August 31, 2010

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

[Submitted online at: www.regulations.gov]


Dear Sir/Madam:

The American Pharmacists Association (APhA) appreciated the opportunity to present at the Food and Drug Administration’s (FDA) July 27-28, 2010 public meeting on issues and challenges associated with the development and implementation of risk evaluation and mitigation strategies (REMS) (Federal Register meeting notice published on June 17, 2010; 75 FR 34453). APhA, founded in 1852 as the American Pharmaceutical Association, represents more than 62,000 pharmacists, pharmaceutical scientists, student pharmacists, pharmacy technicians, and others interested in improving medication use and advancing patient care. APhA members provide care in all practice settings, including community pharmacies, hospitals, long-term care facilities, community health centers, managed care organizations, hospice settings, and the uniformed services.

As mentioned during the meeting, APhA greatly appreciates FDA’s ongoing efforts to gather input from stakeholders on issues related to REMS. We also appreciate FDA recognizing the need to address implementation and logistical challenges for prescribers and pharmacists as REMS are designed. APhA continues to advocate for a standardized, system-based approach that utilizes existing technologies and infrastructures that can be applicable for any REMS program. APhA’s goal is to be a resource for FDA and manufacturers in helping to ensure that REMS programs achieve their intended outcomes, limit burdens on the health care system, and recognize the important role that pharmacists play in safe medication use as part of the health care team.

As follow-up to the public meeting and the questions and answers with FDA, APhA submits the following information to the docket:

- Attachment 1: Statement at the July 27-28, 2010 public meeting;
- Attachment 2: Supplement information for questions and answers at public meeting, including two research articles related to workflow capacity and burden;
- Attachment 3: APhA’s 2009 REMS White Paper referenced in our statement.
Again, thank you for the opportunity to provide comments to FDA on this important issue. We look forward to working collaboratively with FDA, manufacturers, and other stakeholders to develop successful REMS solutions. If you have any questions or require additional information, please contact me at (202) 429-7538, or at mbough@aphanet.org.

Sincerely,

Marcie A. Bough, PharmD
Director, Federal Regulatory Affairs

cc: Brian Gallagher, BSPharm, JD, Senior Vice President, Government Affairs
Kristina E. Lunner, Vice President, Government Affairs
Good afternoon. I am Marcie Bough, a pharmacist and Director of Federal Regulatory Affairs for the American Pharmacists Association (APhA). APhA, founded in 1852 as the American Pharmaceutical Association, represents more than 62,000 pharmacists, pharmaceutical scientists, student pharmacists, pharmacy technicians, and others interested in improving medication use and advancing patient care. APhA members provide care in all practice settings, including community pharmacies, hospitals, long-term care facilities, community health centers, managed care organizations, hospice settings and the uniformed services. Pharmacists, the medication expert on the health care team, play an important role in safe medication use and an important role in risk evaluation and mitigation strategies (REMS) programs.

APhA has been actively involved in many REMS discussions with FDA and other stakeholders throughout the past few years and we appreciate the opportunity to provide continued input at this public meeting. We also appreciate FDA’s efforts in the draft guidance to industry to recognize the implementation and logistical challenges for prescribers and pharmacists that must be addressed as REMS are designed.

My comments reflect APhA’s previous REMS statements and APhA’s November 2009 REMS White Paper published in the Journal of the American Pharmacists Association (JAPhA) that focuses on designing a REMS system to optimize the balance of patient access, medication safety, and impact on the health care system. In the interest of time, I am focusing my comments on two of FDA’s questions included in the meeting notice: Topic C/Questions 4 on issues related to elements to assure safe use (ETASU) on Tuesday; and Topic D on evaluating the effectiveness of REMS programs on Wednesday. For a more comprehensive statement on general REMS issues, please refer to APhA’s White Paper submitted to FDA’s docket and available online at www.japha.org/REMS.

Topic C/Question 4: Issues Related to Elements to Assure Safe Use
For Question 4 related to REMS elements that have affected the health care delivery system, unfortunately, many current risk management programs have presented challenges to practitioners due the lack of standardization and lack of consistency in components between the different programs. The silo effect of programs is not efficient in practice.
For Questions 4b) program design to reduce burden, and 4c) compatibility design with existing technologies to reduce burden, APhA’s comments are grouped as follows:

- Related to system design and infrastructure, any REMS should:
  - Be designed with input from front-line pharmacists and prescribers early in the development process.
  - Utilize a standardized, system-based approach that works for any REMS.
  - Integrate with existing electronic technologies and infrastructures in pharmacy and medical practice systems, including e-prescribing and electronic health records.
  - Consider the role of pharmacist in any REMS program.
  - Be available to any willing provider.
  - Not prevent or delay patient access to needed medications.
  - Be pilot tested prior to a nation-wide launch.
  - Accommodate the varying ways that prescriptions are received at the pharmacy (hand-written, fax, telephone, and electronic).

Various systems are in place that can be connected to or otherwise interoperable with existing standardized, electronic, real-time pharmacy claims adjudication infrastructure.

- Related to the REMS elements and design, any REMS should:
  - Recognize the role pharmacists can play in safe medication use.
  - Use standardized elements and processes to address administrative, logistical, and workflow implementation challenges.
  - Ensure components are workable for all stakeholders.
  - Ensure that programs are flexible enough to adjust to data showing successes or failures of certain components.
  - Define the stakeholder accountability for implementing specific components.

- Related to education design, any REMS should:
  - Provide information to prescribers and pharmacists about any REMS program and materials, requirements, accountability, and logistics to prescribe and dispense.
  - Utilize accredited continuing education materials from accredited providers that include specific information on safety, risks the REMS is designed to mitigate, and outcomes measures that capture practice changes.

Specific to streamlining training of health care providers, if we design for the long-term with a standardized, system-based process, then obtaining and completing educational requirements could be a standard process (for example, online module with online submission) for each REMS if required, not a different process for each REMS program.

If specific verification of education is required, attestation of the successful completion of a program could be sent electronically from the CE provider to the REMS administrator database for inclusion in a seamless verification process linked to the electronic prescription claims adjudication process.
• Related to ETASU design and patient care, any REMS should:
  o Ensure that components of a REMS serve as an adjunct to, not a replacement of
    prescriber/pharmacist dialogue with the patient.
  o Recognize the potential impact of pharmacist-provided clinical care, such as
    medication therapy management (MTM) services, as a potential element to assure
    safe use while recognizing the need for a viable compensation model for
    implementing such REMS requirements.
  • APhA believes that with appropriate time and resources needed to
    implement such elements, pharmacists can further improve REMS
    program effectiveness, patient safety and education, and public health.

