MINUTES OF THE

RISK COMMUNICATION ADVISORY COMMITTEE, FDA

NTSB Conference Center, 429 L'Enfant Plaza S. W. Washington, DC
Thursday, February 26, and Friday, February 27, 2009

Executive Summary

The Risk Communication Advisory Committee (RCAC) and several members of CDER's Drug Safety and Risk Management (DSARM) Advisory Committee met February 26 and 27, 2009.

Ten people spoke during the Open Public Hearing on the first day, and six people spoke on the second day (see below for more detail).

Discussion Topic

The meeting's discussion topic was how to improve the communication of information about prescription drugs to patients. The different types of prescription drug information currently available to patients include Medication Guides, Patient Package Inserts (PPIs), and Consumer Medication Information (CMI). For more detail see below and the meeting materials, transcript, and presentation slides available on the FDA's website: http://www.fda.gov/ohrms/dockets/ac/oc09.html#RCAC

Summary Results

After hearing and discussing the presentations listed in the agenda and presented at the open public hearing, members turned to a set of draft recommendations proposed by the chairman. After discussion of modifications, and acknowledgment of the committee's advisory role, the following set of recommendations was voted upon (in accord with procedures in the recent guidance on voting). The recommendations were supported unanimously by the 15 voting members listed in the roster, except #7, which was voted 14 in favor, 1 against.

1. FDA should adopt a single standard document for communicating essential information about pharmaceuticals, which would replace the current set (PPI, CMI, and MG), through an appropriate consultative process.

2. That standard document should include quantitative summaries of risks and benefits, along with use and precaution information.

3. FDA should adopt the Drug Facts Box format as its standard. It should engage in a process for creating a standard for elaborating information. This adoption should be supported by a rigorous evaluation process, building on existing research.

4. FDA should rely on its existing review processes to derive the authoritative information that the standard document requires, including pharmaceutical company

submissions and expert panel summaries. It should create a process for ensuring up-to-date information on all drugs.

5. FDA-approved and required communications should be subject to rigorous empirical evaluation of their effectiveness.

6. FDA should establish performance standards for the effectiveness of the standard document(s), defined in terms of individuals who have received it.

7. FDA should conduct a systems analysis of the dissemination processes by which the standard document(s) reach consumers at times relevant to their decision making about a product's adoption and use.

8. FDA should identify populations for which the standard document or the dissemination system is inadequate. It should address their needs, where that is within its capabilities, and partner with other organizations, where it is not.

9. FDA should continue to strengthen its practice of relying on the best available social and behavioral science for designing and evaluating communications, including research on textual, numerical, and visual displays. It should foster research relevant to improving the effectiveness and dissemination of its standard document(s). It should include analytical research for identifying the information most critical to the decision making of target audiences.

Members Present

RCAC Members:
Baruch Fischhoff, Ph.D., *Chair*
Craig Andrews, Ph.D.
Christine M. Bruhn, Ph.D.
AnnaMaria DeSalva, B.A.
Sokoya Finch, M.A.
Michael Goldstein, M.D.
Prerna Mona Khanna, M.D., M.P.H.
Madeline Y. Lawson, M.A.
Musa Mayer, M.S., M.A.
John E. Paling, Ph.D.
Ellen M. Peters, Ph.D.
Betsy Lynn Sleath, Ph.D.

DSARM Members:

Terry C. Davis, Ph.D.
Timothy Lesar, Pharm.D.

Sidney Wolfe, M.D. *Consumer Representative*

Bruce Burlington, M.D., *Guest Industry Representative*

Executive Secretary
Lee L. Zwanziger, Ph.D.

Open Public Hearing Speakers

February 26, 2009
Dennis Wiesner, R.Ph.
Paul Johnson, R.Ph.
Tony Lee, Esq.
Marcie Bough, Pharm.D.
Gerald K. McEvoy, Pharm. D.
Saul Shiffman, Ph.D.
Jeffrey E. Fetterman
Pam Budny
Mukesh C. Mehta, R.Ph.
Mary Mease, R.Ph.

February 27, 2009
Claire DeMatteis
Michael J. Miller, R.Ph., Dr.PH.
Cassie Plummer, Pharm.D., MPH
Ellen Hoenig Carlson
Ellen Liversidge
Kala Paul

Presentations, Thursday, February 26, 2009

- Welcome
  Deborah Henderson, Director, Office of Executive Programs, CDER

- Background and Overview of the CMI, PPI, Medication Guides Programs
  Nancy Ostrove, Ph.D., Director for Risk Communication,
  Office of Policy and Planning, FDA
  Jodi Duckhorn, M.A., Team Leader, Division of Risk Management,
  Office of Surveillance and Epidemiology, CDER

- Expert and Consumer Evaluation of Consumer Medication Information – 2008 Final Report
  Carole L. Kimberlin, Ph.D., and Almut Winterstein, Ph.D.
  University of Florida College of Pharmacy

Presentations, Friday, February 27, 2009

- Welcome
  Jeffrey Shuren, M.D., J.D., Associate Commissioner for Policy and Planning

- The effectiveness of the drug facts box in communicating the benefits and side effects of prescription drugs
  Lisa Schwartz, M.D., M.S. and Steven Woloshin, M.D., M.S.
  Outcomes Group, VA Medical Center, White River Junction, VT

- Consumer Medicines Information in Europe; learnings from research, policy and practice
  Dr DK Theo Raynor, Professor of Pharmacy Practice, University of Leeds, UK

- Communicating with patients about prescription drugs and health care: The role of diminished status and other systemic factors in addressing risk and vulnerability
  David P. Moxley, M.S.W., Ph.D., D.P.A., Professor of Social Work
  University of Oklahoma

Risk Communication Advisory Committee Meeting,

February 26, 2009

The Risk Communication Advisory Committee (RCAC) meeting was called to order by Baruch Fischhoff, Committee Chair, at approximately 8:00 a.m., Thursday, February 26, 2009. Three members, Jacob DeLaRosa, Sally Greenberg, and Michael Wolf, could not be present due to patient or family emergencies, or schedule conflicts. Dr. Bruce Burlington also was absent the first day due to a family emergency but participated on the second day. The conflict of interest statement was read into the record, noting that, based on the agenda and financial information reported by participants, no members had conflicts of interest, but that all participants were aware of the need to address conflicts of interest should any arise. All participants introduced themselves. Dr. Fischhoff summarized the history and past meetings of the RCAC, and read aloud the discussion topics (below).

