FDA DOCUMENTATION FOR THE GENERIC CLEARANCE, "TESTING COMMUNICATIONS ON DRUGS PRODUCTS" (0910-0695)

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TITLE OF INFORMATION COLLECTION: Alternative Presentations of Clinical Pharmacology Section of Approved Drug Labeling and Effect on Comprehension, Memory, and Action

DESCRIPTION OF THIS SPECIFIC COLLECTION

1. **Statement of need:**

   Under 21 Code of Federal Regulations (CFR) Part 201.57, specific requirements are enumerated for content and format of labeling for human prescription drug and biological products as identified in 21 CFR Part 201.56. Under 21 CFR 201.57(c)(13), the requirements for labeling covering the Clinical Pharmacology section of the product labeling, identified as Section 12 of the labeling, are listed. Further, the FDA Guidance for Industry ─ Clinical Pharmacology Section of Labeling for Human Prescription Drug and Biological Products ─ Content and Format provides guidelines to enhance clarity and understanding of Section 12, the clinical pharmacology related information, and includes options for presenting information as text, tables, and/or figures. However, even when appropriate information is provided in the labeling, it does not guarantee that healthcare providers (HCP) will fully understand it and use it correctly.

   This proposed study seeks to assess various displays of clinical pharmacology information and increase the cognitive accessibility of clinical pharmacology information in the product labeling so that health care providers (HCPs) can find, understand, remember and use the information in a more efficient and accurate way. The findings will add additional context to the current guidance and future guidances regarding when the various options for presenting information should be utilized. Information determined through this study should positively impact how regulatory reviewers and pharmaceutical industry present clinical pharmacology information in labeling. If HCPs can find, understand, remember, and use labeling information in a more accurate and efficient manner, then public health will be better served through the more appropriate and safe use of drugs.

2. **Intended use of information:**

   Clinical pharmacology information is provided in approved labeling to help physicians and other healthcare providers to select appropriate treatments for specific patients, determine how much and how often they should take a drug, and monitor for both benefits and risks. Specifically, clinical pharmacology information in labeling describes what the body does to the drug and what the drug does to the body. This project examines the "cognitive accessibility" of clinical pharmacology related labeling information ─ the ease with which healthcare professionals can find, understand, remember and use it in an accurate and efficient manner, and seeks to evaluate alternative labeling displays to enhance comprehension of the technical information.

3. **Description of respondents:** Respondents are healthcare providers currently in clinical practice (physicians, nurses, and/or pharmacists) and recruited through various methods (advertising, posting, recruitment) available in the University setting. Projected outcomes of this project will impact reviewers of regulatory submissions (new drug applications, biologics license applications and abbreviated new drug applications), pharmaceutical industry that develop drug labeling, as well as HCPs who will use the label once approved.

4. **Date(s) to be Conducted:** As soon as approved to January 31, 2018.

5. **How the Information is being collected:** The project focuses on product labeling - Section 12 (i.e., Clinical Pharmacology), but will be conducted in a way that may permit application to other sections of the labeling. The proposed work consists of a series of actions, as described below.

Action 1: Design Alternative Displays

All information can be presented in multiple ways, e.g., electronic format, hard copy, interactive online display. The alternative representation approach shows that each type of display can have different cognitive consequences – effects on perception, attention, comprehension, problem solving, and decision making. We plan to develop alternative displays for Section 12 (Clinical Pharmacology) using text, tables, and/or figures. For the project, we will develop similar displays for a fictitious drug, to eliminate possible prior knowledge in test participants.

Alternative displays will also be designed for various other types of clinical pharmacology information. For example, the drug interaction information may benefit from display of data in a table or figure.

Action 2: Conduct Cognitive Accessibility Analysis

After creating alternative displays for major subsections in the Clinical Pharmacology section, we will perform a cognitive accessibility analysis of each display. In addition to measures typically used in health literacy research such as readability scores (to establish the grade level needed to understand them), we will also obtain psycholinguistic measures (such as grammatical complexity and cohesion of idea units) as well as design features (such as the spatial layout of the information). In order to ensure that none of the versions is set up to be a "straw man," each display will contain the same information and be well-designed.