• Related to the growing number of REMS, FDA should consider organizing REMS
  programs based on tiers or levels (similar to Schedules of controlled substances). The
  structure of each level could consist of a standard set of components to choose from
  based on the level or risk for which the REMS is designed to mitigate.

**Topic D: Evaluating the Effectiveness of the REMS**

• Related to Topic D: Evaluating the Effectiveness of the REMS, APhA supports efforts to
  better define and provide guidance on evaluation and assessment of REMS programs and
  outcomes. Efforts used in creating REMS need to be equally matched by efforts to
  evaluate the effectiveness and outcomes of a REMS and its individual components.

Specifically, any REMS program evaluation should ensure that:
  o Patient access to necessary medication is not prevented or delayed.
  o Access standards and provider participation through a REMS network is
    evaluated.
  o Achievable and measurable outcomes are designed and identified with specific
    metrics at the time of approval.
  o Components are proven to be effective in mitigating defined risk(s) and tied to
    metrics to measure successes and/or failures of those components.
  o Components are workable for all stakeholders (including patients, prescribers,
    pharmacists, manufacturers, wholesalers, and system vendors).
  o Stakeholder accountability for implementing specific REMS components are
    defined at the time of approval for a REMS program.
  o Reasons for failures/successes are documented and assessed (for example,
    outcome metrics need to capture the reason for patient failure and/or success,
    rather than just documenting the occurrence).
  o Unintended consequences (for example, decreased patient access, decreased or
    limited provider participation, shifts in risk or prescribing to non-REMS drugs,
    and disruption to delivery of patient care) are monitored.
  • FDA, manufacturers, and stakeholders will need to work together to find
    appropriate ways to document, assess, and report burden (both
    administrative and financial) on the health care system to implement
    REMS programs.
Additional evaluation requirements related to quality include:

- Capturing and reporting the frequency of components not being met, and what those components were; delays in patient access due to components not being met (compliance of a REMS program); and the number of prescriptions being dispensed that require a REMS.
- Allowing for a feedback-loop and continuous quality improvement on REMS programs to re-evaluate, assess and adjust, or discontinue components, throughout the lifecycle of the REMS.
- Requiring REMS programs to include information on where and how to report successes and or failures of REMS programs and components.

Finally, we need to find a balance between appropriate risk management, provider participation, and patient access while appropriately managing burdens on the health care system. Furthermore, these programs need to balance efficiencies and effectiveness so that patients continue to have access to needed medications that are part of a REMS program.

Conclusion

In closing, we appreciate the time and resources FDA has dedicated to this important issue and that FDA has acknowledged the important role of pharmacists and pharmacies in implementing REMS programs. While we recognize FDA does not regulate the practice of pharmacy, FDA’s decisions impact the practice of pharmacy every day. With appropriate time and resources, pharmacists can further improve public health and education for those medications requiring a REMS. Again, APhA continues to advocate for a standardized, system-based approach that utilizes existing technologies and infrastructures that can be applicable to implementing and evaluating these programs. We look forward to continuing to work with FDA, manufacturers, prescribers, pharmacists, and other stakeholders on solutions and outcomes needed to improve the REMS program. Thank you.

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Attachment 2
APhA appreciates that several important REMS issues were recognized and discussed during the public meeting panel question and answer dialogue with FDA, including:

- Opportunities for any willing provider to participate in a REMS program when the provider can meet the requirements of a REMS program;
- Implementing documentation models and establishing compensation models for pharmacist-provided clinical care, such as medication therapy management services, when such services are a required element to assure safe use in a REMS program;
- Identifying best practices for standardizing REMS programs and components;
- Implementing procedures for training attestation and verification; and
- Assessing the burden of REMS programs on pharmacists and the health care system and the capacity of pharmacists to implement REMS programs.

APhA welcomes the opportunity to further discuss these important issues with FDA as FDA continues to work on improving the REMS system. As mentioned at the public meeting, on October 6-7, 2010, APhA is hosting a second REMS meeting with a broad group of stakeholders (FDA has been invited) to discuss standardization and implementation issues and to identify guiding principles for REMS solutions moving forward. We also plans to have participants respond to and discuss a draft model framework for a “tiered” approach to different standardized REMS levels – an issue that APhA and others have advocated. APhA plans to provide the outcomes and publications of this meeting with FDA, Congress, industry, and other stakeholders.

Related to assessing the burden of REMS on pharmacists and the health care system, and assessing the capacity for pharmacists to implement REMS program, at the public meeting APhA offered to provide information to FDA on these issues. While APhA was not able to complete a new member survey in time for this docket submission, such survey information will be provided to FDA when available. In addition, FDA may find the following information helpful related to burden and capacity issues:

- In APhA’s June 2009 comments to FDA on opioid REMS (Docket No. FDA-2009-N-0143, available online at: [http://www.pharmacist.com/AM/Template.cfm?Section=Issues&CONTENTID=20140&TEMPLATE=/CM/ContentDisplay.cfm](http://www.pharmacist.com/AM/Template.cfm?Section=Issues&CONTENTID=20140&TEMPLATE=/CM/ContentDisplay.cfm)) APhA referenced information gathered in a survey to APhA members on lessons learned from existing REMS programs. The questionnaire was sent to 3,907 pharmacists practicing in community, clinic, and...
managed care settings. Based on responses from 275 members (a statistically significant 7% response rate), the following issues regarding existing REMS programs were identified:

- Nearly one-third of respondents selected the following as their top challenges: prescriber and patient registration, verification/documentation of education of prescriber/pharmacist, and verification procedures by pharmacist to process a prescription.
- In addition, respondents said that they had challenges with: verifying that specific lab test/results had been performed by the prescriber; addressing increases in suspect abuse or diversion prescriptions; and the time required to make multiple phone calls to address REMS processing glitches.
- Nearly one-third said that resolving REMS issues has a negative impact on their practice.
- Nearly a quarter of respondents said that they spend several hours or more a week resolving REMS issues.
- A majority said that at least sometimes prescription claims processing was delayed because a REMS component was not met; the average delay being nearly half of a day or more.

  - This new study examines the time pharmacists spent dispensing medications and providing patient care services in 2009. Based on the findings of the research, the researchers propose that the pharmacy profession currently has, and will continue to build, capacity for contributing to the health care system and in providing new provisions of patient care services.

  - This FDA study highlights burdens of risk management programs in place prior to the Food and Drug Administration Amendments Act of 2007 (P.L. 110-85) authorizing the current REMS program. Specifically, the study reports that sixty percent of respondents stated that risk management programs had a negative impact on their daily practice. The study also highlights the need to ensure that pharmacists receive outreach and educational materials about risk management programs.