Discussion Topics (provided to Committee)

The goal as stated in Public Law 104-180 that 95 percent of patients should be receiving useful information by 2006 has not been met, according to the criteria of "useful" specified in the law and described in guidance provided by the long-range action plan and the FDA. In addition, some consumer groups have expressed concern that receiving multiple documents with their prescription drugs at the pharmacy can be confusing. Please comment on the following:

1. Does the existing scientific evidence recommend using multiple communication tools (CMI, PPI, Medication Guides) or a single tool to most effectively communicate prescription drug information to patients? Please describe.

2. In addition to published studies discussed above, what other types of scientific research should be conducted to ensure that FDA is effectively communicating prescription drug information to patients?

3. Based on what you've heard at this meeting and your knowledge of the literature, what is the best format for written patient information? For example, is there evidence supporting use of unstructured narrative, question and answer, tabular, listing of top ten risks, or another format?

4. How should FDA evaluate the effectiveness of different communication tools? Further, what are the most important parts of a complete assessment of a communication tool (for example, did the patient receive the tool, did the patient read the tool, did the patient understand the tool?)

5. Please prioritize the types of research relating to patient information. What projects are most important for moving forward expeditiously? Please include consideration of the following, plus other factors you think important.

- The amount of information patients receive from the pharmacy
- The appropriate balance of risk and benefit information
- The most effective order in which to present information (such as risks, benefits, instructions for use)

- Whether the information should be in a standard format or an "as appropriate for that product" format (An example of standard format is the "Drug Facts" label used on OTC products. Examples of product appropriate formats are a "top ten" most important things to know, or the question-and-answer format now used in Medication Guides)
- The most credible source for this information (i.e.: what source is most trusted by patients: government agency, manufacturers, healthcare professionals such as pharmacists, or other source?)
- How to effectively communicate with patients of differing literacy levels, primary language skills other than English, or underserved patient populations.

Summary of Presentations and Committee Discussions, February 26, 2009

Please see the slides and transcript for further details.

Welcome

Deborah Henderson, Director, Office of Executive Programs, CDER, thanked the RCAC members for their services and summarized the historical background of the meeting topic including FDA's initial efforts toward requiring PPIs, which began in 1968, the Public Law (PL) 104-180 in 1996 that described goals for CMI, the 1998 final rule on Medication Guides, and the 2006 guidance on CMI. FDA has held many public meetings and hearings on the topic, and has heard from stakeholders through individual letters, meetings, and a Citizens Petition (the latter still pending, therefore, not under discussion today), and through federal legislation in the FDA Amendments Act of 2007. The FDA recognizes many challenges, including the overwhelming amount of paper given to patients, the burdens on pharmacies, and the conflicting needs of some patients who desire all risk information, while others need easily accessible highlighted information.

Background and Overview of the CMI, PPI, Medication Guide Programs

Nancy Ostrove, Ph.D., Director for Risk Communication, Office of Policy and Planning, FDA, first highlighted the change in professional and societal attitudes about providing prescription drug information to patients, from 16th century prohibitions on communication, to early (USA) 20th century discouragement, through ongoing attempts to provide information that is adequate in detail but also understandable and useful to patients. She expanded on the previous presentation of FDA's involvement, explaining that PPIs began to be required for oral contraceptives and estrogens because of the ethical need to ensure consent from the healthy patients taking the drugs and hence facing the risks. She noted that PPIs exist for some other drug products but need not be distributed. She also referenced profound cultural changes toward greater patient information and involvement in decision making. Finally, she cited the non-government institutions that, in the 1980s, began to support appropriate communication with patients, such as Ciba Geigy's grant to establish National Center for Patient Information and Education, and the American Medical Association's commitment to provide medication leaflets physicians could hand out to patients when prescribing medicines. Overall, although these actions have sought to encourage patient understanding, the result has been a confusing situation with multiple patient information vehicles.

Jodi Duckhorn, M.A., Team Leader, Division of Risk Management, Office of Surveillance and Epidemiology, CDER, expanded further upon the three current types of written

medication information: Medication Guides, PPIs, and CMI. Medication Guides are written by manufacturers and reviewed by FDA. They may be required for certain self-administered prescription drugs, where information could help prevent serious adverse effects, where the product has serious risks that could affect patients' usage decisions, or where patient adherence to instructions is crucial to the product's effectiveness. Manufacturers are required to provide Medication Guides to pharmacies, which must dispensed with the prescribed drug. Medication Guides aim for a sixth to eighth grade reading level, legibility, and a uniform question/answer format. The FDA Amendments Act of 2007 requires that they be assessed for effectiveness. Ms. Duckhorn explained that the FDA reviews the sponsors' evaluation plans and that, so far, many have been deficient. PPIs, even when not required by regulation, are part of official product labeling and reviewed by FDA, but their distribution is not required. CMI differs in that it is not produced by manufacturers nor reviewed by FDA. Today, patients could receive both a Medication Guide and CMI, or both a PPI and CMI, or CMI alone, when picking up a prescription. In response to PL 104-180, an Action Plan was developed by a consensus conference facilitated by the Keystone Center, which included proposed criteria for good CMI. An assessment in 2001 examined whether sampled CMI were meeting the law's goals of distribution and quality, and found deficiencies. After this, the agency issued guidance. The program was reassessed in 2008, but deficiencies remain.

