PUBLICCITIZEN

1600 20th Street, NW • Washington, D.C. 20009 • 202/588-1000 • www.citizen.org

April 27, 2012

Commissioner Margaret Hamburg M.D.
Food and Drug Administration
Department of Health and Human Services
WO 2200
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

Division of Dockets Management (HFA–305)
Food and Drug Administration
Department of Health and Human Services
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: Docket No. FDA-2012-N-0176

Dear Dr. Hamburg:

These comments from Public Citizen's Health Research Group (PCHRG) come in response to a notice published February 29, 2012, under docket number FDA-2012-N-0176 regarding collection of information by the Food and Drug Administration (FDA) in connection with research entitled "Experimental Study: Examination of Corrective Direct-to-Consumer (DTC) Television Advertising." The proposed research would "examine how corrective advertising may impact consumer misperceptions about prescription drug product safety and efficacy."[1]

This notice was published pursuant to the Paperwork Reduction Act of 1995, enacted to "ensure the greatest possible public benefit from and maximize the utility of information created, collected, maintained, used, shared and disseminated by or for the Federal Government."[2]

We have concerns that the study described in this notice would fail to fulfill that purpose. On the following pages, we shall describe the potential design flaws that could render the results of this study useless. We shall also suggest modifications that, if adopted, could "ensure the greatest possible public benefit" from the resources sure to be expended in carrying out this research.

[1] 27 Fed. Reg. 12307-12308 (2012).

[2] 44 U.S.C. Chapter 35, Section 3501 (1995).

## I. The Proposed Study

The proposed study would select participants affected by a "medium prevalence" medical condition, here defined as one affecting 5-10% of the adult U.S. population. The study would examine the effects of three independent variables:

1. Message exposure
2. Similarity of the original and corrective ads
3. Length of time between exposure to the original and corrective ads

Briefly, the study would be divided into two phases.

1. Phase 1, comparing the effect of exposure to the original ad alone to exposure to the original ad plus the corrective ad
2. Phase 2, a more complex phase comparing two separate sets of elements:
   a. The effect of similarity of design elements in the original ad and the corrective ad
   b. The effect of delay between viewing the original and corrective ads with no delay, a one-week delay, and a one-month delay

## II. Discussion

PCHRG has serious reservations about the proposed study design. Our concerns fall into three categories:

1. Will the participants be a random and representative selection of the target audience?
2. Will the study be adequately powered to ensure meaningful results?
3. Will the study, as designed, yield results useful to policy makers in promoting public health?

### 1. Will the participants be a random and representative selection of the target audience?

Participants, even if at first randomly selected, may later opt out of attending at least two, and possibly more, separate viewings. This could result in an essentially self-selected sample. Also, a study pool defined as those affected by a "medium prevalence" condition (one affecting 5-10% of the adult population) may fail to be representative for certain conditions clustered in particular adult age or sex groups. The notice gave no information on sexual distribution of subjects or the nature of the target ad as it might specifically concern male or female subjects. If the participants in the study are not representative of the population that would be affected by an FDA policy on corrective advertising, inferences drawn from the study would not be useful to policy makers.

**2. Will the study be adequately powered to ensure meaningful results?**

In previous studies conducted under FDA auspices to examine the effects of distraction in DTC advertising on television, we noted that because of the limited numbers of participants in relation to the number of variables, the studies were probably not adequately powered to detect a difference between groups.[3] This result was the likely reason that portions of those studies failed to yield positive results.

When a study is underpowered, it is less likely to detect a statistically significant difference between groups. When this happens, it is impossible to say whether the failure to detect a statistically significant difference occurred because the intervention truly had no effect or because the study design was faulty. An underpowered study that fails to show a statistically significant difference between groups is therefore useless as a source of data for policy makers.

Phase 2 of this study, in particular, involves a large number of variables with what appears to be a relatively modest number of participants. Therefore, to ensure that the study results can be validly interpreted, we would strongly urge that a power analysis be included in the report of the study, and that this power analysis, ideally, be conducted before the study is carried out (*a priori*), rather than afterward, to ensure that the considerable investment (in the form of subjects' involvement and public expense) in conducting the study would result in useful information.