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Pharmacist Contributions to the U.S. Health Care System

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ABSTRACT

Objective: The overall goal for this study was to conduct a segment analysis of the pharmacist workforce during 2009 based upon time spent in medication providing and in patient care services.

Methods: Data for this study were obtained from the 2009 National Pharmacist Workforce Survey in which a random sample of 3,000 pharmacists was selected. Cluster analysis was used for identifying pharmacist segments and descriptive statistics were used for describing and comparing segments.

Results: Of the 2,667 surveys that were presumed to be delivered to a pharmacist, 1,395 were returned yielding a 52.3% overall response rate. Of these, 1,200 responses were usable for cluster analysis. Findings from this study revealed five segments of pharmacists: (1) Medication Providers, (2) Medication Providers who also Provide Patient Care, (3) Other Activity Pharmacists, (4) Patient Care Providers Who also Provide Medication, and (5) Patient Care Providers. The results showed that, in 2009, 41% of U.S. pharmacists were devoted wholly to medication providing (Medication Providers). Forty-three percent of pharmacists contributed significantly to patient care service provision (Medication Providers who also Provide Patient Care, Patient Care Providers who also Provide Medication, and Patient Care Providers) and the remaining 16% (Other Activity Pharmacists) contributed most of their time to business / organization management, research, education, and other health-system improvement activities.

Conclusions: Based on the findings, we propose that the pharmacy profession currently has, and will continue to build, capacity for contributing to the U.S. health care system in new roles for which they have been identified. However, as shifts in professional roles occur, a great deal of capacity is required related to new service provision. Resources are scarce, so an understanding of the most appropriate timing for making such changes can lead to cost-effective use of limited resources for improving patient care.

Acknowledgements

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Introduction

Health care cannot function without medicines and pharmacists serve important roles for helping assure that the use of medicines results in the highest likelihood of achieving desired health and economic outcomes. In addition to the safe and efficient distribution and provision of medications, pharmacists have provided clinical expertise regarding selection, handling, preparation, procurement, and utilization of medications in patients [1] and, more recently, making sure that drugs reach their full potential for patients in society [2]. This implies a use of medications that is safe, effective, appropriate, affordable, cost-effective, efficient, and specific to the needs of a given patient [3-6]. Pharmacists have been identified as important contributors to the healthcare system serving such expanded roles as (1) medication care coordinators for patient-centered medical homes [7-8] and primary care teams [9-12], (2) members of chronic disease management teams that focus on ‘episodes’ of care in which related services are packaged together [11, 13-14], and (3) being the healthcare professional responsible for ensuring optimal medication therapy outcomes through...
medication therapy management (MTM) service provision [3, 11, 15-22].

Continued growth in medication use by society and the expansion of the pharmacist’s role in direct patient care continue to generate demand for pharmacist expertise and services [23]. At the same time, increased efficiencies for pharmacists’ medication providing roles have been achieved through the use of advanced logistics (e.g. centralized fill), technicians, and technology (e.g. bar code scanning, e-prescribing, robotics) [23]. It appears that the pharmacy profession has reached a point in which new roles for pharmacists are being adopted [1-22] and traditional roles are being filled by other workers, systems, or technology [23].

As such points are reached, a great deal of capacity is required related to new service provision as well as strategic decisions regarding educational training, professional training and redeployment, updates to practice acts and regulations, new documentation and billing systems, enhanced information exchange, infrastructure, technology, policy, and new business models [24, 25]. Resources are scarce, so an understanding of the most appropriate timing for making such changes can lead to cost-effective use of limited resources for improving patient care [25].

To help ensure the profession’s capacity for its emerging roles in health care, the pharmacy profession has become more patient focused resulting in reforms for both pharmacy education and practice [26]. On June 30, 2004, the Accreditation Council for Pharmacy Education standards for five-year Bachelors of Pharmacy programs expired and the six-year Doctor of Pharmacy (Pharm.D.) became the sole accredited professional degree for pharmacy in the United States (www.acpe-accredit.org). In addition to the Pharm.D. as the entry-level professional degree for pharmacists, specialized residency training for pharmacists has increased (www.ashp.org). It is estimated that 2,300 (23 percent) of the roughly 10,000 pharmacy school graduates in 2008 sought residency training after graduation (www.ashp.org).

As a result of the evolution in pharmacy education, pharmacists are now trained with a focus and level of expertise in medication therapy management that exceeds any other health care provider’s [15]. Individuals graduating with a Pharm.D. degree have the knowledge, skills and expertise to optimize therapeutic outcomes and improve the medication use system. As a result, pharmacists have gained recognition as “medication therapy experts” [15].

Due to changes in how pharmacists have been trained over time, not all pharmacists currently possess the same set of competencies and experiences. In addition, pharmacists differ in terms of their work activities [27]. In light of the recognition of pharmacists’ expanded roles and the need for strategic decisions regarding the cost-effective use of limited resources, our goal for this study was to conduct a segment analysis of the pharmacist workforce during 2009. Such a segmentation approach would identify key clusters (segments) of the pharmacist workforce and provide a description of their characteristics so that projections could be made regarding future pharmacy profession capacity as cohorts of pharmacists exit the workforce and newly trained pharmacists join the workforce. In light of the expansion of the pharmacist’s role in direct patient care and congruent training in such roles, our segment analysis was based upon pharmacists’ time devoted to medication provision (their traditional role) and to patient care services (their emergent role).

**Study Objectives**

The overall goal for this study was to conduct a segment analysis of the pharmacist workforce during 2009. The objectives were to:

1. Identify segments of pharmacists based upon time spent in medication providing and patient care services.
2. Describe segments according to demographic characteristics.
3. Describe segments according to work contributions.
4. Describe segments by work setting.
5. Describe segments according to work activities.
6. Describe age cohorts and year of licensure cohorts to identify trends that may impact future pharmacist capacity for contributing to the U.S. health care system.

**Methods**

Data for this study were obtained from the 2009 National Pharmacist Workforce Survey in which a random sample of 3,000 pharmacists was selected for a national, cross-sectional, descriptive survey. [27]. Questions comprising each section of the survey were taken from previous workforce surveys conducted by members of the project team [28-29].

We obtained a random sample of 3,000 licensed pharmacists in the United States from KM Lists, Inc., a company that maintains a list of licensed pharmacists in the United States from every state. At the time of our study, this list contained 249,381 unduplicated licensed individuals and was cleaned and updated whenever a state board of pharmacy provided an updated file. They have no states that refuse to give them...
the information. A randomly selected sample of 3,000 names and mailing addresses from this file was selected and provided to us in electronic format. We incorporated this file into a database program to generate mailing labels for the survey.