Committee Questions and Discussion Following Presentation

- Two sources of existing research were suggested: (a) a RAND study commissioned by the FDA, in about 1980, written by David Kanouse, titled "Informing Patients About Drugs," for relevant information; and (b) the work of Dan Morrow.
- A member noted that using multiple vehicles to communicate can increase effectiveness, provided the messages are complementary, without overwhelming the audience with information.
- Regarding the question of how to evaluate drug information for patients, several members pointed out that asking people whether they've understood something is well-known to be unreliable; instead, people should be asked to demonstrate knowledge of key points. They encouraged FDA to insist on rigorous evaluations of communications for effectiveness, including by manufacturers.
- Further to the question of evaluating drug information, a member asked whether there had been research comparing the effectiveness of PPIs, CMI, and Medication Guides. No one was aware of such research, but Ms. Duckhorn explained that it would be difficult to do because generally a drug does not have both a PPI and a Medication Guide.
- Regarding the question of how to communicate effectively with persons of differing literacy or primary language, Ms. Duckhorn explained that there is no regulatory requirement that sponsors provide information in languages other than English. Regarding the evaluation of communications with different groups, she asked how sponsors could locate a sample without either violating HIPAA or using a selected ("cherry-picked") set of physicians for recruitment; this latter question was not settled at the meeting.
- Members requested clarification on the history of mandating PPIs for oral contraceptives and estrogens; FDA representatives explained about the then-novel (but now much more common) idea of prescribing risky drugs to healthy persons. A member explained that there had been an effort to expand the PPI program, but the program was canceled in the early 80s.

- A member referred to research showing that balanced communication of risks and benefits information supports patient adherence to medication.

Expert and Consumer Evaluation of Consumer Medication Information – 2008 Final Report

Carole L. Kimberlin, Ph.D., and Almut Winterstein, Ph.D. of the University of Florida College of Pharmacy, were the principal investigators for the reassessment of CMI[1]. Dr. Kimberlin spoke first, explaining that the 2008 study protocol followed that of the 2001 study. A randomly selected sample of pharmacies (planned as 420, with 365 being completed) was visited by professional shoppers posing as patients with new prescriptions for two example drugs, to see what written information they would receive. An expert panel reviewed the information in light of the criteria of the Action Plan, and a sample of consumers also assessed the consumer communication criteria for CMI. The results were that 94% of the pharmacies visited provided CMI leaflets, which were highly variable in length, problematic with respect to the criteria of directions for use, and monitoring for safety, as well as format. Readability and usefulness were particularly problematic, although most of the information was accurate.

Dr. Winterstein continued by presenting some examples, which she put into the context of manuals for personal computers and home appliances. She noted that the latter are generally better formatted, include troubleshooting information, and appear in several languages. She also suggested that improper use of these products might have much less health effect than improperly used prescription drugs.

She reported results of some additional analyses, going beyond the 2001 and 2008 protocol evaluations. First, there were no significant differences in quality between CMI produced by different publishers. However, different CMI from the same publisher could vary substantially in length and quality between pharmacies, for reasons that are not clear. She also noted that, in the study protocol, CMI items were scored for including certain information but were not assessed at all as to whether they included extraneous or repetitive information or multiple disclaimers, so that information overload remains a possibility. She raised the issue of individualization of information: drugs may be used for different conditions, some of which are evidence-based but off-label (non-FDA-approved) uses. She noted that CMI that explains the benefits and risks for a condition entirely different from the patient's diagnosis might be confusing. It is not clear, however, how our system could provide individualized information.

Committee Questions and Discussion Following Presentation

- A member described a study of risk communication involving use of a potentially dangerous paint stripping compound, highlighting two results: First, there was a potentially simple message, i.e. that users could take a couple of easy steps to ensure ventilation and then could use the product safely, Second, the information about these steps was included in labels of some but not all products; when included, it appeared confusingly in various locations. The author's conclusion was that the decentralized and non-research-based approach to providing information was not successful.

[1] Kimberlin, CL and Winterstein, AG. "Expert and Consumer Evaluation of Consumer Medication Information – 2008 Final Report, provided to the committee as background and available http://www.fda.gov/ohrms/dockets/ac/09/briefing/2009-4408b1-00-Index.html

- Regarding the amount of information to provide, a member noted the contrast between the suggestion to provide or highlight only the most likely adverse event information on the one hand, and the sense of betrayal experienced by patients and caregivers (including several who submitted written comments) who suffered an unexpected and devastating adverse event. Later in the discussion, another member commented that information has to be chosen strategically, in order to communicate what is most important in particular situations. The question of how to prioritize information, by usefulness, arose several times in the meeting.
- Several members commented that patient information appears to be directed toward two very different purposes – communication with the patient and insulating the manufacturer from possible liability – and noted that the legally insulating language may interfere with patient communication.
- Regarding the type of evaluation that should be done for patient information documents, particularly Medication Guides that target particular problems, a member pointed out that content-based evaluation (assessing whether the document meets certain criteria for the inclusion and display of information) , is at best only a surrogate for patient understanding and action (i.e., performance-based testing).

Summary of Open Public Hearing Presentations, February 26, 2009

Please see the slides (where applicable) and transcript for further details.

- Dennis Wiesner, RPh (CIPP), Senior Director, Pharmacy - Privacy - Government and Industry Affairs National Association of Chain Drug Stores, advocated a single document that would be short, simple, and easily understood, in place of the multiple documents potentially given to patients today.

- Paul Johnson R.Ph., Senior Clinical Manager, Wolters Kluwer Health - Clinical Solutions, pointed out that consumer medication information has improved significantly from the 2001 to the 2008 study, although problems with software and printing (e.g., font size, selected locally) remain.

- Tony Lee, Esq., Director of Public Policy, National Community Pharmacists Association, presented the view of his organization that, because the existing situation results in communication that is too complex, one document would be preferable (see slides).

- Marcie Bough, Pharm.D., Director, Federal Regulatory Affairs, American Pharmacists Association, commented that patients receive too much information and that, in particular, there are too many Medication Guides, and went on to provide specific suggestions for improving Medication Guides, CMI, and PPIs.