**3. Will the study, as designed, yield results useful to policy makers in promoting public health?**

To answer this question, it is important to acknowledge the wide range of design possibilities in corrective television advertising.[4] The 2007 Amendments to the Food, Drug, and Cosmetic Act require that the "major statement"[5] in DTC television and radio advertising relating to side

---

[3] *See* Levin J, Sorscher S, Wolfe S. Comments to FDA on Direct-to-Consumer Drug Advertisements. Public Citizen. February 27, 2012. *Available at* http://www.citizen.org/documents/comments-to-fda-on-direct-to-consumer-drug-advertisements.pdf (last accessed April 27, 2012).

[4] 75 FR 15376 March 29, 2010 Docket No. FDA-2009-N-0582 Proposed Rule re presentation of Major Statement, 77 FR 4273 January 27, 2012 Docket No. FDA-2009-N-0582 Proposed Rule Extension to review Distraction Study, etc.

[5] "The 'major statement' is a term that is relevant only to broadcast (TV or radio) ads for prescription drugs. It refers to the presentation of the drug's most important risks. This presentation must be spoken. It also can be included in the video part of TV advertisements." Food and Drug Administration, Drug Advertising: A Glossary of Terms. *Available at* http://www.fda.gov/Drugs/ResourcesForYou/Consumers/PrescriptionDrugAdvertising/ucm072025.htm#M (last accessed April 27, 2012).

effects and contraindications of an advertised prescription drug intended for humans be presented in a "clear, conspicuous and neutral manner."[6] We have previously discussed methods to achieve this requirement, such as simultaneous presentation of text and audio tracks, as well as elimination of elements that may defeat this purpose (such as distracting information).[7] While there may be disagreement as to what should be required, it is clear that the manner of presentation of the major statement can affect viewer comprehension.

We believe that corrective television advertising intended to correct consumer "misperceptions about prescription drug product safety and efficacy"[8] should logically be held to the same standard as that required for the initial "major statement." We would therefore require the information contained in the corrective advertisement to be presented in a "clear, conspicuous and neutral manner" and apply this standard not only to corrections pertaining to the major statement, but to all material in the corrective advertisement relevant to safety and efficacy.

A corrective advertisement ideally would contain direct, easy-to-understand wording, few or no distracting elements, and reinforce, rather than distract from, the corrective material by having large text clearly displayed on the screen accompanying a slowly and clearly enunciated audio track read at a reasonably high volume. We shall call this a "clear and conspicuous" corrective advertisement.

On the other hand, a corrective advertisement might present corrective material with confusing wording, distracting elements; with little or no clearly legible text; and with rapid, poorly enunciated reading of the corrective material at a low volume. We shall call this an "unclear and inconspicuous" corrective advertisement.

A study that tests the effectiveness of clear and conspicuous advertising might provide policy makers with useful information about best practices for corrective advertising but would not provide useful information about what types of corrective advertising should be prohibited as ineffective. On the other hand, a study that tests the effectiveness of only unclear and inconspicuous corrective advertising would probably show that corrective advertising does not

---

[6] "In the case of an advertisement for a drug subject to section 353(b)(1) of this title presented directly to consumers in television or radio format and stating the name of the drug and its conditions of use, the major statement relating to side effects and contraindications shall be presented in a clear, conspicuous, and neutral manner." 21 U.S.C. Section 352(n).

[7] *See* Levin J, Sorscher S, Wolfe S. Comments to FDA on Direct-to-Consumer Drug Advertisements. Public Citizen. February 27, 2012. *Available at* http://www.citizen.org/documents/comments-to-fda-on-direct-to-consumer-drug-advertisements.pdf (last accessed April 27, 2012); *see also* Wolfe S., Levin J. Letter on Regulation of Direct-to-Consumer Marketing. Public Citizen. June 28, 2010.

