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PhRMA

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Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane; Room 1061
Rockville, MD 20852

Re: Docket Number 03N-0017; Agency Information Collection Activities: Proposed Collection; Comment Request; Impact of Risk Management Programs on the Practice of Pharmacy; 68 *Federal Register* 7124

Dear Sir/Madam:

The following comments on the above noted information collection activity are submitted on behalf of the Pharmaceutical Research and Manufacturers of America (PhRMA). PhRMA represents the country's leading research-based pharmaceutical and biotechnology companies. Our member companies are devoted to inventing medicines that allow patients to lead longer, happier, healthier, and more productive lives. In 2001, our members invested over $30 billion in the discovery and development of new medicines.

PhRMA appreciates the opportunity to provide input on FDA's request for comment on a proposed information collection concerning the "Impact of Risk Management Programs on the Practice of Pharmacy."

PhRMA generally believes that information collections, including surveys, can be useful for the performance of FDA's functions, and that answers to the questions that guide the data collection can have practical utility. However, this particular survey, as proposed, will not provide clear and useful information. Therefore, the survey should be revised with particular attention paid to sampling methodology, enhancing response rates, and enhancing the quality, utility, and clarity of the information collected. PhRMA offers the following general comments on each of these topics for your consideration and would be happy to work with the FDA in revising this study to help maximize its usefulness for the agency and the public health. PhRMA also provides comments on specific survey questions in an Attachment to this letter. These comments are also designed to enhance the quality, utility and clarity of the information collected and to ensure that the stated goals of the information collection are met.

Sampling Methodology

The proposed sampling universe is too broad to provide valuable feedback to FDA. The vast majority of risk management (RM) programs affect pharmacists that dispense to ambulatory patients, mostly in the outpatient setting, and to a lesser degree, hospital-based pharmacists (e.g., for Tikosyn®). However, it is unclear how pharmacists employed by academia, regulatory agencies, or pharmaceutical manufacturers would be able to contribute to this survey by answering the questions that concern RM programs. The primary focus should be on community pharmacists who currently dispense medications with accompanying RM programs.

03N-0017

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If the sampling frame FDA proposes to use (licensed pharmacists listed with State Boards of Pharmacy) cannot distinguish between community dispensing pharmacists and others, then a different sampling frame should be chosen. Otherwise, many more pharmacists than necessary will be subjected to an initial mailing. The proposed survey design would require many pharmacists who do not have relevant experience to answer all of the questions – with outcomes that would not be especially useful. This constitutes an unnecessary burden. At the very least, even if other sampling frames cannot be identified, the pharmacists should be screened for their experience in dispensing RM program medications before being asked to respond to the entire questionnaire. Having an active pharmacist license does not mean that the individual dispenses medications in his or her position. A straightforward way to ensure that the respondents have this experience would be to word Question 1 as: "Are you currently employed in a position that requires that you dispense prescription medications?" If a potential respondent answers "no," indicating that he or she has little or no current experience, that person should be instructed to stop at that point and return the questionnaire.

It is also important to recognize that the environment and procedures in chain vs. independent pharmacies differ significantly. Ideally, the sampling frame should be stratified to obtain an equal distribution of pharmacists working in chain vs. independent pharmacies. If such stratification is not possible, a question should be added to allow FDA to analyze these groups separately. This suggested question should replace the current Question 2, which does not make this distinction.

If FDA is interested in how RM programs are being implemented in institutional settings, like nursing homes and hospitals, separate questions that are applicable to those settings should be added. The current questions concerning special prescription stickers and Medication Guides are mainly applicable to the retail pharmacy setting.

PhRMA is not aware of data to support FDA's stated expectation of a 75 to 85 percent response rate for a mailed survey, with only one follow-up mailing and no monetary incentive. Further, there appears to be no cover letter or other accompanying explanation or incentive that provides a compelling reason for a busy pharmacist to complete the questionnaire. Most mailed surveys have response rates significantly lower than 75 percent, and more often lower than 50 percent.

PhRMA questions the need for a sample of 5,000 pharmacists, regardless of whether it is a stratified or simple random sample. A sample of 384 should suffice to obtain a reasonably precise estimate (plus or minus 5 percentage points) of population parameters, regardless of the size of the population. This is using the most conservative assumptions about how respondents will answer. Even given a desire to obtain precise estimates for each of the four geographic regions, as mentioned in the *Federal Register* notice, 384 in each of these subgroups, or a total of 1,536 would be sufficient. This is far below the 3,750 return that a 75 percent response rate would offer.

Enhancing Response Rates

There are a number of ways that response rates may be enhanced. Inclusion of the following elements may enhance the likelihood that sampled pharmacists will participate.