- Gerald K. McEvoy, Pharm. D. Assistant Vice President, Drug Information, and Editor in Chief, AHFS Drug Information and Consumer Medication Information, American Society of Health-System Pharmacists, agreed that progress had been made in the information provided by vendors. He also noted that consumer-centered research is needed, with a goal of producing one document (not modeled on physician labeling) (see slides).

- Saul Shiffman, Ph.D., Senior Scientific Advisor, Pinney Associates (Bethesda, MD) (and professor of health psychology and pharmaceutical sciences, University of

Pittsburgh) presented a small demonstration study, sampling non-college educated adults and oversampling elder subjects, for evaluating comprehension of drug information similar to the usability testing of nonprescription drug information (see slides).

- Jeffrey E. Fetterman, President & CEO, ParagonRx, summarized a small study on patient understanding of Medication Guides and commented on other results, regarding usability, and on principles of adult learning to propose some ways to improve documents on prescription drugs (see slides).

- Pam Budny, Manager of Regulator Affairs at Eli Lilly and Company, presented the company's position that patient-directed medication information needs improvement. It should be a single document, provided to patients with each prescription. The documents' content and format should be specified in regulations, prepared and tested by sponsors, and approved by FDA.

- Mukesh C. Mehta, Vice President of Thomson Reuters Health Care, suggested the following: written information about prescription drugs might best be provided by the prescriber; not all pharmacists are aware of required Medication Guides; and, the question is not only whether patients receive written information, but also whether they read and understand it.

- Mary Mease, currently of Quintiles and formerly of FDA, speaking on her own behalf, suggested that the revision of patient-directed information should proceed toward a vision of what it should be, not limited to written formats, and that there should be interaction between FDA and stakeholders on questions like testing comprehension in drug-naïve patients.

<u>Committee Questions and Discussion for Open Public Hearing</u>

- Several committee members inquired about the Citizen's Petition, acknowledging that FDA could not comment, but that any petitioners present could. Several speakers provided clarifying comments distinguishing the Petitioners' aspirations for improved health care and counseling, from possible legal or regulatory standards for written information.
- Observing that many speakers had advocated moving toward one type of document, a member asked the speakers for any data demonstrating that this would be more effective. No specific data were offered; one speaker suggested not pushing for one document until data were available, and another held that general observations suggest that one document would be an improvement over the current situation.
- Several members inquired further about uptake, workflow, and distribution in pharmacies affecting prescription drug information for patients, but these questions were not fully settled.

Summary of Committee's Further Comments and Discussion, February 26, 2009

- Several members commented at various points about aspects of the overall healthcare system that should be considered in ensuring that patients get useful information about their prescription drugs, including oral counseling by physicians

and pharmacists. FDA representatives welcomed the discussion as reflecting the system-wide nature of the challenge of providing patients with adequate and understandable information about prescription drugs. Agency personnel noted, however, that FDA has authority and capacity to regulate only drug products, not healthcare more generally.

- A member suggested viewing some well-developed documents (perhaps starting from the existing three types but working toward streamlining) as a basis for providing adequate information to patients, but not requiring a single vehicle to be ideal for all patients. In particular, when patients experience difficulties due to different primary language or lower health literacy or numeracy, then the health care system should include helpers to interpret the information, and these helpers should be accessible to patients who need them. Meanwhile, at least a good vehicle for information would be available.
- A member pointed out that patients receive information about their drugs from different perspectives at different points when treating a health problem, i.e., patient understanding of a medicine when first taking it differs from continuing to take it and incorporating it into their ongoing self-care. When designing studies, therefore, investigators should consider the situation in which communication effectiveness is to be evaluated. Another member later re-emphasized that studies should be designed to take into account a broad spectrum of users, including various types of patients, and that pilot tests should include the very different situations of drugs for chronic use and for acute uses (e.g., antibiotics).
- One member inquired whether other committee members supported continued private sector responsibility for CMI, given that the goals stipulated in PL 104-180 had not been met. Several members agreed that it was not a good idea and made further comments. However, as the discussion began to look like a non-simultaneous vote, Dr. Fischhoff explained the FDA voting guidance and encouraged members to plan to return to this topic, with others, the following day after full discussion of the proposal(s).
- A member commented that regulations mandating that information be provided can have good effects, referring to a study by Bonnie Svarstad, showing stronger state-level regulations about pharmacy counseling to be correlated with improved counseling and communication.
- A member commented that a single communication vehicle that would be understandable by patients would be better than the current situation, and also would make translation into other languages more feasible. While acknowledging that she had no confirmatory data at hand, she suggested that it is very likely that many people believe the CMI received with their drugs must be FDA-approved, so she would support FDA regulation. However, she was concerned that FDA approval of information should not serve as a legal shield from liability for the manufacturer.
- A member commented that while research results and methods generally relevant to many areas of the meeting topic exist, applications such as the amount of information patients need about drugs may be impossible to specify in the abstract. One approach would be to develop a pilot project with six different types of drugs (this could also be extended to devices), and use them to develop a template for communication, so that the public can become familiar with the format. She pointed out that the project would require expertise beyond social science, and eventually might be incorporated into the early drug review process by having medical reviewers prioritize the information patients most need to know. The member also commented that shorter, more concise messages generally are better

communicated, and could be followed by a second tier of more detailed information. The pilot communication should be tested with a convenience sample of individuals diverse in age, education, literacy and numeracy, or in a sample of actual users identified by partnering with professional associations that can recruit in member pharmacies.

- A member pointed out that many patients receive medicines as free samples in the doctor's office; further consideration of written information for patients should, therefore, include that situation.
- Another member stressed testing formats for communication, noting that it is already well established that grouping and ordering information is important for better understanding, and that there has been some previous work (referring to Alan Levy's article, "Performance Characteristics of Seven Nutrition Label Formats").
- In further comments on testing, several members noted that the population should include also diverse ethnic and racial characteristics, as well as different languages.
- Several members suggested in different contexts that one way to move forward would be to hold contests, for example, for CMI designs specified to be understandable in user performance testing, or for graphics arts students to develop icons for use in CMI with entries then subject to empirical user testing.

