Experimental Study of Patient Information Prototypes

0910-Number

SUPPORTING STATEMENT

Submitted by

Office of Medical Policy
Center for Drug Evaluation and Research

Food and Drug Administration

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A. JUSTIFICATION

1. Circumstances Making the Collection of Information Necessary

In order to make informed decisions about health care and to use their medications correctly, consumers need easy access to up-to-date and accurate information about the benefits, risks, and safe use of their prescription drugs. Consumers currently receive multiple pieces of paper with their prescription drugs from the pharmacy, containing information that is developed and distributed through various sources. Written prescription drug information is provided through a voluntary effort (Consumer Medication Information)[1] as well as through FDA mandated use of Medication Guides[2] and Patient Package Inserts (PPI).[3] Patients describe a wide range of experiences and varying degrees of satisfaction with information currently provided at the time medicines are received at the pharmacy. In some cases, the written documents are difficult to read and understand, duplicative and overlapping, incomplete or contradictory. FDA has held multiple public meetings to solicit feedback on providing balanced, comprehensive, and up to date prescription drug information to consumers.

Since 1968, FDA regulations have required that PPIs written specifically for patients be distributed when certain prescription drugs or classes of prescription drugs are dispensed. PPIs are required for estrogens and oral contraceptives, are considered part of the product labeling, and are to be dispensed to the patient with the product. In the 1970s, FDA began evaluating the general usefulness of patient labeling for prescription drugs resulting in a series of regulatory steps to help ensure the availability of useful written consumer information. Other PPIs are submitted to FDA voluntarily by manufacturers and approved by FDA, but their distribution is not mandated by regulation. In 1979, FDA proposed regulations that would have required

[1] Public Law 104-180-Aug.6, 1996, Title VI, Effective Medication Guides
[2] 21 CFR 208
[3] 21 CFR 310.501.21, CFR 310.515

written patient information for all prescription drugs[4] and in 1980, finalized those regulations.[5] In 1982, the regulations were revoked based, in part, on assurances that the effort could be handled more efficiently within the private sector.[6]

In 1995, FDA proposed the Prescription Drug Product Labeling: Medication Guide Requirements, designed to set specific distribution and quality goals and timeframes for distributing written information to patients.[7] The Agency then published a Final Rule that established a program under which Medication Guides would be required for a small number of drugs considered to pose a serious and significant public health concern.[8]

In thinking about the best communications for patients, evidence suggests that both the content (e.g., organization) and format (e.g., white space) of a document will impact the comprehension of patient information. Research on reading behavior and document simplification suggests that the use of less complex terminology presented in shorter sentences with a more organized, or *chunked*, structure should improve consumer processing for at least three reasons. First, it should decrease the *cognitive load* engendered by the current physician-directed format. Second, a more structured and organized patient information document should present a less imposing processing demand, increasing consumers' willingness and self-perceived ability to read and understand the presented material. Research with the format of over-the-counter (OTC) drug labels,[9] the nutrition facts label,[10] and other information formats[11]

[4] FDA Proposed Regulation, Patient Package Inserts for Prescription Drugs, 44FR 40015; July 6, 1979
[5] FDA Final Regulation, Patient Package Inserts for Prescription Drugs, 47 FR 39147, September 12, 1980
[6] Revocation of PPI Final Rule, 47 FR 39147, September 7, 1982
[7] FDA Proposed Regulation, Prescription Drug Product Labeling; Medication Guide Requirements, 60 FR 44182, August 24, 1995
[8] 21 CFR 208, Subpart B-General Requirements for a Medication Guide, Section 208.20, Content and Format of a Medication Guide, December 1, 1998
[9] Aikin, K.J. (1998). Consumer Comprehension and Preference for Variations in the Proposed Over-The-Counter Drug Labeling Format, Final Report; Vigilante, W.J. & Wogalter, M.S. (1997). The preferred order of overt-the-counter (OTC) pharmaceutical label components. *Drug Information Journal*, *31*, 973-988.
[10] Levy, A.S., Fein, S.B. & Schucker, R.E. (1992). More effective nutrition label formats are not necessarily more preferred. *Journal of the American Dietetic Association*, *92*(10), 1230-1234.
[11] Lorch, R. & Lorch, E. (1995). Effects of organizational signals on text-processing strategies. Journal of

demonstrates that information presented with section headings, graphics (such as bullets), and other design elements is more easily read than information presented in paragraph format. Consumers are more likely to engage in behavior they believe they can successfully complete.[12] Third, a patient information document that provides readers with clearer "signals" regarding the most important information should help readers prioritize the importance of the presented information. This should increase the probability that the set of information identified as important is subjected to more complete mental processing, thereby increasing the communication of that information.[13]

As part of FDA's efforts to improve the patient information received with prescription drugs, a Risk Communications Advisory Committee meeting was held on February 26-27, 2009. At this meeting, committee members discussed issues such as the ones described above and listened to stakeholder problems regarding the design and distribution of patient information. Following the advisory committee meeting, the working group created four prototypes to aid discussion at a public workshop to be held later in the year.