A mailed questionnaire with multiple follow-up was designed using principles from Dillman [30] in which a four-contact approach was utilized: (1) pre-notification letter, (2) survey packet, (3) postcard reminder, and (4) survey packet remailed to non-responders. Surveys were returned to the University of Minnesota, College of Pharmacy and processed for data entry. A database structure was created and responses coded according to the survey code book. Data were extracted from the database and analyzed for this report using a two-step cluster analysis, with SPSS version 16.0 statistical software. The SPSS two-step cluster analysis uses a scalable cluster algorithm. The first step of the analysis is to ‘pre-cluster’ each case (record) into many small sub-clusters through a sequential clustering approach. The second step of the analysis is to ‘cluster the sub-clusters’ resulting from step one into the final cluster solution using an agglomerative hierarchical clustering method. The log-likelihood distance measure (a probability-based distance) is applied for each step of the analysis so that both continuous and categorical variables can be used if so desired.

For our analysis we utilized two continuous variables for defining clusters: (1) percent time spent in medication providing activities and (2) percent time spent in patient care activities at each respondent’s primary place of employment. These were two of the six work activities we included for the 2009 survey which were defined as:

- **Medication Providing**: preparing, distributing, and administering medication products, including associated consultation, interacting with patients about selection and use of over-the-counter products, and interactions with other professionals during the medication providing process.

- **Patient Care Services**: assessing and evaluating patient medication-related needs, monitoring and adjusting patients’ treatments to attain desired outcome, and other services designed for patient care management.

- **Business / Organization Management**: managing personnel, finances, and systems.

- **Research**: discovery, development, and evaluation of products, services, and/or ideas.

- **Education**: teaching, precepting, and mentoring of students/trainees.

- **Other Activities**: any activities not described in other categories.

Our primary goal was to identify pharmacist segments and describe them using descriptive statistics within the context of the new roles for pharmacists that we mentioned in the introduction of this paper. It should be noted that medication providing is an important patient care service and our use of the terminology “patient care services” may be confusing. For clarification, it should be noted that “medication providing” primarily uses the medication as the unit of focus for service provision. It is typically focused on prescription order fulfillment but includes an array of professional activities in which pharmacists are responsible to the technical functions of providing a prescription product, assuring that the correct drug product is provided, identifying and resolving drug-drug interactions, conversing with prescribers about dose or directions, and patient counseling about proper use.

For the purpose of this study, the designation “patient care services” uses the patient as the unit of focus and can be provided independent from any medication being provided to the patient. This service typically is a team-based clinical role providing patient-centered medication therapy management, health improvement, and disease prevention services [31].

After pharmacist segments were identified, we described them using Chi-Square and Analysis of Variance (ANOVA) statistics.

**Results**

Of the 3,000 individuals contained in our random sample, 333 (11%) were considered “undeliverable or not applicable” for the study. Of the 2,667 surveys that were presumed to be delivered to a pharmacist, 1,395 were returned yielding a 52.3% overall response rate. Responses received on August 15, 2009 or later were not included for analysis. Thus, 1,391 surveys were entered into our data file (52.2% usable response rate).

For inclusion in cluster analysis, respondents needed to report both their percent time devoted to medication providing and to patient care services. Respondents who reported that they were: (1) retired, do not practice pharmacy at all, (2) employed in a career not related to pharmacy, or (3) unemployed were not asked the work activity questions and, thus, not included for analysis. Respondents who were included for analysis were those who
reported that they were: (1) practicing as a pharmacist, (2) employed in a pharmacy-related field or position, or (3) retired, but still working in pharmacy or employed part-time as a pharmacist. A total of 1,200 respondents provided usable responses for cluster analysis.

Cluster analysis identified five segments of pharmacists that we labeled as: (1) Medication Provider, (2) Medication Provider who also provides Patient Care, (3) Other Activity Pharmacist, (4) Patient Care Provider who also Provides Medication, and (5) Patient Care Provider. Figure 1 shows the proportion of pharmacists in each of the five segments and Table 1 provides a description of each segment in terms of time devoted to medication providing and patient care services.

Table 2 provides summary comparisons among the five segments in terms of (1) demographic characteristics, (2) work contributions, (3) work settings by column %, (4) work settings by row %, (5) time currently spent in work activities, and (6) time desired to spend in work activities. Chi-square and Analysis of Variance statistics were used for describing the segments. In light of the exploratory nature of our cluster analysis to identify segments, we treated ANOVA findings as exploratory as well. Complete results (including post hoc analysis ANOVA testing) are available from the corresponding author. The five pharmacist segments are discussed next.

MEDICATION PROVIDERS
In our study, this group (41% of pharmacists employed in pharmacy or in a pharmacy-related field) devoted an average of 88% of their time to medication providing and only 5% to patient care services as defined in this study. Table 2 shows that they were the oldest of the five segments, on average. Fifty-nine percent of this segment were male, only 17% had a PharmD degree, and only 3% had residency training. This segment contributed the fewest hours worked per week of any segment and 43% of respondents who worked in ‘other, setting not licensed as a pharmacy’ were identified as being in the “Other Activity Pharmacist” segment of pharmacists. Other Activity Pharmacists are currently spending about their desired time in the various work activities we studied.

OTHER ACTIVITY PHARMACISTS
This segment (16% of pharmacists employed in pharmacy or in a pharmacy-related field) devoted an average of only 5% of their time to medication providing and only 3% to patient care services as defined in this study. Table 2 shows that they were the third oldest of the five segments, on average. Sixty percent of this segment were male, 42% had a PharmD degree, and 19% had residency training. This segment contributed the most hours worked per week of any segment and 93% were working in urban areas with a population over 50,000. The findings showed that 45% of this segment of pharmacists worked in ‘other, setting not licensed as a pharmacy,’ and 30% worked in a hospital setting. In addition, 83% of respondents who worked in ‘other, setting not licensed as a pharmacy’ were identified as being in the “Other Activity Pharmacist” segment of pharmacists. Other Activity Pharmacists are currently spending about their desired time in the various work activities we studied.

MEDICATION PROVIDERS WHO ALSO PROVIDE PATIENT CARE
This segment (25% of pharmacists employed in pharmacy or in a pharmacy-related field) devoted an average of 65% of their time to medication providing and 19% to patient care services as defined in this study. Table 2 shows that they were the second oldest of the five segments, on average. Fifty-two percent of this segment were male, only 17% had a PharmD degree, and only 4% had residency training. This segment contributed an average of 38 hours worked per week and 79% were working in urban areas with a population over 50,000. Two-thirds of this segment of pharmacists worked in community pharmacy practice settings (67%) and one-quarter (25%) worked in hospital practice settings. The results showed that the Medication Providers who also Provide Patient Care would like to decrease the proportion of time they devote to medication providing (from 65% to 52%) and increase the proportion of time they devote to patient care services (from 19% to 31%).