The meeting was adjourned at approximately 5:00 p.m. for the evening, to reconvene the next day.

Risk Communication Advisory Committee Meeting,

February 27, 2009

Dr. Fischhoff called the meeting back to order at approximately 8:00 a.m., Friday, February 27, 2009. The conflict of interest statement was read into the record. The Chairman welcomed all attendees and, after Committee members quickly reintroduced themselves, he opened the presentations and discussions of the day. The Committee returned to discussion of the topics listed above and heard additional presentations listed on the agenda and summarized below.

Summary of Presentations and Committee Discussions, February 27, 2009

Welcome

Jeffrey Shuren, M.D., J.D., Associate Commissioner for Policy and Planning, thanked the RCAC for input and described FDA actions responding to RCAC recommendations.

- Based on the committee's recommendations at its first meeting about a proposed template for FDA recall press releases, FDA staff members made revisions to the template, which is now in clearance. More generally, the advice of the first meeting emphasized the need to pretest FDA's messages; FDA is building and plans to pilot soon an infrastructure and a process to do this.
- The second meeting addressed two topics specified in the FDA Amendments Act. One was how direct-to-consumer advertising relates to communicating to subsets of the general population, such as the elderly, children, racial and ethnic minority groups, and to increasing access to health information and decreasing health

disparities for these populations. The Agency has been collecting information, reviewing published research and will soon be drafting the report to Congress. The second topic concerned a required study on the appropriateness of including in televised direct-to-consumer advertisements a statement encouraging consumers to report negative side effects of prescription drugs to MedWatch (as is currently required for printed direct-to-consumer prescription drug ads). RCAC members' comments informed revisions in the protocol.

- At the third meeting, the RCAC passed a set of resolutions with recommendations to FDA, including that "FDA should consider risk communication as a strategic function to be considered in designing its core processes" and that "FDA should engage in strategic planning of its risk communication activities." That resounded very strongly within the Agency. The FDA has established a Communications Council as an internal management committee to facilitate intra-agency communication and coordination of risk communication activities. Further, the FDA received funding in the Fiscal Year 2008 Supplemental Budget to hire additional staff with social and behavioral science expertise, and also to conduct risk communication-related research. The FDA also committed to develop a risk communication strategic plan. Drafting of that plan is underway and our goal is to complete that by the end of the fiscal year. The impact of these and other Committee advice has raised the profile of risk communication in the Agency among both managers and staff.

<u>The effectiveness of the drug facts box in communicating the benefits and side effects of prescription drugs</u>

Lisa Schwartz, M.D., M.S. and Steven Woloshin, M.D., M.S. of the Outcomes Group, VA Medical Center, White River Junction, VT presented. Dr. Woloshin began, noting that in the past, patients were not the intended audience for prescription drug information, but that has changed, as is especially obvious in direct-to-consumer drug advertisements. He argued that in order to make good decisions about drugs, patients need facts about the drugs, such as data on how well the drug works. Neither advertising nor the patient directed information discussed in the meeting thus far usually includes such data, however. When such data are mentioned, they may be in the form of relative risk, which can be difficult to interpret. Both drug ads and Medication Guides emphasize side effects associated with the drug, again often without data on the likelihood of adverse events. Their team has developed a prototype prescription drug facts box modeled on the existing nutrition facts box in food labeling. Since conceiving the idea in 2002, they have carried out two preliminary studies and two national, randomized trials[2]. In the most recent randomized trial, they identified participants from a random digit dial national sample, then randomized them to receive either two ads with drug facts boxes or the same two ads with the standard brief summary.

Dr. Schwartz continued the presentation, describing the two national trials designed to see whether using the drug facts box prototype or standard brief summaries made a difference in drug choice. In the first, participants were presented with advertisements for two fictional drugs for treating heartburn. The drugs were described as having similar

[2] Schwartz LM, Woloshin S and Welch HG. The Drug Facts Box: Providing Consumers with Simple Tabular Data on Drug Benefit and Harm. *Medical Decision Making*. 2007; 27: 655-662 and Schwartz LM, Woloshin S, and Welch HG. Communicating Drug Benefits and Harms With a Drug Facts Box: Two Randomized Trials. *Annals of Internal Medicine*. **150**(8). 21 April 2009., both suggested as background for the meeting.

side effects but different levels of effectiveness. The second study used ads for two fictional drugs to prevent second heart attack. The benefit of these drugs was numerically smaller relative to the drugs in the first trial. In both trials, the group receiving the brief summary tended to overestimate drug benefit more than the group receiving the drug facts box prototype. The researchers' overall conclusion is the drug facts box improved subjects' knowledge of prescription drug benefits and side effects, resulted in better choices between drugs for current symptoms, and corrected the over-estimation of benefit in the setting of prevention. Finally, she reported that they had been working on a pilot project with FDA medical reviewers to produce ten drug facts boxes for different drugs and to develop a handbook for writing them. They urge the FDA to start producing drug facts boxes as part of the review process for new drugs either in a stand-alone form or as part of other CMI efforts.

Committee Questions and Discussion Following Presentation

- Responding to a question about usability for patients with different characteristics, Dr. Schwartz noted that while they had not done subgroup analyses, participants with less education tended to do less well with the information in the prototype drug facts boxes, but they still did better than with the standard brief summaries.
- Several questions arose about the flexibility of the drug facts box format; for example, if the same drug were to have substantially different benefits in different groups of people, there might need to be more than one drug facts box. Dr. Woloshin said they'd assumed that a box would be needed for each indication. A member noted that pharmacies generally don't know the reason for prescribing a particular drug for a particular patient and that the boxes for some drugs could be quite different. How to handle that has not yet been addressed.
- Another question was how to deal with changing risk and benefit information. Dr. Schwartz said they'd considered dating the versions of each box.
- Responding to a question about testing different formats for presenting numerical information and future research, Dr. Schwartz said they had struggled with the problem of using percents or frequencies, but had not yet tested the alternatives.
- A member observed that the drug facts box presentation facilitates comparison of risks and benefits for a drug, and between different drugs, but that the comparisons are complicated. For example, data on benefits and risks of different drugs might be of different sorts because of coming from studies with different designs. Dr. Woloshin affirmed that they encourage rigorous comparative trials.