This public workshop was held on September 24-25, 2009. During the workshop stakeholders from industry, consumer advocacy, and academia converged to discuss desirable features for a single-document patient leaflet, if one were to be developed, consumer tested, and distributed. Participants were divided into six groups to address the pros and cons of the four prototypes with the goal of deciding which features participants appreciated and did not

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Educational Psychology, *87*(4), 537-544; Lorch, R. & Lorch, E. (1996). Effects of organizational signals on free recall of expository text. *Journal of Educational Psychology*, *88*(1), 38-48; Lorch, R., Lorch, E. & Inman, W. (1993). Effects of signaling topic structure on text recall. *Journal of Educational Psychology*, *85*(2), 281-290.

[12] Wood, R. & Bandura, A. (1989). Impact of conceptions of ability on self-regulatory mechanisms and complex decision making. *Journal of Personality and Social Psychology*, *56*(3), 407-415.

[13] Lorch, R. & Lorch, E. (1995). Effects of organizational signals on text-processing strategies. Journal of Educational Psychology, *87*(4), 537-544; Lorch, R. & Lorch, E. (1996). Effects of organizational signals on free recall of expository text. *Journal of Educational Psychology*, *88*(1), 38-48; Lorch, R., Lorch, E. & Inman, W. (1993). Effects of signaling topic structure on text recall. *Journal of Educational Psychology*, *85*(2), 281-290.

appreciate. Responses were varied but several key findings emerged. In general, participants liked the prototype based on the OTC Drug Facts label but expressed concern that the totality of the important information may not fit in such a format. Some people expressed a desire for as much information as possible, although few people recommended pursuing the current Medication Guide format.

Given the information obtained from workshop participants, the working group refined several prototypes and designed a study to investigate the usefulness of two possible patient information formats from a user perspective. The results of this study will inform FDA as to the usefulness and parameters of various format options for a patient information document.

2. **Purpose and Use of the Information Collection**

The purpose of this study is to investigate the usefulness of two possible prototypes for patient medication information (PMI). FDA has an interest in providing useful and accessible information to patients when they retrieve their prescriptions at the pharmacy. In order to ensure that a standard format of information is most useful, we propose approaching this issue both qualitatively and quantitatively. These approaches will allow us to provide information about the readability, usefulness, and understandability of the two formats in a variety of populations, including those with the medical condition in question, people with low literacy levels, and members of the general public. We will compare the two prototypes to each other and to the existing Medication Guide format in order to obtain empirically based information about the most comprehensible and preferred document. This study will inform future policy with regard to PMI.

3. **Use of Improved Information Technology and Burden Reduction**

Automated information technology will be used in the collection of information for the second phase of this study. The contracted research firm will collect data through Internet administration. The participant will self-administer the Internet survey via a computer, which will record responses and provide appropriate probes when needed. In addition to its use in data collection, automated technology will be used in data reduction and analysis. Burden will be reduced by recording data on a one-time basis for each respondent, and by keeping surveys to less than 20 minutes.

4. **Efforts to Identify Duplication and Use of Similar Information**

To our knowledge, only one published study has investigated a new prototype in an attempt to improve upon current patient information provided at the pharmacy.[14] In this study researchers used focus groups to solicit feedback on a simplified prototype for patient medication information (PMI) and found that their version, which incorporated several plain language recommendations, was generally found to be easy to read and understand. This qualitative research suggests that simplifying patient information will be welcomed by the target audiences of the information sheets. Aspects of this prototype have been incorporated into the current prototype designs.

Although the cited study provides important information for FDA, the current study is a more systematic investigation of multiple prototypes. Two prototypes have been developed through a procedure involving scientific literature review, extensive public and expert feedback, and internal deliberation. It will involve both a qualitative and a quantitative phase. Thus, we are aware of no research that duplicates the current effort.

5. **Impact on Small Businesses or Other Small Entities**

[14] Papay, J.I., Fritz, D., Cantu, T., Ellis, M., & Debussey, S. (2010). Assessment of a simplified format of written patient prescription drug information. *Drug Information Journal, 44*, 375-391.

No small businesses would be involved in this data collection.