Action 3: Conduct Literature Review

We will conduct a literature review to examine existing research on how physicians and other healthcare providers use the product labeling. A preliminary review of Agency-related materials (e.g., MedWatch reports, CDER Advisory Committee transcripts, "Dear Healthcare Professional" letters) may also be conducted, to determine whether they are useful in identifying incomplete understanding of the label. We will also assemble references concerning key cognitive principles that can be used to enhance cognitive accessibility.

Action 4: Develop Testing Methods

Two major types of testing methods will be developed to guide subsequent on-line testing (Action 5).

   a.   *Cognitive Testing Methods*

We will develop methods for testing the effects of the alternative displays on cognition. They will include cognitive tasks that examine attention, comprehension, memory, and decision making. For example, participants will study one of the displays, get information about hypothetical patients, and decide whether the drug is appropriate for them.

   b.   *MetaCognition Testing Methods*

We will also develop methods for determining how well providers like the alternative displays and how well they think they understand the information in each (This may be accomplished via online testing, direct observation, interviews or surveys). These "metacognition" questions are useful, since positive ratings suggest that people are more likely to read the information and are more mentally engaged in material they like and value. However there is often a gap between cognition (what people actually know and understand) and metacognition (what they think they know and understand) – people tend to overestimate their true knowledge and understanding. Therefore, we will compare results on cognitive and metacognitive tests, but actual cognition will be the main indicator of whether a given display is successful.

Action 5: Implement Testing Methods

We will translate the cognitive and metacognitive testing methods into software for online data collection. The testing software to be used permits presentation of carefully-controlled cognitive tasks as well as metacognition questions. The screen displays that participants see will look attractive and be user-friendly.

Action 6: Conduct a Pilot Test

We will conduct a pilot test of the cognitive and metacognitive methods with a small sample of healthcare professionals. Participants will be recruited from an opt-in internet panel of physicians and/or other healthcare providers (physician's assistants, nurses, nurse practitioners, pharmacists). On a random basis, each participant sees only one of the displays for a given subset of clinical pharmacology information. During the Study Phase, they study the information for a fixed amount of time (determined by the amount of information in the displays and past studies in the Medical Cognition Lab). During the Test Phase, they participate in cognitive tasks that assess attention, comprehension, memory, and decision making. Then they see the alternative displays again – both the one they studied and the other(s) – and answer the metacognition questions. The primary independent variable is display version and the dependent variables include accuracy (percent correct) on the cognitive tasks and ratings on Likert scales for the metacognition questions. The results will be used to determine whether any modifications of the testing methods are needed. They should also provide preliminary evidence about the relative

effectiveness of the alternative displays, prior to launch of a full study with a large sample of healthcare providers (to be conducted with other support).

Action 7: Develop Knowledge, Tools, & Standards

A check-list for assessing the cognitive accessibility of drug information will be prepared. It will enable labeling developers to increase the communication effectiveness of labeling information. For example, if a check-list for certain information yields a low cognitive accessibility score, labeling developers can either modify the display in terms of the features that scored low in the check-list or consider shifting to an alternative type of display. The check-list will also enable regulators to assess the cognitive accessibility of sections in the labeling.

6. **Confidentiality of Respondents:**

   Personally identifiable information is collected only to the extent necessary, is not retained and is justified accordingly.

7. **Amount and justification for any proposed incentive**

   No incentives are offered.

8. **Questions of a Sensitive Nature**

   No names or personally identifiable information is collected. Some personal information will be collected, including age, provider category (e.g., physician or pharmacist), year of educational degree, years in practice, specialty, and type of clinical setting (e.g., private practice, hospital).

9. **Description of Statistical Methods**

   Responses in the cognitive tasks are scored for accuracy, with 1=correct and 0=incorrect; in rare, pre-specified cases, partial credit of 0.5 may be awarded. The main statistical analysis is a one-way analysis of variance, with type of display as the factor (e.g., text vs. table). This analysis is performed on accuracy scores for the cognitive tasks and on ratings scores in the metacognition questions. The criterion for statistical significance is $p < .05$ or better.

BURDEN HOUR COMPUTATION *(Number of responses (X) estimated response or participation time in minutes (/60) = annual burden hours):*

Type/Category of Respondent	No. of Respondents	Participation Time (minutes)	Burden (hours)
Prescribers[a]	50	30	25
Pharmacists	50	30	25
Nurses	50	30	25
Total	150		75 hours

[a] Includes Physicians, Nurse practitioners, and Physicians assistants.

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