Consumer Medicines Information in Europe; learnings from research, policy and practice

Dr DK Theo Raynor, Professor of Pharmacy Practice, University of Leeds, UK, spoke by video conference from Leeds. Patient-focused research on CMI in Europe and Australasia in the past 20 years has been running in parallel with what has been happening in the U.S., leading to some common lessons. Currently, most drugs in the U.K. and across the European Union are given to the patient in original packs which pharmacies re-label. As a result, each pack must be provided a patient leaflet. The leaflet is written by the manufacturer according to strict guidance (including readability guidelines), and leaflets for new drugs must be successfully tested with people from the target patient group ("User-Testing") before they are granted a license. In collaboration with colleagues at Wisconsin and Sydney, his group compared the readability and

usability of CMI from Australia, the UK, and the U.S.[3] Although Australian leaflets achieved very good compliance, they often are not distributed. The U.K. leaflets did slightly less well, and the U.S. leaflets were further behind on these criteria. The U.S. sample had only 50 percent compliance for contraindications and precautions, as well as problems with legibility and comprehensibility.

Dr. Raynor's group has produced a worldwide review of the research in English-language CMI.[4] They found widespread dissatisfaction but positive guidance including that: people don't want written information to substitute for spoken information from the prescriber, people value information that was set in the context of their particular illness and contained a balance of benefit and harm information, and people vary in their need and desire for detail. People want drug information both to help make the initial decision about using the drug, and if they use it, to help with ongoing decisions about continued use and for understanding symptoms if they occurred.

Regarding user testing, he highlighted two options for determining whether people can find and understand the information they need: content-based (using readability formulae and check lists) or performance-based. He reminded the audience that readability formulae are based on word and sentence length and, therefore, a written passage can have the same readability score whether written backwards or forwards.

He concluded by listing points of common understanding: unit-of-use packaging guarantees delivery of the CMI, as a system depending on another party to print and add it makes delivery less likely; in all cases, written CMI should supplement, not replace, counseling; performance–based user testing is crucial in evaluating effectiveness; standardization through a template may be helpful to increase usability and meet content guidelines, but it is also important to account for differences among drug types; and finally, the inclusion of more benefits information to produce a more balanced leaflet would help meet patients' concerns.

<u>Committee Questions and Discussion Following Presentation</u>

- Responding to a question regarding the presentation of quantitative information about risks and benefits, Dr. Raynor reported that EU and UK documents do not currently include data on benefits. For adverse events, however, the documents include both specific quantitative information and verbal descriptors (e.g., "common") in five bands. Their research suggests that both are better than either the verbal descriptor or a percentage alone, although more work is needed.
- Responding to a question about distribution in the different national systems studied, Dr. Raynor said that all have problems; in the US, the problem seemed to be that patients might receive several documents. Having pharmacies print out the

[3] Raynor DK, Svarstad B, et al. Consumer Medication Information in the United States, Europe, and Australia: A Comparitive Evaluation. *Journal of the American Pharmacists Association*. 2007; 47(6): 717-724, suggested as background for the meeting.

[4] Raynor DK, Blenkinsopp A, et al. A systematic review of quantitative and qualitative research on the role and effectiveness of written information available to patients about individual medicines, Health Technology Assessment HTA NHS R&D HTA Programme, Executive Summary: *Health Technology Assessment* 2007; Vol. 11: No. 5, suggested as background for the meeting.

documents can cause other problems, in that the pharmacy might not always do it, or might include other distracting items like advertisements.

Communicating with patients about prescription drugs and health care: The role of diminished status and other systemic factors in addressing risk and vulnerability

David P. Moxley, M.S.W., Ph.D., D.P.A., Professor of Social Work, University of Oklahoma, described the Detroit-based Leaving Homelessness Intervention Research Project, which has been going eight years, focusing on homeless older African-American women. The project includes communicating around health in highly risky situations. It addresses the spectrum of social, economic, physical, psychological and other problems the participants are facing from a perspective of finding and building their strengths. The project defines "health" as the participants possessing the adaptive resources to function effectively in the face of daily exigencies and challenges. Homelessness wears down adaptation, flexibility, and functioning, and stimulates the onset of serious health problems such as arthritis. These bad effects can be worsened by bad experiences with health care—for example, being prescribed expensive corrective shoes, advised to avoid walking, or being prescribed medicines that must be taken regularly with food when a regular food supply is not available.

Small and personalized helping resources that truly represent the person, with short links between the person and the sources of help, are very important. Many participants face substantial practical issues with medication management, such as losing medication while on the streets or moving around, degradation of the containers, theft, loss through being arrested and imprisoned, and the need for heroic efforts to store medication, for example, when refrigeration is needed.

In facilitating the use of medication, personal control becomes an important part of the self-efficacy aims of the project. The adaptation the person makes to homelessness can influence communication. A person who does not trust health care workers, or is unable to concentrate because of stress or hunger, will be less receptive to medication directions. Strengthening self efficacy may improve receptivity to communication about self care. Medication management could be addressed in supportive group conditions. At the least, it could be very helpful to facilitate medical "homes" for homeless persons, because moving about and sporadically accessing healthcare can result in dangerous actions like abruptly stopping medication and suffering ill effects. Continuity of care could help both access and trust for better communication.

Committee Questions and Discussion Following Presentation

- Dr. Moxley agreed with a member's comment that a standard format for prescription drug information could help caregivers to help individuals such as those in the project. He also reported that a substantial majority of participants had, and used, cell phones and email accounts accessible on public terminals.

Summary of Open Public Hearing Presentations, February 27, 2009

Please see the slides (where applicable) and transcript for further details.