6. **Consequences of Collecting the Information Less Frequently**

The proposed data collection is one-time only. There are no plans for successive data collections.

7. **Special Circumstances Relating to the Guidelines of 5 CFR 1320.5**

This collection of information fully complies with 5 CFR 1320.5. There are no special circumstances.

8. **Comments in Response to the Federal Register Notice and Efforts to Consult Outside the Agency**

In accordance with 5 CFR 1320.8(d), FDA published a 60 day notice for public comment in the FEDERAL REGISTER of May 4, 2010 (Vol. 75, No. 85; see Appendix C). FDA received five comments. In the following section, we outline the observations and suggestions raised in the comments and provide our responses. Four of the five comments expressed support for the conductance of the research to explore issues of quantitative benefit information. They all described the collection of data as a worthy endeavor which will provide useful information on how best to communicate information to patients about their prescription drugs.

Comment 1. The first comment stated that FDA's approach to examining the content and format of the prototypes is reasonable. This comment provided minor suggestions regarding how to improve the study, most of which are currently addressed in the questionnaire. For example, we have included time measurement, questions about the safe use of the product, and scenario-based questions in the questionnaire for the second phase of our study. We have incorporated other suggestions into the qualitative first phase of our project. In this phase, we

will present participants with all versions of the prototypes to assess their preferences and will be able to probe participants more thoroughly about their reactions and responses to the prototypes.

Comment 2. This comment provided a statement of support for the approval of this data collection, claiming the study will have practical utility.

Comment 3. This comment provided support for the research proposed in this document and reported that the components identified by FDA are consistent with those found in their own research. The comment suggested the inclusion of a visual system for identifying drug products and the inclusion of a variety of font sizes for people with visual impairments. FDA fully supports the presentation of information for special populations. However, the scope of the present study is to determine one format out of several that works with a range of participants. After this step, we can move toward incorporating special features, such as pictures or large font, to accommodate patients with varying needs.

Comment 4. Part of comment 4 was outside the scope of the proposed data collection; i.e., regarding the proper channels for distribution of PMI. Regarding the parts of the comment that focused on the proposed research, the comment generally discussed omissions in the current proposed prototypes. These additional pieces of information have all been discussed at length at various public and expert meetings, including the public workshop in September of 2009, the Brookings Institute Expert Workshop in July of 2010, and the Part 15 hearing in September of 2010. When improving medication documents for patients, there is always a trade-off between the desire to keep it simple and the desire to provide more information. Although a small number of individuals reported the desire for exhaustive information, the great majority of the feedback FDA has received and the literature the Agency has reviewed suggests that the information in the currently proposed prototypes is a reasonable collection of the important

information that patients need to safely use their medications. Moreover, research suggests that providing large amounts of information will not serve patients well, but may instead impede their understanding of the information.[15] Finally, the proposed research itself is designed to address the issue of whether the information in the prototypes is optimal. The first phase of the research will involve qualitative interviews, wherein participants will have ample opportunity to tell us what they want and need to know. The second phase of the research will involve quantitative assessment of the comprehension of important information in the document. Thus, we believe our two-pronged approach will address some of the concerns raised in this comment and we must defer to the volumes of other feedback we have received regarding the limiting of information in PMI.

Comment 5. Comment 5 had five main concerns with the study. First, the comment suggested that FDA reach out to CMI publishers as early as possible in the development of the prototypes. FDA concurs with the importance of doing this and, in fact, has already done so multiple times and in multiple venues. Several CMI publishers participated in the public workshop held in September of 2009 and spoke at the Part 15 hearing in September of 2010.

Second, the comment claims that FDA has not used an evidence-based strategy to develop the PMI prototypes. We disagree. FDA developed the prototypes based on the scientific literature. As described in the first section of this document, the prototypes were based on recommendations to include chunks of information that would reduce cognitive load and facilitate processing by including plenty of white space, headings, and maintaining a readable font size. From this first step, public feedback was obtained and incorporated, and feedback from communications experts was obtained and incorporated, resulting in the current prototypes.

[15] See, for example, Day, R.S. (2010, September 27). *PMI: From concept to compliance.* Development and distribution of Patient Medication Information for prescription drugs: Part 15 Public Hearing, FDA White Oak Campus, Silver Spring, MD.

At this stage, we are proposing the continuation of the gathering of evidence by conducting the proposed two-part study to examine the PMI prototypes.