PATIENT CARE PROVIDERS WHO ALSO PROVIDE MEDICATION
This segment (12% of pharmacists employed in pharmacy or in a pharmacy-related field) devoted an average of 33% of their time to medication providing and 43% to patient care services as defined in this study. Table 2 shows that they were the youngest of the five segments, on average. Sixty-four percent of this segment were female, 40% had a PharmD degree, and 25% had residency training. This segment contributed the second fewest hours worked per week of any segment and 88% were working in urban areas with a population over 50,000. The results showed that 54% of this segment of pharmacists worked in hospital settings, 23% worked in community pharmacy practice settings, and 16% worked in ‘other, licensed pharmacy settings.’ The Patient Care Providers Who Also Provide Medication would like to decrease only slightly the proportion of time they devote to medication providing (from 33% to 26%), keep the time they devote to patient care about the same (43% actual and 44%
desired), but increase slightly the proportion of time they devote to research and education.

PATIENT CARE PROVIDERS
In our study, this group (6% of pharmacists employed in pharmacy or in a pharmacy-related field) devoted an average of just 5% of their time to medication providing and 82% to patient care services as defined in this study. Table 2 shows that they were the second youngest of the five segments, on average. Fifty-nine percent of this segment were female, 53% had a PharmD degree, and 26% had residency training. This segment contributed the second highest number of hours worked per week of any segment and 92% were working in urban areas with a population over 50,000. Almost two-thirds (64%) of this segment worked in hospital pharmacy practice settings and less than 1% of respondents who worked in community practice settings were identified as being in the “Patient Care Provider” segment of pharmacists. Patient Care Provider Pharmacists are currently spending about their desired time in the various work activities we studied.

AGE AND YEAR OF LICENSURE COHORTS
Tables 3 and 4 summarize comparisons for U.S. pharmacist age and year of licensure cohorts and provide insight regarding future pharmacy profession capacity as cohorts of pharmacists exit the workforce and newly trained pharmacists join the workforce. For example, Table 3 shows that pharmacists over the age of 60 are typically male, not likely to hold a PharmD degree, and not likely to have residency training. In comparison, pharmacists who are 35 years old or younger are very different, with most being female, holding a PharmD degree, and a significant proportion having residency training. It is not surprising that younger pharmacists are more likely to comprise the ‘Other Activity Pharmacist,’ ‘Patient Care Provider who also Provides Medication,’ and ‘Patient Care Provider’ segments and that older pharmacists are more likely to comprise the ‘Medication Provider’ and ‘Medication Provider who also Provides Patient Care’ segments in light of trends in pharmacist training. Table 4 shows similar findings when Year of Licensure cohorts are described. The transformations that took place among years of licensure cohorts are particularly striking for the gender, holding a PharmD degree, and residency training variables.

Discussion
We identified five pharmacist segments using data from a survey of a random sample of pharmacists conducted in 2009. The findings showed that recent transformations in pharmacy education regarding the Doctor of Pharmacy (Pharm.D) degree as the sole accredited professional degree for pharmacy in the United States and the increase in pharmacist residency training has created new competencies which translate into capacity in the pharmacy profession for taking on expanded responsibility for optimizing medication use in the U.S. health care system.

The findings showed that, in 2009, 41% of U.S. pharmacists were devoted wholly to medication providing (Medication Providers). Forty-three percent of pharmacists contributed significantly to patient care service provision (Medication Providers who also Provide Patient Care, The Patient Care Providers who also Provide Medication, and The Patient Care Providers) and the remaining 16% (Other Activity Pharmacists) contributed most of their time to business/organization management, research, education, and other health-system improvement activities. However, pharmacists who are most visible to the public in community pharmacy practice settings and almost eight out of 10 pharmacists who are “Medication Providers” work in these publicly visible and accessible settings. Such visibility of Medication Providers may give a public impression that is not completely accurate regarding the capacity for pharmacist provision of patient care and for the complete scope of pharmacist contributions to the U.S. health care system.

The findings also showed that older pharmacists, who are more likely to exit the workforce before younger pharmacists will, are most likely to be in the “Medication Provider” segment of pharmacists. Thus, as over 10,000 new pharmacists are being licensed each year under the new paradigm of training and the older pharmacists exit the workforce, the capacity of the pharmacist workforce for provision of patient care is likely to be even more pronounced.

The findings also suggest that pharmacists who may be in the “Medication Provider” or the “Medication Provider who also Provides Patient Care” segments, but not likely to exit the workforce in the near future, would be open to retraining and redeployment. These pharmacists reported that they would like to spend less time in medication providing and more time in provision of patient care services (see Tables 3 and 4). We propose that the majority of these pharmacists would be willing to move into more patient care services roles as training and opportunities for redeployment present themselves. These findings are consistent with the Holland-Nimmo practice change model [32-36] and guidance for making this transition already exists for the pharmacy profession [32-36].

Based on our findings, we propose that the pharmacy profession currently has, and will continue to build, capacity
for contributing to the U.S. health care system in roles for which they have been identified which include: (1) medication care coordinators for patient-centered medical homes [7-8] and primary care teams [9-12], (2) members of chronic disease management teams that focus on ‘episodes’ of care in which related services are packaged together [11, 13-14], and (3) being the healthcare professional responsible for ensuring optimal medication therapy outcomes through medication therapy management (MTM) service provision [3, 11, 15-22]. However, as shifts in professional roles occur, a great deal of capacity is required related to new service provision as well as strategic decisions regarding educational training, professional training and redeployment, updates to practice acts and regulations, new documentation and billing systems, enhanced information exchange, collaborative practice models, infrastructure, technology, policy, and new business models. Resources are scarce, so an understanding of the most appropriate timing for making such changes can lead to cost-effective use of limited resources for improving patient care [25]. In the next section of this paper, we propose several ideas to consider as pharmacist capacity is further developed and integrated into the U.S. healthcare system.

Ideas for Consideration as Pharmacist Capacity is Developed and Integrated into Healthcare

Our findings indentified five clusters (segments) of pharmacists and our description of these segments provided insight regarding how the pharmacist workforce might evolve in terms of capacity for patient care over time. In light of these findings, we offer eight ideas for consideration as pharmacist capacity is further developed and integrated into the U.S. healthcare system.