- Clair DeMatteis, Executive Vice President and General Counsel to Catalina Marketing Corporation, the parent company of Catalina Health Resource, which produces written medication information including CMI. Ms. DeMatteis pointed out

that current regulations are confusing and the resulting communication documents voluminous, repetitive, and likewise confusing. Therefore, they advocate a single, FDA-regulated document.

- Michael J. Miller, RPh, Dr.PH., Department of Pharmacy: Clinical and Administrative Sciences, The University of Oklahoma, summarized two recently completed research projects in which participants received a 30-minute telephone interview about NSAID risk awareness, with results that highlight the importance of health literacy (see slides).

- Cassie Plummer, Pharm.D. MPH, Drug Information Pharmacist, iGuard, Inc. introduced iGuard as a web-based medication monitoring service for patients and summarized a study of participants' experience with Medication Guides. Most wished to receive Medication Guides at their pharmacy, and nearly half wanted Guides at both the pharmacy and the doctor's office (see slides).

- Ellen Hoenig Carlson of AdvanceMarketWorx, referred to the work of Dr. John Medina, recommending four points: consumers don't pay attention to boring things; we have to repeat so the audience can remember; we need to stimulate more than one sense; and among the senses, vision is the most important (see slides).

- Ellen Liversidge, a Board Member of the Alliance for Human Research Protection, cited atypical antipsychotics as an example of lack of FDA vigilance. She noted that in June of 2007, she spoke before a committee of the FDA, asking that atypical antipsychotics have Medication Guides, but none have appeared.

- Kala Paul, a neurologist and president of the Corvallis Group, emphasized that user testing shows that many people have difficulty understanding written medication information, especially where numeracy is required, so that whatever the FDA does should be tested in actual patients, including older and lower literacy patients.

Summary of Committee's Closing Comments and Discussion, February 27, 2009

- Two short videos were shown of patients with lower health literacy, illustrating the profound efforts and confusion of individuals attempting to read, understand, and use prescription medications as directed.
- In further discussion of events at the meeting so far, a member commented that the use of a format like the drug facts box in prescription drug advertising could have positive effects on consumer understanding, but also could prompt individuals to make decisions about a medication before discussing it with a healthcare provider, and concluded that further research should address the downstream effects of communication formats. In reply, Ms. Henderson pointed out that the data FDA reviews regarding drug regulation comes from clinical trials designed to yield conclusions about populations, whereas medical care decisions must involve the judgment of a healthcare provider advising an individual patient about using a drug for a particular need.

After hearing and discussing the presentations listed in the agenda and presented at the open public hearing, members turned to a set of draft recommendations proposed by the

chairman. Dr. Fischhoff noted first that everyone should understand the statements of the committee to be advisory only and, therefore, should focus on the general sense of a recommendation rather than the literal wording. Dr. Ostrove also noted that agency actions have to reflect many considerations, so that even an action informed by a recommendation may diverge in implementation, to which both Dr. Fischhoff and another member agreed, but pointed out that the Committee could provide the agency with concrete recommendations to start from.

- Members then discussed the general thrust of the recommendations. Comments included:
    - Patient information should be evaluated not only for whether the written material meets predetermined criteria of completeness and readability, but also for whether patients can understand and act upon it.
    - Patient information should be performance tested with individuals similar to those likely to use the product, including, for example, older persons of lower health literacy and numeracy.
    - Supporting the development of one document in place of Medication Guides, PPIs and CMI does not rule out, but is consistent with, developing tiered information.
    - There are many different drug boxes in use or in the literature, including the model presented at the meeting and the current FDA-mandated OTC Drug Facts Box.
    - Icons (for example, the circle with a diagonal slash to show that something is prohibited) can be helpful for readers at all levels of literacy, but must be performance tested.
    - Concrete use directions should be included, tailored to the individual patient when technologically possible.

- Members then discussed individual recommendations, first addressing any final wording concerns. Please see the list of attendees for names of the fifteen voting members (industry representatives do not vote).

    - After noting that FDA would not necessarily draft patient information, and that healthcare providers should be consulted, members agreed unanimously to the following recommendation:

      1. FDA should adopt a single standard document for communicating essential information about pharmaceuticals, which would replace the current set (PPI, CMI, and MG), through an appropriate consultative process.

    - The second recommendation, very similar to previous RCAC advice, was agreed unanimously without further discussion:

      2. That standard document should include quantitative summaries of risks and benefits, along with use and precaution information.

    - After several comments indicating that at present it is not clear how a drug facts box format might best be integrated with tiered information, how it might affect subsequent consumer decision making, and what further development might be needed, Dr. Fischhoff specified that the recommendation should be read in the spirit of a drug facts box being a conceptual standard, that further

work should address how to provide more detailed information, and that any adoption should be supported by rigorous evaluation building on existing research. With that, the members agreed unanimously to the following recommendation:

3. FDA should adopt the Drug Facts Box format as its standard. It should engage in a process for creating a standard for elaborating information. This adoption should be supported by a rigorous evaluation process, building on existing research.

- Introducing the fourth recommendation, Dr. Fischhoff commented that the FDA has the most authoritative information through the drug review process, and should build on that base. Additional individual comments included that this is the model for developing labeling, that any such information should be updated with new postmarketing data, and that the process adopted should eventually be extended to drugs already approved. The members then agreed unanimously to the following recommendation:

  4. FDA should rely on its existing review processes to derive the authoritative information that the standard document requires, including pharmaceutical company submissions and expert panel summaries. It should create a process for ensuring up-to-date information on all drugs.

- The next recommendation was proposed using the word "usability," reflecting a human factors approach. Several members suggested using "effectiveness" instead, reflecting a healthcare environment. Comments about this and the next recommendation suggested adding target completion dates but that was decided to be left to the FDA. Another comment was that the proposed standards might be impossibly high if "effectiveness" meant observed behavior change, but was answered by the observation that "effectiveness" should be understood simply as indicating that users could locate and express key information. The members then agreed unanimously to the following recommendation:

  5. FDA-approved and required communications should be subject to rigorous empirical evaluation of their effectiveness.

- In discussing the next recommendation, members noted that it should refer to the standard document and to related documents, and that the phrase "individuals who have received it" should be understood as including patients and lay caregivers or others who provide additional interpretative help. The members then agreed unanimously to the following recommendation:

  6. FDA should establish performance standards for the effectiveness of the standard document(s), defined in terms of individuals who have received it.

