not available for diagnostic purposes. The agency should not proscribe Bio-Rad's unified labeling on the basis of a concern applicable to other device labeling that refers to unapproved uses of the specific device, because Bio-Rad's labeling will not create such uses for devices not available in the United States. Plainly, Bio-Rad's control product could not be misused without the presence of such a product.

Bio-Rad Does Not Control Approval of Analyte Test Kits. Second, FDA argues that permitting off label uses in labeling, with disclaimers that a device is not approved/cleared for such a use, circumvents the product approval system by permitting the making of unapproved product claims, thus discouraging premarket submissions for review. However, whether Bio-Rad's control may be used with a particular test kit depends on whether the test kit manufacturer has received clearance or approval for such use. FDA cannot justify its suppression of Bio-Rad's labeling by arguing that suppression will encourage a premarket submission because the effect is too remote on the test kit manufacturers, who are responsible for the submissions.

Controls are in Support of the Pre-established Character of Individual Test Kits. Third, Bio-Rad's in vitro controls have no independent function and only serve the purpose of benchmarking laboratory equipment used to run specific in-vitro diagnostic tests. As such, the controls can only have use if they are validated for a specific IVD. To the extent a test kit is unavailable in the United States, it is inconceivable that Bio-Rad's international labeling will result in a person creating a test kit to coincide with the control without also obtaining an FDA clearance or approval to market the device and have the opportunity for reimbursement. To suggest that a statement in labeling alluding to the use of a control outside of the United States will result in the development of the same product for illegal domestic use is unreasonable. Critically, it is important to appreciate that use of a Bio-Rad IVD control limited to use only in those test kits for which it can be validated, and no one is going to validate a test kit merely because of Bio-Rad's international label.

II. THE FIRST AMENDMENT REQUIRES THE FDA TO PERMIT DISCLAIMERS AND STATUTORY POLICY FAVORS THIS APPROACH.

A. The First Amendment Requires That FDA's Restrictions Be Narrowly Drawn.

Even if ODE's policy of disallowing references to unapproved uses were permissible under the First Amendment, the factors distinguishing Bio-Rad's circumstances from the usual case would preclude suppression of the labeling.² Under recent cases, FDA's regulation of commercial speech is permissible only if the speech is false or inherently misleading,³ or if the regulation meets three criteria. These criteria are: (1) the government seeks to advance a substantial interest by restricting speech; (2) the restriction directly advances the substantial interest; and (3) the restriction does not burden substantially more speech than necessary. *See Central Hudson Gas & Electric Corp. v. Public Service Commission of New York*, 447 U.S. 557 (1980); *Washington Legal Foundation v. Friedman*, 13 F. Supp 2d 51,66-74 (D.D.C. 1998) (*WLF I*)⁴.

² Bio-Rad's labeling is considered commercial speech, subject to less protection than "pure speech." *See, e.g., Washington Legal Foundation v. Friedman*, 13 F. Supp. 2d 51 (D.D.C. 1998) (*WLF I*); *see also Central Hudson Gas & Electric Corp. v. Public Service Commission of New York*, 447 U.S. 557 (1980). In *WLF I*, the court relied on three factors to conclude that Continuing Medical Education (CME) seminars, peer-reviewed articles, and textbook reprints were commercial speech: (1) whether the speech is concededly an advertisement; (2) whether the speech refers to a specific product; and (3) whether the speaker has an economic motivation for disseminating the speech.

³ False and misleading commercial speech receives no constitutional protection. "The First Amendment's concern for commercial speech is based on the informational function of advertising. Consequently, there can be no constitutional objection to the suppression of commercial messages that do not accurately inform the public about lawful activity. The government may ban forms of communication more likely to deceive the public than inform it or commercial speech related to illegal activity." *Central Hudson*, 447 U.S. 557, 565.