- An introductory letter from FDA explaining why it is important for selected respondents to fill out and return this questionnaire. As mentioned above, there appears to be no compelling reason for a pharmacist to participate in this survey. In the absence of a compelling reason or a monetary incentive, an informational incentive, such as an offer to send a report of the results directly to the respondent, may be the next best thing.
- Assurance that responses will be confidential, at least, and anonymous, if that's the case, and that data will only be used in aggregate form.
- A clear signal on the outside of the envelope that the questionnaire is sponsored by FDA. There is, however, some risk to doing this if the pharmacists see it as a way to advance a political agenda rather than a way to give truthful responses. In any case, especially if the envelope will be mailed to a pharmacy rather than a home address, the envelope needs to be marked so as to have it "stand out" from junk mail. Without a way to distinguish the survey, it may be opened by someone else and never get to the sampled pharmacist.

In addition, PhRMA recommends a more comprehensive follow-up plan. One follow-up may not suffice for a mail questionnaire. It would also be better if the follow-up requests were not mailed to those who have already responded. However, if concern for anonymity overshadows the cost concerns of multiple follow-ups, the subsequent mailing should clearly state that it is only for those who have not already sent in the questionnaire.

Enhancing the Quality, Utility, and Clarity of the Information

The stated intent of this study is to "evaluate pharmacists' knowledge of risk management programs, identify barriers of compliance, and assess the impact of these programs on the practice of pharmacy" with the overall goal of "obtaining information that will help FDA understand how risk management programs affect the practice of pharmacy and gain insight on practical interventions for future risk management programs."

Knowledge. We are assuming that "knowledge" of risk management (RM) programs is being assessed by questions about respondents' experience with handling components of specific RM programs. However, knowledge is not identical to experience. The respondents may not understand why, and by whom, these RM programs are being instituted, which may affect their willingness to deal with the components of the program. The survey should be revised to include questions about what educational programs might be helpful in facilitating compliance with RM programs.

Barriers to Compliance. How are barriers to compliance being measured beyond Question 20? It appears that this question is the only one that is focused on this critical question. Given that, we have the following concerns about its presentation and validity.

- Because of the question's placement and lack of a clear heading indicating a change in focus, respondents are likely to answer it (and Questions 18 and 19) in the context of the previous "patient information" section. Thus, these questions need a new section heading and introductory sentence or two to clarify the scope of the queries.
- The dichotomous yes or no answer format does not provide useful comparative feedback about the **extent** to which the respondent has encountered each of the potential barriers. This could be done easily with a minor change to the format that would allow indication of the severity of the problem. Without this, if a pharmacist checked "yes" to every one of these, there would be no way to determine which was the greatest and which the least

problematic barrier to compliance. Alternatively, respondents could be asked which problem has posed, for them personally, the greatest barrier to effective implementation of RM programs.

Impact of Programs on Pharmacy. There are no specific questions that examine the impact on the practice of pharmacy of any of the 3 different risk management components examined (use of special prescription stickers, Dear Health Care Professional/Pharmacist letters, labeling/patient information/Medication Guides). Yet assessing the impact of these programs on pharmacy is one of the research's stated goals. This is a serious limitation of the data collection as proposed. Questions should be included that ask pharmacists to describe the qualitative and quantitative deviations from normal work flow that result from RM programs. For example, does dispensing medications with stickers utilize different resources than dispensing similar medications without stickers, and, if so, how? How do RM programs affect time to fill prescriptions or the quality of the pharmacist-patient relationship? Time and resources are both major issues for pharmacies; we could also assume that programs that increase either are likely to pose compliance problems. One way of getting some measure of impact within the current questionnaire format, at least on time spent, would be to ask how much additional time was needed with regard to each of the problems experienced in Question 20.

Finally, the flow and wording of many of the proposed questions can be improved to enhance the quality, utility, and clarity of the information collected. Specific comments on the questions are included in the Appendix.

CONCLUSIONS

In summary, PhRMA recommends that the proposed survey be revised in the following ways to be more useful to FDA's performance and improve its utility:

Sampling Methodology

- The primary focus should be on community pharmacists who are most likely to dispense medications associated with RM programs.
- The sampling frame should be stratified to obtain an equal distribution of pharmacists working in chain vs. independent pharmacies.
- The survey should be accompanied by an explanation or incentive that provides a compelling reason for a pharmacist to complete it.
- The sample size should be reduced.