Third, the comment expresses concerns that the use of a fictitious drug (and only one) may limit the generalizability of the findings of the study. The use of a fictitious drug eliminates the confound of prior knowledge when asking participants about the information they see. Rheutopia was selected to be a very close amalgam of an existing class of drugs. This class was chosen because it has a complicated set of risks, it is given by injection (an unusual administration), and it has multiple indications. FDA's reasoning is that if successful PMI can be developed for such a complex drug, PMI for drugs with simpler profiles will be attainable. It is true we are investigating only one drug in the current study; this decision was based on resource constraints. One research study cannot accomplish all goals. Future studies may be used to assess the applicability of the results in other drug classes.

Fourth, the comment expresses concern that the research will not include a variety of different populations and that the lack of detail provided in the Federal Register notice suggests that very little knowledge will be gained from the research. Regarding the first part, the revised research proposed in this document includes low literacy individuals with chronic disease, general population individuals, and individuals with one of the medical conditions that Rheutopia treats. FDA believes these are the populations most relevant to this particular type of drug, as well as other chronic diseases. In terms of the detail provided, the questionnaire, which provided extensive detail about the exact questions proposed, was available upon request during the first comment period and will continue to be available during the second comment period.

Fifth and finally, the comment suggested that comparing variations of a short, one-page document limits the findings because there will be no comparison to a longer document, which

may perform better. FDA concurs. In the revised research currently proposed, we have included a control condition. A subset of individuals will be randomly assigned to see the Medication Guide format for Rheutopia. Thus, we will compare two proposed one-page prototypes with an existing document that would be currently required for Rheutopia if it were a real drug.

External Reviewers

In addition to public comment, DDMAC discussed the prototypes and the research design and protocol with a panel of 19 experts convened by the Brookings Institution on July 21, 2010. The names of these individuals can be found in Appendix A. After the workshop, several experts provided detailed written feedback to FDA, which was incorporated into the design of the study.

9. **Explanation of Any Payment or Gift to Respondents**

Participants completing formative interviews in the first phase of the research will receive $75 cash incentive for completing a 60-minute interview.

After additional discussion with the University of North Carolina (UNC) team who is assisting with the recruitment for the current study, we have concluded that a $40 payment for this study is inadequate given the specific and particular patient population we are trying to recruit. The nature and scope of the tasks they will be asked to complete warrants a greater incentive, particularly for a primarily low literacy population. The interview guides for this study are intensive, particularly for low literacy participants who may already be intimidated by the research process. They will need an additional motivator to participate.

Secondly, many of the subjects will not have access to their own car but will rely on family members or friends to bring them, increasing the burden on not only themselves but family members or friends. As a result, participants often have to pay for their gas in order to

come for their visits to doctor's appointments and research studies. The sharp rise in gas prices may make travel for unnecessary endeavors less likely. If they are unable to drive themselves or obtain a ride, they may rely on the city buses or the Medicaid van for transportation to the hospital, however, this will add more time and burden for the participants.

Lastly, some participants may also have to pay for childcare in order to come in for the visit. While doctor's appointments are critical to their ongoing healthcare, research studies are not a necessity for their health. As such, adequate compensation must be provided to encourage participation.

For comparison, here is some information from other UNC studies that are currently ongoing:

- A study that is much less involved (and started 10 years ago) pays $50.00 per visit to the research subject. This same study also reimburses $10.00 for a phone call lasting less than 5 minutes. Due to price of gas, the sponsor (federal agency) added an additional $25.00 gift card to the $50.00 in the last year.

- Other studies reimburse a minimum of $25.00 for a quick follow-up visit that lasts less than 15-30 minutes.

- Most studies pay $100.00 for a screening visit which generally takes less time than the currently proposed study.

For the second phase pre-test and main experiment conducted with Knowledge Networks (KN), survey specific incentives are provided to respondents for surveys lasting longer than 16 minutes (which is the case for this survey). The exact value of the incentives offered for this study are 10,000 points, equivalent to $10 if the Panelist asks for the incentive in cash, for completing the study. No points are offered if the person does not complete the study.

Panelist may receive value from these points in a variety of ways including receiving a check for the dollar value (1,000 points = $1). These options now include purchasing sweepstakes

tickets where the prize may be much larger, either in dollar value or a product with substantial value such as an iPod or some other well know gift. KN will soon be expanding these offerings to include a larger catalog of products.

Survey participation is rewarded with a variety of incentives (small cash awards, gift prizes, raffle opportunities).

Further, steps are taken to ensure that panel members are not overburdened with survey requests. The primary sampling rule is to assign no more than one survey per week to members. This level of survey frequency helps to keep panelists engaged as part of the panel. On average, most KN panelists participate in about two surveys a month. This is closer to four per month for panel segments that may be in higher demand depending on the projects being fielded.