⁴ The status of *WLF I* as legal precedent is clouded by the complicated subsequent history of the case. The court entered summary judgment against the government in *Washington Legal Foundation v. Henney*, 56 F. Supp. 2d 418 (D.D.C. 1998) (*WLF II*), finding unconstitutional the CME guidance as well as the FDAMA provisions that superseded the enduring materials guidance's. When the D.C. Circuit heard FDA's appeal of the district court's judgment, FDA announced in its argument that the agency would narrow its application of the unconstitutional policy and provisions. In light of the narrowed interpretation, the Circuit Court dismissed FDA's appeal and vacated in part the district court's judgment insofar as it declared the CME guidance and FDAMA provisions. *See Washington Legal Foundation v. Henney*, 202 F.3d 331 (D.C. Cir. 2000) (*WLF III*). Following this decision, the district court denied *WLF*'s motion to reinstate the injunction against use of the guidance documents. *Washington Legal Foundation v. Henney*, 128 F. Supp 3d 11 (D.D.C. 2000)(*WLF IV*). Still, none of these subsequent decisions invalidated the *WLF I* holding, which was confirmed by the district court's decision in *WLF II*. The Appeals court noted that its vacating the district court's injunction did not mean it was criticizing the district court's reasoning or conclusions. *See WLF III* at 337, n.7.

Is the Speech False and Misleading? FDA has argued that promotional materials for pharmaceuticals that are not false become inherently misleading when distributed by a manufacturer without FDA having reviewed the claims. *WLF I* at 67. Courts have rejected this argument, and refused to find such materials to be false and misleading for purposes of the *Central Hudson* test. See *Western States Medical Center v. Shalala*, 69 F. Supp. 2d 1288, 1300-1301 (D.Nev. 1999), *aff'd in relevant part* 238 F.3d 1090 (9th Cir. 2001), *aff'd* 122 S. Ct. 1497 (2002); *cf. Washington Legal Foundation v. Henney*, 56 F. Supp. 2d 81, 86 (*WLF II*) ("The government...cannot justify a restriction of truthful, non-misleading speech on the paternalistic assumption that such restriction is necessary to protect the listener from inadvertently misusing the information.") (D.D.C. 1999). Thus, provided the disclaimer is adequate, FDA cannot credibly argue that Bio-Rad's unified labeling is false or misleading and thus outside First Amendment protection.

What is the Nature of the Government's Interest? Under the second prong of the *Central Hudson* test, FDA has successfully defended its restrictions on promotional materials by arguing that its restrictions promote the public health and safety and preserves the integrity of premarket review processes. See *Western States Medical Center*, 122 S. Ct. at 1505; *WLF I* at 71. We do not dispute that the government's interest in requiring manufacturers to make submissions to FDA for product approval/clearance before new claims for a device may be made in labeling, and that such interest is substantial.

Nonetheless, the FDA's regulation of the speech is unlawful because it fails to satisfy the two remaining requirements of the *Central Hudson* test.

What is the Relationship Between the Interest and the Regulation? Restrictions on speech that advance a substantial government interest fail if they advance the substantial interest only indirectly. Although the most direct means of advancing FDA's substantial interest in premarket review of unapproved uses is requiring a submission, courts have found that the prohibition on references to such uses amounts to the same thing, and that such a prohibition directly advances FDA's interest in ensuring manufacturers submit data on likely uses of their devices. See *e.g., WLF I*. However, FDA has suppressed labeling for IVD controls marketed by Bio-Rad to encourage premarket submissions that would be made by analyte test kit manufacturers; Bio-Rad only labels and markets its controls for legally available assays. Thus, the relationship between FDA's interest in premarket submissions and its means of effecting that interest is indirect and impermissible under the *Central Hudson* test. Further, to the extent suppressing truthful statements in Bio-Rad's unified labeling is intended to regulate post-market promotion and use of the controls, FDA is attacking truthful speech in order to indirectly ensure compliance with the misbranding and adulteration provisions of the

Act. This indirect method of effecting FDA's interest in compliance with the Act is similarly impermissible under *Central Hudson*. Importantly, it is also unsupported by the Act, see section II.B., *infra*.

Has FDA used the Least Restrictive Alternative? Further, FDA's concern that manufacturers will adopt disclaimers of unapproved uses as a standard practice hinges on a justification that is highly suspect in First Amendment case law, namely, that consumers will be unable to make intelligent decisions on the basis of complete, true information. Courts have repeatedly rejected such reasoning. In *WLF I*, the D.C. District Court wrote:

If there is one fixed principle in the commercial speech arena, it is that 'a State's paternalistic assumption that the public will use truthful, nonmisleading commercial information unwisely cannot justify a decision to suppress it.'...To endeavor to support a restriction upon speech by alleging that the recipient needs to be shielded from that speech for his or her own protection, which is the gravamen of FDA's claim here, is practically an engraved invitation to have the restriction struck.