Enhancing Response Rates – Inclusion of the following elements will result in a greater likelihood that sampled pharmacists will participate:

- A cover letter explaining why it is important for selected respondents to participate. This letter should include an offer to send a report of the results directly to the respondent and assurance that responses will be kept confidential.
- Disclosures on the outside envelope that will make the survey mailing "stand out" from the clutter of other mailings.
- A more comprehensive follow-up plan.

Enhancing the Quality, Utility, and Clarity of the Information

- The survey should be revised to include questions about what educational programs might be helpful in facilitating compliance with RM programs.
- Question 20 should be revised to measure barriers to compliance through the inclusion of: (1) a new section heading and introductory sentence or two to clarify the scope of the queries, and (2) a change to the format that would allow indication of the severity of the problem.
- The survey should include questions that examine the impact on the practice of pharmacy of any of the 3 different risk management components examined (use of special prescription stickers, Dear Health Care Professional/Pharmacist letters, labeling/patient information/Medication Guides), as this is the stated goal of the research.
- Revisions to the questions as described in the Appendix.

PhRMA hopes that these comments will prove useful to FDA as the Agency moves ahead with this survey.

Sincerely,

Attachment: Comments on Survey Questions

ATTACHMENT

PhRMA Comments on Survey Questions:

The following comments are offered in the spirit of improving the questionnaire.

Questions 1 and 2: These questions were commented on in *Sampling Methodology*. PhRMA recommends that Question 2 be replaced with a question that distinguishes respondents working in chain vs. independent pharmacies. If the question is retained, it should be reworked so that the wording is consistent with the response requested. Specifically, asking a respondent to choose what settings "best" describe where they are currently practicing pharmacy is internally inconsistent. "Best" implies a singular response. Either "best" should be deleted, allowing multiple responses, or it should be retained, and only one response should be solicited.

Introduction to prescription stickers section: The initial explanation is insufficient to distinguish between a sticker a prescriber places on a prescription to signal that he or she did something or made some decision vs. a sticker that a pharmacist places on the bottles in which they dispense medications. The description in parentheses gives no real context for why physicians use these stickers but does potentially bias the results by stating "to ensure that safety risks have been addressed." PhRMA suggests alternative wording along the lines of: "Some medications are supposed to be dispensed only when the prescriber affirms that certain actions have been taken by the patient or prescriber. The prescriber does this by putting a 'special sticker' on the prescription. This is different from the instruction or warning stickers that pharmacists put on bottles of dispensed medications." To reinforce this distinction, we recommend that each reference to a "special sticker" be highlighted somehow, for example, by bolding or putting it in quotation marks.

In addition, some of the medications that are now stickered (e.g., Accutane and Lotronex) were not stickered in the past. Pharmacists may not accurately recall their experiences as a function of when stickers were required vs. when they were not. Therefore, we suggest attaching a timeframe to the sticker question to place the responses in the timeframe of when stickers were required.

Questions 3 and 4: PhRMA suggests that the clarity of these questions would be increased by revising them as follows: "Have you ever received a prescription for a medication that required a 'special sticker' on the prescription for you to dispense the medication?" and "Have you ever received by fax or telephone a prescription for a medication that required a 'special sticker' on the prescription for you to dispense the medication?"

Questions 5 and 6: The placement of these questions should be immediately prior to Question 4, since they ask about the consequences of receiving a physical prescription order with a missing sticker, not about faxed or telephoned orders. In addition, how useful is "ever received" in Question 5? Is this just meant to be a screener for Question 6? In either case, without timeframes or amount quantification, the validity and usefulness of the information is suspect. What if the special sticker was missing more than once and the respondent took different actions on different occasions? Which occasion will the respondent choose to refer to in

answering Question 6? Will the respondent reference the most salient, which is likely to be the one that "stands out," or the most representative?

Question 5 could be more informative if asked as "About how often do you receive prescriptions for medications that require a 'special sticker' on the prescription for you to dispense the medication, but the 'special sticker' is missing?" The response set could be in percentage of time (e.g., 90-100% of the time; 75-89% of the time; 50-74% of the time; 25-49% of the time; 0-24% of the time), or to more subjective intervals (see suggestion in Question 10 comments).

There are a number of ways to quantify Question 6 to make it more useful. At the very least, the question should specify which occasion is being asked about (e.g., the most recent, or what is the most common/representative procedure followed). It would also be useful to know whether the respondent's pharmacy has a standard procedure in place for how to deal with missing stickers on medications with RM programs.