[8] 27 Fed. Reg. 12307-12308 (2012).

work at all, again failing to provide policy makers with useful information about how to regulate corrective advertising. Therefore, in order to provide valid, useful, generalizable data, the proposed study should include evaluation of both 1) a truly informative, non-distracting, clear and conspicuous corrective advertisement and 2) an unclear and inconspicuous corrective advertisement.

Ideally, the clear and conspicuous advertisement would contain simultaneous text in its video portion. This text would be clearly legible even on small screens and simultaneously read aloud distinctly and slowly. Such a corrective advertisement would not contain distracting images, bizarre social contexts, or, indeed, any images except those designed to assist in comprehending the corrective message.

The unclear and inconspicuous corrective advertisement would contain distracting elements and lack clarity in its presentation of the corrective material — similar to what might be expected in a real-world scenario where a pharmaceutical company may be tempted to distract consumers from important safety and efficacy information that could negatively impact sales.[9]

The current study design fails to pose and answer questions that will be useful to policy makers in promoting public health. While the study does purport to compare different versions of corrective advertising, these versions are designed to test only whether there is an effect from (a) the corrective ad's similarity to the original ad, and (b) the time delay between the original ad and the corrective ad. Both research questions will fail to yield useful information. First, there is no evidence that similarity to the original ad has any effect on viewer comprehension of a corrective message. Instead of focusing on similarity to previous misleading advertising, the study should focus on whether the corrective message is presented in a manner that is clear and conspicuous. Based on the description in the February 29 notice, we have grave concerns that none of the versions of corrective advertising presented in this study will have a sufficiently clear and conspicuous message to demonstrate that corrective advertising is effective at correcting misinformation.

Second, while time delay may be an important factor, the current study addresses only the time difference of one week versus one month between viewing the original misleading ad and seeing the corrective ad. In the real world, a consumer is likely to experience multiple viewings of the original, misleading ad and will have to wait months or years before the regulatory process forces a corrective advertising campaign. The conditions in the study are so different from real-world circumstances that no valid conclusions may be drawn from them that could be applied to FDA policy.

For these reasons, we suggest that the design of each of the proposed experiments be modified to include a group exposed to both a clear and conspicuous corrective advertisement and

[9] For an example of unclear and inconspicuous messages in real-world corrective advertising, we would direct the study authors to the corrective advertisement for YAZ®, which is described in Appendix B, *infra*.

another group exposed to an unclear and inconspicuous corrective advertisement. The results of each of these groups should be compared head-to-head with each other as well as with the "no exposure" control group (which is already described in the current study design).

**III. Critique of the References Offered in the Instant Notice**

Unfortunately, the references offered in the instant notice seemed less concerned with presenting corrective advertising in a manner most likely to inform the consumer about the safety and efficacy of a given product and more concerned with determining whether the corrective advertisement might be bad for sales. Furthermore, the only example of application of a judicial remedy to enforce corrective advertising cited by one of these references distorted the clear intent of the opinion cited.

For a more extensive discussion of these references, please see Appendix B to this comment.

**IV. Conclusion**

We urge the FDA to consider these points in order to create the best possible design for this study on corrective television advertisements.

1. The study participants should be a random and representative selection of the target audience.
2. The study should be adequately powered.
3. The study should include in its design a comparison of the efficacy of unclear and inconspicuous and clear and conspicuous advertisements as defined herein.

Attention to these matters would provide the best possible information to FDA policy makers and most likely satisfy the purposes of the Paperwork Reduction Act of 1995: to "ensure the greatest possible public benefit from and maximize the utility of information created, collected, maintained, used, shared and disseminated by or for the Federal Government."

Sincerely,

Joan Levin, J.D., M.P.H.
Formerly of the Health Research Group

Sarah Sorscher, J.D., M.P.H.
Research Associate, Health Research Group
Public Citizen

Sidney Wolfe, M.D.
Director, Health Research Group
Public Citizen

**Appendices**:

A. References Selected for Inclusion with the Instant Notice
B. YAZ: An Example of "Unclear and Inconspicuous" Corrective Advertising

**Appendix A. References Selected for Inclusion with the Instant Notice.[10]**

Four references were specifically cited by the FDA in the instant Notice.