13 F. Supp.2d at 69-70 (citations omitted); *see also Western States Medical Center*, 122 S. Ct. at 1507 (characterizing FDA's concern as "a fear that people will make bad decisions if given truthful information about drugs" and rejecting "the notion that the Government has an interest in preventing the dissemination of truthful commercial information in order to prevent members of the public from making bad decisions with the information.") Importantly, as we discussed in section I.C., references in Bio-Rad's labeling for IVD controls to unapproved/uncleared test kits that are unavailable domestically have different consequences than labeling for typical devices, because such off label uses do not relate directly to the use of the control and are dependent on the status, availability, and/or validation of the referenced kits.

The corollary to courts' rejection of paternalistic government approaches to the regulation of speech is the view that "the preferred remedy [for potentially misleading speech] is more disclosure, rather than less." *See Pearson v. Shalala*, 164 F.3d at 650, 657 (D.C. Cir. 1999), *quoting Bates v. State Bar of Arizona*, 97 S. Ct. 2691 (1977); *see also Western States Medical Center*, 122 S. Ct. at 1560 ("we have made clear that if the Government could achieve its interests in a manner that does not restrict speech, or that restricts less speech, the Government must do so.") In *Pearson*, the D.C. Circuit Court found that FDA's refusal to permit certain claims for dietary supplements, without considering whether disclaimers qualifying the claims could mitigate the asserted misleading effect, violated the First Amendment, and cited several Supreme Court precedents for the proposition that disclaimers are "constitutionally preferable to outright suppression." *Id* at 657. The Supreme Court recently expressed this view in the FDA context. *See Western States*

Medical, 122 S. Ct. at 1508 (rejecting a prohibition on speech and stating that the government's interests "could be satisfied by the far less restrictive alternative of requiring each compounded drug to be labeled with a warning that the drug had not undergone FDA testing and that its risks were unknown.")

Given the ruling in *Pearson* and other cases expressing a preference for disclaimers over prohibitions on speech, FDA bears the burden of establishing that its substantial interest in encouraging premarket review submissions for unapproved/uncleared uses requires the complete suppression of truthful information in labeling because disclaimers are inadequate to avoid false or misleading messages. As the D.C. District noted in *WLF II*, permitting such information, with the qualification that FDA has not approved the use, should not defeat FDA's interest because "manufacturers are...undoubtedly aware of the value of FDA approval as an indication of safety and reliability, certainly important factors for health care providers choosing between competing products." *WLF II*, 56 F. Supp.2d at 87. FDA's argument that rejecting Bio-Rad's unified labeling is necessary because the practice of labeling for unapproved uses in the aggregate will discourage premarket submissions runs afoul of the doctrine that the government must regulate speech using the least restrictive alternative. The First Amendment prohibits FDA from suppressing speech when a disclaimer is a viable option, and to date FDA has shown no basis for rejecting as inadequate Bio-Rad's disclosures that certain test kits are not approved/cleared in the United States.

B. The Act Expresses a Preference for Disclaimers Over Suppression.

The Act also supports the argument that a disclaimer, rather than suppression, is the appropriate means to regulate potential unapproved uses associated with a device subject to premarket notification review. See § 513(i)(1)(E) of the Act (a provision enacted as part of the "Food and Drug Administration Modernization Act of 1997" ("FDAMA")). Section 513(i)(1)(E) provides in relevant part:

[a]ny determination by the Secretary of the intended use of a product shall be based upon the proposed labeling submitted in a report for the device under section 510(k). However, when determining that a device can be found substantially equivalent to a legally marketed device, the director of the organizational unit responsible for regulating devices...*may require a statement in labeling that provides appropriate information regarding a use of the device not identified in the proposed labeling if, after providing an opportunity for consultation with the person who submitted such report, the Director determines and states in writing-*

- (I) that there is a reasonable likelihood that the device will be used for an intended use not identified in the proposed labeling for the device; and
- (II) that such use could harm⁵

(emphasis added). Congress enacted this provision to address industry's concern about FDA's practice of demanding that sponsors of premarket notifications submit information on possible uses of devices other than the use proposed for the device in the context of a premarket notification submission. Under this provision, when FDA believes a potentially harmful off-label use of a device is reasonably likely, FDA may "require limitations in the labeling that proscribe the unlabeled use." H. Rep. No. 105-307, at 24 (1997).