First, what are future training needs for pharmacists to connect their capacity with future health care system needs? We suggest that continual improvements to Doctor of Pharmacy (Pharm.D.) training will be needed; especially the development of team-based, interprofessional training that will help health care providers learn about and experience team-based patient care. Also, expansion of pharmacy residencies (with suitable funding for such training) could help meet the advanced training needs for pharmacists. We propose that efforts to create “industry norms” that would require pharmacy residency training as a condition for certain types of pharmacist employment would help position such residencies for legitimate consideration of graduate medical education (GME) funding. Such norms also could provide assurances to other healthcare professionals regarding pharmacists’ competence for providing patient care.

Second, community pharmacy practice business models are still focused primarily on medication providing. There are new models emerging in community pharmacies that utilize advanced logistics (e.g. centralized fill), technology (e.g. bar code scanning, e-prescribing, robotics), technicians, specialty pharmacy services, corporate (in-house) pharmacies, and new patient care service models. However, we believe that it is important to monitor the rate of discontinuance for some community pharmacy business models as well as monitoring the adoption of new business models that would help pharmacists fulfill their potential in the health care system [24-25]. Where and how pharmacists might contribute to ensure access to medications and associated services are questions that will need to be addressed. In addition, supply and demand balance or imbalance for pharmacists should be monitored as these changes occur.

Third, pharmacy practice acts and other health profession practice acts (that define scope of practice) will need updating on an ongoing basis to reflect and accommodate new roles for health professionals and for team-based care. In pharmacy, the National Association of Boards of Pharmacy (www.napb.net) could take the lead for updating the Pharmacy Model Practice Act that could be utilized by state boards of pharmacy as they develop their states’ practice acts. New thinking about what embodies pharmacy practice in the health care system is continually needed. Agreement on such things as provider status and scope of practice is needed, including consensus from other health care fields and systems.

Fourth, significant work and progress are needed regarding the alignment of payment policies for not only supporting new roles and services but also to provide adequate payment for the providers of these services and evidence of cost-effectiveness for payers of these services. According to the 2008, 2009, and 2010 Medication Therapy Management Digests and Environmental Scans [37-40], the most significant barriers to offering Medication Therapy Management services for pharmacist providers were related to billing, staffing adjustments, and payment levels. For the payers of these services, the most significant challenges to overcome were related to getting patients to engage in the service offerings, evidence of tangible outcomes, and having sufficient numbers of service providers in their patient population service areas. Alignment of payment policies would help overcome some of these barriers for both providers and payers.

Fifth, we propose that flexibility in medical / health care home designs could create innovative and responsive practice structures that integrate pharmacist expertise for
medication therapy coordination and management under varying geographic regions, practice setting types, and patient population types [8]. Balancing such flexibility with the need for standards of care is a challenge that needs to be addressed in the reforming health care system.

Sixth, all members of collaborative health care teams, including pharmacists, must have access to necessary patient health and treatment records to support and inform their patient care service and decision-making functions [8]. Such access should include both the authority and responsibility to input information into these records to facilitate team-based collaborative care. Coming to consensus about what information is (1) proprietary, (2) related to business functions, and (3) related to patient health and treatment is not an easy task. However, we believe it will have immense impact on the ability of pharmacists to contribute their full capacity to the developing health care system.

Seventh, discussion regarding pharmacists’ contributions to patient care that is comprised of bundles of services into “episodes of care” will be important. By packaging related services together in a way that supports high-quality, lower-cost care, providers, payers, and patients could begin to view episodes of care as a unified patient care experience rather than a series of disparate services. For example, products and services associated with the treatment of diabetes could be bundled in a way to influence overall pay-for-performance outcome measures. Pharmacist capacity for medication coordination throughout the whole episode of care could be valuable for improving quality and avoiding waste in medication therapy. As mentioned previously, payment redesign in addition to care redesign will need to be addressed to bring pharmacists’ full capacity to fruition.

Finally, we suggest that efforts to help bring the U.S. health consumer’s perceptions of pharmacists and the roles they play in health care more in line with pharmacists’ true capacity for patient care would be helpful in making transformations in health care. We believe that consensus within the pharmacy profession and collaborative health care teams overall regarding processes of pharmacist-provided patient care and language that is used as care is provided to patients would have more impact on changing patients’ perceptions than public service campaigns or advertising. For example, pharmacists who hold a Pharm.D. degree could be referred to as the patient’s Doctor of Pharmacy. This would not only identify the practitioner’s training but also identify his or her area of expertise. This idea is similar to telling patients that they will see their Doctor of Internal Medicine or their Doctor of Orthopedics.

Another example of building consensus for the purpose of creating clear expectations to patients would be to refer to medication therapy and coordination visits in a common way. Currently, the term “Medication Therapy Management” is being used. Bringing consensus to the term used and placing it into common usage would help advance the public’s perception of pharmacists’ roles in the health care system. We believe that the public should be clear regarding the different roles that their prescription order fulfillment pharmacist has in comparison to their medication therapy management pharmacist. This is similar to the different roles that are identified with different physicians (e.g. internal medicine physician and surgeon).

Limitations

The results and our interpretation of them should be tempered with the limitations of the study. The results are based on respondents’ self reports, raising questions regarding the extent to which respondents gave socially desirable responses.

Pharmacist respondents were geographically diverse in that all regions of the United States were represented in proportion to the U.S. population and in proportion to our sampling frame [27]. However, some individual states were over-represented (e.g. Montana) and some states were under-represented (e.g. New Mexico) [27]. Thus, while we achieved good geographic coverage, some states were disproportionately represented in this study. To overcome this limitation, we analyzed only aggregate data and not state- or region-specific data.

Non-response bias is another limitation. It is possible that responders were more interested in the topic we studied or had stronger opinions about the questions we asked than those who chose not to respond. Our evaluation of non-response bias showed that late responders were more likely to be: working as a pharmacist, younger, and having a PharmD degree than early responders. These same characteristics are likely to be reflected in the non-responders to this study and should be considered when interpreting the reported findings.

For our analysis, usable data from respondents working in pharmacy or a pharmacy related field were used. While our findings are representative of pharmacists working in pharmacy or a pharmacy related field, it should be noted that our analysis did not include licensed pharmacists who were outside of these domains (retired, unemployed, or working outside of a pharmacy related field).
The definitions we used for medication providing and patient care services were newly developed for the 2009 survey and differed from previous national pharmacist workforce surveys conducted in 2000 and 2004 [27-29]. Thus, no comparisons were possible to previous years. However, we developed the work activity definitions based upon what we learned from earlier surveys, namely that pharmacists view medication providing and associated patient counseling as a unified process and service. We reflected that notion for our 2009 survey and defined patient care services as being separate from the medication providing process. Our findings suggest that responders were able to interpret our new definitions in the manner in which we developed them and that our findings can be considered an accurate reflection of pharmacist work.