1. Darke, P.R., L. Ashworth, and R. J. B. Ritchie, "Damage from Corrective Advertising: Causes and Cures," Journal of Marketing, vol. 72, pp. 81-97, 2008. (Hereinafter "Darke 2008").
2. Mazis, M.B. and J. E. Adkinson, "An Experimental Evaluation of a Proposed Corrective Advertising Remedy,: Journal of Marketing Research, vol. 13, pp. 178-183, 1976. (Hereinafter "Mazis 1976").
3. Mazis, M.B., D.L. McNeill, and K.L.Bernhardt, "Day-After Recall of Listerine Corrective Commercials." Journal of Public Policy & Marketing, Vol 2, pp. 29-37, 1983. (Hereinafter "Mazis 1983").
4. Singer, N., A Birth Control Pill that Promised Too Much, New York Times, Feb. 11, 2009, p. B1 (Hereinafter "Singer 2009").

It appeared from the choice of references herein that the primary concern of FDA in this selection was the well-being of companies required to produce corrective advertising, rather than the health and safety of the consumer viewing these advertisements.

Darke 2008 was primarily concerned with damage to the reputation of the particular product, as well as to the reputations of other products of that company, other products for similar uses or indications, other companies of similar products, and even advertising in general.

Mazis 1976 focused on confusion that could result in consumers believing that some other attribute of the product besides the targeted one was problematic. Presumably, this could similarly cut into sales.

Mazis 1983 similarly explored the above-mentioned kind of confusion. This article made reference to a leading Federal Trade Commission (FTC) case involving corrective advertising[11] of an over-the-counter (OTC) product, Listerine. The authors presented this case as follows: "Courts have held that while advertisers may be forced to include corrective statements, their ability to promote their products cannot be significantly impaired."[12]

However, even a cursory examination of this case reveals that this court allowed for a far-reaching remedy of potentially long duration. In finding lack of foundation for Warner-

[10] 77 FR 12308. These references were not available in the online docket folder at www.regulations.com. We wish to thank the FDA contact official for providing copies of the first three sources.

[11] Warner-Lambert Company v. FTC, 562 F. 2nd 749 (D.C.Cir.1977), cert. denied, 98 S. Ct. 1575 (1978).

[12] Mazis 1983 at p. 29.

Lambert's claims that Listerine could prevent colds and sore throats, the trial court had ordered the dissemination of the following corrective message: "Contrary to prior advertising, Listerine will not help prevent colds or sore throats or lessen their severity." On appeal from that order, only the words "contrary to prior advertising" were omitted, so as not to humiliate the company. [13]

Not only was this corrective message to be applied to all advertising for this product, it was to be applied until the company had "expended on Listerine advertising a sum equal to the average annual Listerine advertising budget for the period of April 1962 to March 1972, approximately ten million dollars."

The court justified this extensive ruling by explaining that future users of the product who may have seen earlier advertisements needed to be advised, and that the measure of the money spent on advertising rather than a specific time duration was exacted to assure that the company could not avoid corrective advertising by withholding ads for a substantial period.

The Listerine case is not a singular occurrence of judicial enforcement of FTC oversight of OTC advertising.[14] If strenuous remedies, including the equivalent of the entire advertising budget for a substantial period of time, are enforced where arguably the only consumer risk was the price of a product that might be worthless to prevent colds and sore throats, how much more should potential consumers of a prescription drug that might have truly deleterious adverse effects be warned against using the drug for unapproved indications?

---

[13] Warner-Lambert Company v FTC, op. cit.