Section 513(i)(1)(E) restricts the agency from delaying 510(k) decisions because of possible off-label uses not stated in labeling. Although the provision does not speak directly to FDA's refusal to clear labeling that refers to unapproved/uncleared uses; nonetheless, it articulates the policy that the appropriate remedy for potential off-label use is information proscribing or limiting the use. This policy supports the practice of designing unified labeling that identifies unapproved/uncleared test kits with a disclaimer identifying the kits as such. Significantly, implicit in the legislative policy behind section 513(i)(1)(E) is that off label uses that could cause harm are properly and effectively mitigated by disclosure.

C. The Disclaimer Must be Sufficient.

While First Amendment law and the Act support disclaimers as the appropriate means of qualifying information on a device's label about an unapproved use, Bio-Rad believes that reasonable regulation to ensure the sufficiency of the disclaimer is appropriate. For purposes of the commercial speech analysis under the First Amendment, the disclaimer must be adequate to counter concerns that the labeling as a whole is false and misleading, or that an unapproved use is being promoted. In addition, the disclaimer must comply with section 502(C) of the Act, which provides that a device is misbranded:

If any word, statement, or other information required by or under authority of this Act to appear on the label or labeling is not prominently placed thereon with such conspicuousness (as compared with other words, statements, designs, or devices, in the labeling) and in such terms as to

⁵ The provision requires the Director of CDRH to notify the device's sponsor of limitations that must appear in the labeling. Section 513(i)(1)(E) was scheduled to sunset on November 19, 2002; however, Congress underscored its support of the provision by making it a permanent part of the statute in the Medical Device User Fee and Modernization Act of 2002, signed into law by President Bush on October 26, 2002.

render it likely to be read and understood by the ordinary individual under customary conditions of purchase and use.

The agency issued a regulation implementing this authority for device labels, see 21 C.F.R. § 801.15, but has not issued regulations prescribing specific requirements under section 502(c) for general device labeling or for IVD labeling.⁶ Because section 502(c) applies equally to labels and labeling, the agency is likely to interpret the provision as imposing the same requirements on labeling as the agency has imposed by regulation on labels. Thus, a disclaimer required by the Act to appear in labeling should be in a typeface close in size to the typeface of the statement it is disclaiming,⁷ and must be easy for the reader to find. Bio-Rad has designed its unified labeling specifically to comply with these requirements.

In sum, First Amendment case law required FDA to permit references to unapproved test kits in the context of Bio-Rad's product labeling so long as the labeling contains appropriate disclaimers. This limitation on FDA's 510(k) review authority was enacted in FDAMA in instances where an off label use would be "reasonably likely." Thus, under the case law and the policy incorporated into the Act in FDAMA, the agency must permit Bio-Rad to distribute unified labeling with its devices, provided the labeling disclaims references to unavailable test kits by noting that they have not been reviewed and approved/cleared by FDA. The model labeling submitted with this petition satisfies these requirements and must be allowed by FDA.

⁶ Although not directly applicable to Bio-Rad's labeling, FTC's requirements for disclaimers in advertisements provide useful guidelines. To satisfy FTC's requirements, disclaimers must be sufficiently prominent, understandable, presented in a way that consumers are likely to read (or hear) the disclaimer, and in reasonable proximity to the statement the disclaimer is qualifying. See "FTC Advertising Enforcement Disclosures in Advertisement," www.ftc.gov.

⁷ The agency requested comment on the prominence of disclaimers relevant to the text being disclaimed in its May 16, 2002 *Federal Register* notice. Specifically, the agency sought response to the following questions:

Should disclaimers be required to be in the same (or smaller or larger) size of type and given equal prominence with claims? Is there any relevant authority or social science research on this issue?

67 *Federal Register* at 34,944.

C. Environmental Impact

No Environmental Impact Statement is required because the action requested falls within the categorical exclusion described in 21 C.F.R. § 25.30.


D. Economic Impact

No economic impact information has been requested by FDA.

E. Certification

The undersigned certifies that, to the best of the knowledge and belief of the undersigned, this petition includes all information and views on which the petition relies and that it includes representative data and information known to the petitioner, which are unfavorable to the petition.

On behalf of Bio-Rad Laboratories,



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Attachments

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

B. Example of Bio-Rad's Unified Labeling

- Lyphochek Tumor Marker Control