Our cluster analysis was based upon one national sample of pharmacists. In order to test the stability of our cluster analysis, we replicated our analysis using data from the 2009 Minnesota Pharmacy Workforce Survey [41]. Using those data, the same five clusters were achieved with extremely similar results for the descriptions of each cluster. Findings from that analysis are available from the corresponding author.

Finally, all of the respondents to this survey were first licensed before 2007. Therefore, even though our survey was conducted in 2009, our sampling frame had a lag time so that pharmacists newly licensed from 2007 through the present were not included in the sample. This limitation must be considered, especially when interpreting findings related to year of licensure, age, or other time dependent variable. Thus, it is likely that we underestimated the proportion of pharmacists working in patient care areas since younger pharmacists typically took on those roles.

Conclusions

Findings from this study revealed five segments of pharmacists: (1) Medication Providers, (2) Medication Providers who also Provide Patient Care, (3) Other Activity Pharmacists, (4) Patient Care Providers who also Provide Medication, and (5) Patient Care Providers. The findings showed that older pharmacists, who are most likely to exit the workforce before younger pharmacists do, are most likely to be in the “Medication Provider” segment of pharmacists. Thus, as over 10,000 new pharmacists are being licensed each year under the new paradigm of training and the older pharmacists exit the workforce, the capacity of the pharmacist workforce for provision of patient care will be even more pronounced. We conclude that recent transformations in pharmacy education regarding the Doctor of Pharmacy (Pharm.D) degree as the sole accredited professional degree for pharmacy in the United States and the increase in pharmacist residency training has built capacity in the pharmacy profession for taking on expanded responsibility for optimizing medication use in the U.S. health care system.

The findings also suggest that pharmacists who may be in the “Medication Provider” or “The Medication Provider who also Provides Patient Care” segments, but not likely to exit the workforce in the near future, would be open to retraining and redeployment. These pharmacists reported that they would like to spend less time in medication providing and more time in provision of patient care services. We propose that the majority of these pharmacists would be willing to move into more patient care services roles as training and opportunities for redeployment present themselves.

Based on our findings, we propose that the pharmacy profession currently has, and will continue to build, capacity for contributing to the U.S. health care system in new roles for which they have been identified. However, as shifts in professional roles occur, a great deal of capacity is required related to new service provision as well as strategic decisions regarding educational training, professional training and redeployment, updates to practice acts and regulations, new documentation and billing systems, enhanced information exchange, collaborative practice models, infrastructure, technology, policy, and new business models. Resources are scarce, so an understanding of the most appropriate timing for making such changes can lead to cost-effective use of limited resources for improving patient care.
References


Figure 1: Proportion of U.S. Pharmacists by Segment in Descending Size

![Figure 1: Proportion of U.S. Pharmacists by Segment in Descending Size](image_url)

Table 1
Description of Pharmacist Segments

<table>
<thead>
<tr>
<th>Pharmacist Segment</th>
<th>Segment Size (% of total)</th>
<th>Mean Percentage Time (+/- s. d.) Devoted to Medication Providing</th>
<th>Mean Percentage Time (+/- s. d.) Devoted to Patient Care</th>
</tr>
</thead>
<tbody>
<tr>
<td>1: Medication Provider</td>
<td>n = 496 (41%)</td>
<td>88% +/- 9</td>
<td>5% +/- 4</td>
</tr>
<tr>
<td>2: Medication Provider who also Provides Patient Care</td>
<td>n = 303 (25%)</td>
<td>65% +/- 11</td>
<td>19% +/- 7</td>
</tr>
<tr>
<td>3: Other Activity Pharmacist</td>
<td>n = 193 (16%)</td>
<td>5% +/- 8</td>
<td>3% +/- 6</td>
</tr>
<tr>
<td>4: Patient Care Provider who also Provides Medication</td>
<td>n = 142 (12%)</td>
<td>33% +/- 17</td>
<td>43% +/- 11</td>
</tr>
<tr>
<td>5: Patient Care Provider</td>
<td>n = 66 (6%)</td>
<td>5% +/- 8</td>
<td>82% +/- 13</td>
</tr>
<tr>
<td>Total</td>
<td>N = 1,200</td>
<td>58% +/- 34</td>
<td>17% +/- 21</td>
</tr>
</tbody>
</table>
Table 2
Comparison of U.S. Pharmacist Segments