[14] The FTC may order the advertiser to correct the misinformation through compelled advertising. E.g., Novartis Corp. v. FTC, 223 F.3d 783 (D.C. Cir. 2000); Warner-Lambert Co., 86 F.T.C. 1398 (1975), modified, 92 F.T.C. 191 (1978), aff'd, 562 F.2d 749 (D.C. Cir. 1977); England's Best, Inc., No. 932-3000 (9/8/94). The Commission has explained that it will require corrective advertising where "(1) the challenged ads have substantially created or reinforced a misbelief; and (2) the misbelief is likely to linger into the future." Novartis Corp. 5/17/99, CCH Trade Reg. Rep. ¶24, 339. Advertising for Doan's pills stated it has an ingredient other analgesics lack and it is made for back pain, but because there is no evidence that it is more effective than other analgesics in relieving back pain, for one year and eight million dollars of advertising future ads and packaging must state: "Although Doan's is an effective pain reliever, there is no evidence that Doan's is more effective than other pain relievers for back pain". Novartis Corp. v. FTC, 223 F.3d 783 (D.C. Cir. 2000). See WebTV Networks, Inc., Consent Order C-3988 122/12/03); U.S. v. Bayer Corp., CV 00-132 (D.N.J. 1/11/00); Exxon Corp., 124 F.T.C. 249 (1997) (Fifteen second commercial to air in eighteen markets and brochures at service stations for two years to counteract advertising that high octame gasoline would reduce maintenance); Schering Plough, 123 F.T.C. 1301 (1997). (distribute 150,000 consumer brochures advising to re-apply sunscreen after vigorous activity after advertising sunblock last all day).

In selecting these articles as its sole references for this notice, the FDA displays, at the very least, a profound misunderstanding of the role of corrective advertising in protecting the health and safety of consumers.

**Appendix B. YAZ: An Example of "Unclear and Inconspicuous" Corrective Advertising**

In 2008, FDA investigated Bayer, the maker of YAZ, for a series of misleading DTC television ads that broadened the drug's indication, overstated its efficacy, and minimized its risks.[15] YAZ was approved for the prevention of pregnancy, treatment of premenstrual dysphoric disorder (PMDD), and treatment of moderate acne.[16] The drug's label made clear, however, that YAZ should be taken to treat acne or PMDD only by women who had already selected oral contraception as their primary form of birth control, and that the drug caused serious side effects, including blood clots, heart attack, and stroke.

The original advertisement for YAZ contained language suggesting that it was suitable for PMS, not only for PMDD, and could treat all forms of acne, in addition to being otherwise misleading.[17] In fact, there was no evidence that this drug was effective for the treatment of PMS. The ads also minimized the drug's risks through distracting, fast-paced visuals. On October 3, 2008, the FDA issued a warning letter concerning YAZ, citing numerous deficiencies and

---

[15] Food and Drug Administration. Warning Letter: YAZ (drospirenone and ethinyl estradiol) tablets, Bayer Pharmaceuticals. Abrams T, FDA Warning Letter to Reinhard Franzen, President and Chief Executive Officer, Bayer HealthCare Pharmaceuticals, Re: NDA # 21-676, 21-873, 22-045. October 3, 2008. *Available at* http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/EnforcementActivitiesbyFDA/WarningLettersandNoticeofViolationLetterstoPharmaceuticalCompanies/ucm053993.pdf (last accessed 4/27/12).

[16] Ibid.; See also Singer N. "A Birth Control Pill that Promised Too Much." New York Times. February 11, 2009, p. B1. (Hereinafter "Singer 2009").

[17] PMS stands for Premenstrual Syndrome. PMDD stands for Premenstrual Dysphoric Disorder, comprising a more severe constellation of symptoms.