Question 7: Is the respondent being asked to comment on the helpfulness of special stickers as a communication tool for him or herself, or for pharmacists in general? The way the question is worded appears to be the latter. But does the respondent have the expertise, or even sufficient experience, to judge this? We suggest revising the question to focus on the respondent's own experience. In addition, we suggest using "effective" rather than "helpful" because effective is a clearer concept than helpful. Thus: "How effective have 'special stickers' been as a communication tool between you, in your pharmacist role, and physicians with whom you interact?" Further, the response set proposed is likely to get nothing but "somewhats" because the respondents are unlikely to use the extreme anchors. We recommend either using a 5 or 7 point scale anchored by "extremely" and "not at all," or a 4 point scale without a clear neutral point, such as "very," "moderately," "somewhat," and "not very."

Question 8: PhRMA recommends clarifying that the referenced communication between pharmacists and physicians be regarding medication or drug risks. The wording should also be made consistent with Questions 12 and 17 so that the respondents are not confused.

Question 10: Clarify that these are the letters they personally have received. The response alternatives are not well spaced. Specifically, there is a much greater interval between "often" and "rarely" than between "always" and "often" or between "rarely" and "never." We suggest using the response alternatives that FDA has successfully used in its own surveys in the past: "always," "usually," "sometimes," "rarely or never."

Question 11: PhRMA has the same concern as expressed for Question 7. We recommend that the survey ask pharmacists how helpful Dear HCP/Pharmacist letters are for manufacturers communicating with the respondent, since he or she is not likely to be an expert in determining how useful it is for others. PhRMA suggests wording along the lines of "How effective have 'Dear Pharmacist' or 'Dear Healthcare Professional' letters been in manufacturers effectively communicating with you as a pharmacist?" See comments on Question 7 for suggested response alternatives.

Additional suggestion for this section: Given that FDA has expressed some concern that these letters may not be the most effective way for manufacturers to communicate with health care professionals, this questionnaire provides an opportunity to query pharmacists about the

effectiveness of other ways sponsors communicate with pharmacists (e.g., FDA- and sponsor-supported web sites, pharmacy newsletters).

Introduction to Medication Guide etc. section. It is overstating the case to assert that patient labeling is always produced for the purpose of informing patients of drug risks. Drug risks are only one component of patient labeling; communicating instructions for use is the primary focus of some labeling, and providing a balanced view of the product is the primary focus of other labeling. We recommend that this first sentence be revised as follows: "*Medication Guides* and *Patient Package Inserts* are manufacturer-produced, FDA-approved information for patients about the medications they have been prescribed. *Patient information leaflets or sheets* are also designed to give patients information about their prescribed medications. However, they are not produced by pharmaceutical manufacturers nor are they approved by FDA."

Question 13: PhRMA is concerned that the wording of this question will produce a "yea-saying" response bias because of its relatively challenging wording. What pharmacist is going to say that she or he is not familiar with the term, given its description in the preceding paragraph? We recommend deleting this question.

Question 14: The response alternatives given to this question don't match the way the question is worded. As worded, the question suggests a "yes-no" answer. We recommend: "For each of the 3 patient information categories below, please indicate your understanding of when the patient literature should be given to the patient with the dispensed medication." We also recommend revising, to improve clarity, "Always Optional" to "Never required to be given out."

Question 15: PhRMA has the same concern about the response scale proposed here as for Question 10. The alternatives are not equally spaced. If an even more quantitatively-based response is desired, one solution would be to use the response alternatives suggested in our comments on Question 5.

Question 16: The question and the response alternatives are not consistent. We agree with the "effectiveness" specified in the question, and recommend that the response alternatives be changed to be consistent with this, keeping in mind our recommendations on Question 7.

Question 18: It is not clear whether this refers to patient education materials or educational materials for the pharmacist. Without this clarification, the results from this question would have no practical utility. We are also not sure which research question this particular item addresses. What is the usefulness to FDA of these data? Further, even drugs without risk management programs provide educational materials (for patients and health care professionals). In order to get a sense of whether products with risk management programs get the same, less, or more of this kind of information, we recommend including in the listing some products that do **not** have a risk management program.

Question 20: See comments under *Barriers to Compliance* and *Impact of Programs on Pharmacy*. Also, some of the items in Question 19 that form the basis for answers to Question 20 are oral dosage forms, but are not "pills" (e.g., Actiq, Tikosyn). Therefore, use of the term "pill" in Question 20 undermines the credibility of the questionnaire as being directed toward pharmacists, who are likely to know the difference between varying oral dosage forms. We recommend substituting "medication" for "pill." For ease of responding, we recommend grouping the "problems" as a function of their source – the prescriber (e.g., Prescriber

complains about ...), patient (Patient wants ....), or the pharmacist's own experience (You had difficulty ...). Also, we recommend separating into 2 sub-items the item about difficulty in confirming that the prescriber vs. the patient is registered. In the current proposal, these are confounded.