10. **Assurance of Confidentiality Provided to Respondents**

All respondent data will be kept private to the extent permitted by law. The experimental instructions will include information explaining this to respondents.

No personally identifiable information will be sent to FDA. All information that can identify individual respondents will be kept by the independent contractor in a form that is separate from the data provided to FDA. The information will be kept in a secured fashion that will not permit unauthorized access. These methods will all be approved by FDA's Institutional Review Board (Research Involving Human Subjects Committee, RIHSC) and RTI's Institutional Review Board prior to collecting any information.

All electronic data will be maintained in a manner consistent with the Department of Health and Human Services' ADP Systems Security Policy as described in the DHHS ADP Systems Manual, Part 6, chapters 6-30 and 6-35. All data will also be maintained in consistency

with the FDA Privacy Act System of Records #09-10-0009 (Special Studies and Surveys on FDA Regulated Products).

Knowledge Networks (KN) has a security policy which is monitored for compliance. This policy involves separating identifying and nonidentifying data into different database systems. Only IT and Panel Management staff with a need to know have access to personally identifying information. Throughout the interview process, questionnaire data is copied to a secured, centralized database for data processing. Data is backed up onsite every three hours and replicated to a disaster recovery site every minute. This data is retained. Access to the backups is restricted to KN's senior IT staff, all of whom have signed a confidentiality agreement. Access to survey result data is allowable for relevant KN research staff but explicitly denied to anybody who may deal with panel information. On a case by case basis, an individual client project can be restricted to individual people due to client need or restriction. In addition, Knowledge Networks enforces a strict password policy to ensure that access isn't leaked or circumvented. KN's network perimeter security is maintained via firewall.

11. **Justification for Sensitive Questions**

This data collection will not include sensitive questions. The complete list of questions is available in Appendix B.

12. **Estimates of Annualized Burden Hours and Costs**

The total annual estimated burden imposed by this collection of information is 850 hours for this one-time collection (Table 1).

Table 1. Estimated Annual Reporting Burden[a]

Activity	No. of Respondents	Annual Frequency per	Total Annual Responses	Hours per Response	Total Hours

		Response			
Phase I, screener	400	1	400	2/60	13
Phase I, interviews	90	1	90	1	90
Phase II, screener	2,600	1	2,600	2/60	87
Phase II, Pretest	30	1	30	20/60	10
Phase II, questionnaire	1,300	1	1,300	30/60	650
Total					850

[a]There are no capital costs or operating and maintenance costs associated with this collection of information.

These estimates are based on FDA's experience with previous consumer studies.

Table 2. Estimated Annual Recordkeeping Burden

Activity	No. of Recordkeepers	Annual Frequency per Recordkeeping	Total Annual Records	Hours per Record	Total Hours
N/A	N/A	N/A	N/A	N/A	N/A

[a]There are no capital costs or operating and maintenance costs associated with this collection of information.

These estimates are based on FDA's experience with previous consumer studies.

13. **Estimates of Other Total Annual Costs to Respondents and Record Keepers**

There are no costs to respondents. There are no record keepers.

14. **Annualized Cost to the Federal Government**

The estimated cost to the Federal Government for the collection of data is $1,613,294.00.

This includes the costs paid to the contractors to program the study, draw the sample, collect the

data, and create a database of the results. The cost also includes FDA staff time to design and manage the study, to analyze the resultant data, and to draft a report.

15. **Explanation for Programs Changes or Adjustments**

This is a new data collection.

16. **Plans for Tabulation and Publication and Project Time Schedule**

Conventional statistical techniques for experimental data, such as descriptive statistics, analysis of variance, and regression models, will be used to analyze the data in the second phase. The Agency anticipates disseminating the results of the study after the final analyses of the data are completed, reviewed, and cleared. The exact timing and nature of any such dissemination has not been determined, but may include presentations and articles at trade and academic conferences, publications, and Internet posting.

Table 3. Project Timetable

Task	Estimated Completion Date
External Peer Review	September, 2010
RIHSC Review	November, 2010
30-day FR notice publication	November, 2010
OMB Review of PRA package	January, 2010
Phase I Data Collection	February, 2011
Phase I Data Analysis	April, 2011
Receipt of Phase I Data and Methods Report from Contractor	April, 2011
Phase II Data Collection	July, 2011
Phase II Data Analysis	September, 2011
Draft Report	November, 2011

Internal Review of Draft Report	January, 2012
Revisions	February, 2012
Final Report	March, 2012

17. **Reason(s) Display of OMB Expiration Date is Inappropriate**

No exemption is requested.

18. **Exceptions to Certification for Paperwork Reduction Act Submissions**

No exceptions are requested.