"The symptoms of PMDD are similar to those of PMS. However, they are generally more severe and debilitating and include a least one mood-related symptom." Storck, SS. Premenstrual dysphoric disorder. MedlinePlus. December 22, 2012. *Available at* http://www.nlm.nih.gov/medlineplus/ency/article/007193.htm (last accessed 4/27/12). "Premenstrual dysphoric disorder (PMDD) is a severe, sometimes disabling form of premenstrual syndrome (PMS). Although regular PMS and PMDD both have physical and emotional symptoms, PMDD causes extreme mood shifts that can disrupt your work and damage your relationships. About 30 percent of menstruating women have PMS. Up to 8 percent of women with PMS have symptoms that meet the diagnostic criteria for PMDD." Gallenberg, MM. What's the difference between premenstrual dysphoric disorder (PMDD) and premenstrual syndrome (PMS)? How is PMDD treated? Mayo Clinic. June 22, 2010. *Available at* http://www.mayoclinic.com/health/pmdd/AN01372 (last accessed 4/27/12).

misleading features in the television advertising for that product.[18] Pursuant to a settlement with the FDA and 27 state attorneys general,[19] corrective advertising was released purporting to correct these misleading statements.

However, the corrective advertising that ultimately aired simply stated that YAZ was "for the treatment of PMDD, … not for the treatment of PMS" and proceeded to define the two conditions in a manner that could leave consumers with the impression that the purpose of the correction was to clarify definitions, rather than to rectify an important error.[20]

The YAZ corrective advertisement provides an example of current unclear and inconspicuous corrective advertising. Viewers may not have found it clear from this corrective presentation that YAZ is *not* to be taken for PMS, that it should not be taken at all for the treatment of acne or PMDD unless a woman had already chosen oral contraception as her form of birth control, and that previous ads had misstated the drug's risks and benefits.

The cited advertisement utilizes numerous techniques to distract viewers from the corrective message. The narrator in these advertisements speaks quickly, presenting a great deal of information within a very short time frame.[21] The unlikely social context is also confusing: viewers may well spend the bulk of the commercial wondering why detailed labeling information is being narrated by a woman dressed for a night out at the club.

We believe that this ad was unlikely to effectively impart the new, corrective information about YAZ to most viewers. On the contrary, this corrective ad, with its tone and setting, might as easily have come across not as a corrective advertisement, but as an additional promotion for the use of this product for PMDD, without stressing its inappropriateness for the less severe symptoms of PMS.

---

[18] Abrams T, FDA Warning Letter to Reinhard Franzen, President and Chief Executive Officer, Bayer HealthCare Pharmaceuticals, Re: NDA # 21-676, 21-873, 22-045. October 3, 2008. *Available at* http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/EnforcementActivitiesbyFDA/WarningLettersandNoticeofViolationLetterstoPharmaceuticalCompanies/ucm053993.pdf (last accessed 4/27/12).

[19] Singer 2009.

[20] An example of a corrective video for YAZ (drospirenone and ethinyl estradiol) tablets, Bayer Pharmaceuticals, may be viewed at http://www.youtube.com/watch?v=EO-G8O0lHq0 (last accessed 4/27/12).

[21] We believe that virtually all of the information in both the original and corrective advertisements for this product would best be communicated by a physician familiar with the symptoms and medical history of the patient, rather than through a 30- or 60-second television message viewed by a lay person. We noted this previously in our comments pursuant to Docket No. FDA-2009-N-0582 regarding DTC television advertising.

The televised corrective advertising for the prescription drug YAZ presents, in our opinion, an unclear and inconspicuous presentation that would be likely to lead to the very "consumer misperceptions about prescription drug product safety and efficacy" with which the instant notice is concerned.

In urging the agency to adopt an adequately populated and powered study, we strongly caution against using the YAZ corrective advertisement as a model, except as an example of an unclear and inconspicuous treatment of the correction. Standing alone, the YAZ corrective advertisement at best serves as a putatively corrective treatment, replete with distractions and statements likely to confuse viewers.

An experiment based solely on an unclear and inconspicuous advertisement such as the YAZ corrective advertisement, without a balancing clear and conspicuous advertisement, would not assist the FDA in making a thoughtful and well-informed policy decision for future corrective advertising. Confining the exposure of a study group to such a poorly designed corrective ad would decrease the likelihood of demonstrating the efficacy of corrective advertising in general and would be less likely to demonstrate that a corrective ad could adequately convey needed information. Certainly such an "unclear and inconspicuous" ad could not, by itself, provide data useful for determining whether well-designed corrective advertising could promote public health.