- The next two proposals referred to delivery of the information, and some members suggested that the proposals are unnecessary, especially if information is required to be given with (eventually) every drug; when asked, fourteen of the fifteen voting members agreed to the following recommendation (Dr. Davis disagreeing that it was necessary).

7. FDA should conduct a systems analysis of the dissemination processes by which the standard document(s) reach consumers at times relevant to their decision making about a product's adoption and use.

- The eighth recommendation had been discussed with the seventh and was agreed on unanimously without further discussion:

  8. FDA should identify populations for which the standard document or the dissemination system is inadequate. It should address their needs, where that is within its capabilities, and partner with other organizations, where it is not.

- The final recommendation of the meeting was introduced as an appreciation and support for FDA to continue to strengthen and expand use of social and behavioral science, and after modification for consistency (e.g., the word "effectiveness" and attention to the differing needs of different audiences), members agreed unanimously to the following recommendation:

  9. FDA should continue to strengthen its practice of relying on the best available social and behavioral science for designing and evaluating communications, including research on textual, numerical, and visual displays. It should foster research relevant to improving the effectiveness and dissemination of its standard document(s). It should include analytical research for identifying the information most critical to the decision making of target audiences.

The meeting was adjourned at 2:00 p.m.

For further details of presentations and discussions, please see transcript and slides, both posted at http://www.fda.gov/ohrms/dockets/ac/oc09.html#RCAC.

Appendix: FDA Discussion Topics

The FDA had provided the Committee with a set of discussion topics, read into the record by Dr. Fischhoff and referred to in discussion throughout the meeting, but not formally treated as questions for voting. For convenience, we have gathered below some summary comments already mentioned that explicitly or implicitly address the FDA discussion topics.

Discussion Topics

The goal as stated in Public Law 104-180 that 95 percent of patients should be receiving useful information by 2006 has not been met, according to the criteria of "useful" specified in the law and described in guidance provided by the long-range action plan and the FDA. In addition, some consumer groups have expressed concern that receiving multiple documents with their prescription drugs at the pharmacy can be confusing. Please comment on the following:

1. Does the existing scientific evidence recommend using multiple communication tools (CMI, PPI, Medication Guides) or a single tool to most effectively communicate prescription drug information to patients? Please describe.

> Member comments: Many members indicated that the current situation is untenable and not supported by evidence, and that a single document would be preferable. Members also held that it should be developed in light of research and should be evaluated for effectiveness by both content testing and performance testing in diverse users. Members noted that consistently using a single form of document will allow members of the public to develop familiarity and skill in using it. Members also indicated that the document should be tiered, as some individuals (or individuals at different points in their condition and decision-making process) simply need basic information that is readily accessible, while others need more detail).

2. In addition to published studies discussed above, what other types of scientific research should be conducted to ensure that FDA is effectively communicating prescription drug information to patients?

> Member comments: Members strongly and repeatedly advised FDA to ensure that documents for communicating prescription drug information to patients and other individuals be user tested with performance standards, not just content tested by pre-determined criteria. Performance standards must be defined, and should include knowledge of key facts about the product in question. Identifying the key facts about a particular product will depend on medical knowledge.

3. Based on what you've heard at this meeting and your knowledge of the literature, what is the best format for written patient information? For example, is there evidence supporting use of unstructured narrative, question and answer, tabular, listing of top ten risks, or another format?

> Member comments: Various members commented that a drug facts box format had certain clear advantages, such as gathering different types of information together and providing a standard ordering of information. Given that members have consistently and strongly supported including numerical information about risks and benefits in the current and previous meeting(s), members commended a tabular sort of format as an effective way to display quantitative information. However, it was also noted that there was little discussion and little data presented about various other formats, so further work should be done in developing a standard.

4. How should FDA evaluate the effectiveness of different communication tools? Further, what are the most important parts of a complete assessment of a communication tool (for example, did the patient receive the tool, did the patient read the tool, did the patient understand the tool?)

> Member comments: Many members strongly advised FDA to incorporate performance testing, not just content testing, into standards of evaluating different communication tools. In suggesting what sort of users to test, many members strongly advised the FDA to ensure that users of varying age, education, health literacy and numeracy, background, and other characteristics

be included, describing structured sampling as a methodology that could be used to consider different types of needs.

5. Please prioritize the types of research relating to patient information. What projects are most important for moving forward expeditiously? Please include consideration of the following, plus other factors you think important.

- The amount of information patients receive from the pharmacy
- The appropriate balance of risk and benefit information
- The most effective order in which to present information (such as risks, benefits, instructions for use)
- Whether the information should be in a standard format or an "as appropriate for that product" format (An example of standard format is the "Drug Facts" label used on OTC products. Examples of product appropriate formats are a "top ten" most important things to know, or the question-and-answer format now used in Medication Guides)
- The most credible source for this information (i.e.: what source is most trusted by patients: government agency, manufacturers, healthcare professionals such as pharmacists, or other source?)
- How to effectively communicate with patients of differing literacy levels, primary language skills other than English, or underserved patient populations.

Member comments: As noted above, the members have consistently placed a high priority on clearly communicating both risk and benefit information, and on testing documents with target users. It was suggested that some of the above questions could be addressed in a pilot project with different types of drugs, and the results used to develop other drug-specific communications. Various members have recommended exploring partnerships to build the capacity of the overall medical product and health care delivery system to address the needs of individuals who are otherwise marginalized due to such factors as speaking other languages or currently being homeless.

I certify that I attended the February 26 and 27, 2009, meeting of the Risk Communication Advisory Committee and that the minutes reflect what transpired.

//s//.
Lee L. Zwanziger, Ph.D.
Executive Secretary

//s//.
Baruch Fischhoff, Ph.D.
Chair