<table>
<thead>
<tr>
<th>Demographic Characteristics</th>
<th>Medication Provider (n = 496)</th>
<th>Medication Provider who also provides Patient Care (n = 303)</th>
<th>Other Activity Pharmacist (n = 193)</th>
<th>Patient Care Provider who also Provides Medication (n = 142)</th>
<th>Patient Care Provider (n = 66)</th>
<th>Overall (n=1,200)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Age (years) ANOVA p&lt; 0.001</td>
<td>52.0</td>
<td>50.2</td>
<td>49.2</td>
<td>45.6</td>
<td>47.4</td>
<td>50.1</td>
</tr>
<tr>
<td>Female Gender (%) X² p &lt; 0.001</td>
<td>41%</td>
<td>48%</td>
<td>40%</td>
<td>64%</td>
<td>59%</td>
<td>47%</td>
</tr>
<tr>
<td>Hold PharmD Degree (%) X² p &lt; 0.001</td>
<td>17%</td>
<td>17%</td>
<td>42%</td>
<td>40%</td>
<td>53%</td>
<td>26%</td>
</tr>
<tr>
<td>Residency Training (%) X² p &lt; 0.001</td>
<td>3%</td>
<td>4%</td>
<td>19%</td>
<td>25%</td>
<td>26%</td>
<td>9%</td>
</tr>
<tr>
<td>White/Caucasian Ethnicity (%) X² p = 0.047</td>
<td>88%</td>
<td>85%</td>
<td>87%</td>
<td>77%</td>
<td>86%</td>
<td>86%</td>
</tr>
<tr>
<td>Work Contributions Mean Hrs Worked /Wk ANOVA p&lt; 0.001</td>
<td>35.6</td>
<td>38.0</td>
<td>44.7</td>
<td>37.2</td>
<td>39.8</td>
<td>38.1</td>
</tr>
<tr>
<td>Work Part Time (30 hrs per week or less) (%) X² p &lt; 0.001</td>
<td>29%</td>
<td>20%</td>
<td>13%</td>
<td>30%</td>
<td>18%</td>
<td>24%</td>
</tr>
<tr>
<td>Work in Urban Area with Population Over 50,000 (%) X² p = 0.002</td>
<td>79%</td>
<td>79%</td>
<td>93%</td>
<td>88%</td>
<td>92%</td>
<td>83%</td>
</tr>
<tr>
<td>Practicing as a Pharmacist (%) X² p &lt; 0.001</td>
<td>89%</td>
<td>93%</td>
<td>45%</td>
<td>94%</td>
<td>97%</td>
<td>84%</td>
</tr>
<tr>
<td>Current Work Setting (Column %) X² p &lt; 0.001</td>
<td>Community Pharmacy a 78%</td>
<td>67%</td>
<td>10%</td>
<td>23%</td>
<td>1%</td>
<td>-</td>
</tr>
<tr>
<td>Hospital Setting</td>
<td>15%</td>
<td>25%</td>
<td>30%</td>
<td>30%</td>
<td>54%</td>
<td>64%</td>
</tr>
<tr>
<td>Other, Licensed Pharmacy Setting b</td>
<td>7%</td>
<td>7%</td>
<td>15%</td>
<td>16%</td>
<td>27%</td>
<td>-</td>
</tr>
<tr>
<td>Other, Setting Not Licensed as a Pharmacy c</td>
<td>&lt;1%</td>
<td>1%</td>
<td>45%</td>
<td>7%</td>
<td>8%</td>
<td>-</td>
</tr>
<tr>
<td>Current Work Setting (Row %) X² p &lt; 0.001</td>
<td>Community Pharmacy a (n = 645) 60%</td>
<td>32%</td>
<td>3%</td>
<td>5%</td>
<td>&lt;1%</td>
<td>-</td>
</tr>
<tr>
<td>Hospital Setting (n = 325)</td>
<td>23%</td>
<td>24%</td>
<td>17%</td>
<td>23%</td>
<td>13%</td>
<td>-</td>
</tr>
<tr>
<td>Mean % of Time Currently Spent in Work Activities</td>
<td>Medication Providing ANOVA p&lt; 0.001</td>
<td>Patient Care Services ANOVA p&lt;0.001</td>
<td>Business / Organization Management ANOVA p&lt;0.001</td>
<td>Research ANOVA p&lt;0.001</td>
<td>Education ANOVA p&lt;0.001</td>
<td>Other ANOVA p&lt; 0.001</td>
</tr>
<tr>
<td>-----------------------------------------------</td>
<td>-------------------------------------</td>
<td>--------------------------------------</td>
<td>-----------------------------------------------</td>
<td>------------------------</td>
<td>------------------------</td>
<td>------------------------</td>
</tr>
<tr>
<td>Other, Licensed Pharmacy Settingb (n = 126)</td>
<td>29%</td>
<td>65%</td>
<td>88%</td>
<td>5%</td>
<td>2%</td>
<td>1%</td>
</tr>
<tr>
<td>Other, Setting Not Licensed as a Pharmacyc (n = 104)</td>
<td>1%</td>
<td>2%</td>
<td>83%</td>
<td>10%</td>
<td>5%</td>
<td>-</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Mean % of Time Desired to Spend in Work Activities</th>
<th>Medication Providing ANOVA p&lt; 0.001</th>
<th>Patient Care Services ANOVA p&lt;0.001</th>
<th>Business / Organization Management ANOVA p&lt;0.001</th>
<th>Research ANOVA p&lt;0.001</th>
<th>Education ANOVA p&lt;0.001</th>
<th>Other ANOVA p&lt; 0.001</th>
</tr>
</thead>
<tbody>
<tr>
<td>Other, Licensed Pharmacy Settingb (n = 126)</td>
<td>71%</td>
<td>52%</td>
<td>5%</td>
<td>7%</td>
<td>26%</td>
<td>6%</td>
</tr>
<tr>
<td>Other, Setting Not Licensed as a Pharmacyc (n = 104)</td>
<td>16%</td>
<td>31%</td>
<td>8%</td>
<td>9%</td>
<td>44%</td>
<td>81%</td>
</tr>
</tbody>
</table>

a “Community Pharmacy Practice” included: independent, chain, mass merchandiser and supermarket pharmacies.

b “Other, Licensed Pharmacy Setting” included: nursing home, long term care, health maintenance organization, nuclear, clinic-based, mail service, central fill, and home health/infusion pharmacies.

c “Other, Setting Not Licensed as a Pharmacy” included: pharmacy benefit administration, academic, government administration, pharmaceutical industry, consulting companies, professional associations, and other organizations that were not licensed as a pharmacy.

d Other includes activities such as: computer analysis, audit control, continuing education, grants, committee work, communications, consultation, data analysis, drug information services, formulary management, systems implementation, inspections, investigations, information technology work, manufacturing, marketing, medication safety, meetings, policy work, problem resolution, quality assurance, regulatory issues, and writing.
### Table 3
Comparison of U.S. Pharmacist Age Cohorts

<table>
<thead>
<tr>
<th>Age Cohort (years of age)</th>
<th>Female Gender</th>
<th>Hold PharmD Degree</th>
<th>Year of First Licensure</th>
<th>Residency Training</th>
<th>% in Cluster 1 Medication Provider</th>
<th>% in Cluster 2 Medication Provider who also provides Patient Care</th>
<th>% in Cluster 3 Other Activity Pharmacist</th>
<th>% in Cluster 4 Patient Care Provider who also Provides Medication</th>
<th>% in Cluster 5 Patient Care Provider</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; or equal to 30 (n = 32)</td>
<td>78%</td>
<td>84%</td>
<td>2004</td>
<td>31%</td>
<td>41%</td>
<td>6%</td>
<td>22%</td>
<td>13%</td>
<td>19%</td>
</tr>
<tr>
<td>31 to 35 (n = 116)</td>
<td>64%</td>
<td>67%</td>
<td>2000</td>
<td>22%</td>
<td>33%</td>
<td>23%</td>
<td>16%</td>
<td>23%</td>
<td>5%</td>
</tr>
<tr>
<td>36 to 40 (n = 141)</td>
<td>70%</td>
<td>40%</td>
<td>1995</td>
<td>11%</td>
<td>37%</td>
<td>31%</td>
<td>15%</td>
<td>13%</td>
<td>5%</td>
</tr>
<tr>
<td>41 to 45 (n = 140)</td>
<td>69%</td>
<td>32%</td>
<td>1991</td>
<td>11%</td>
<td>38%</td>
<td>24%</td>
<td>16%</td>
<td>18%</td>
<td>5%</td>
</tr>
<tr>
<td>46 to 50 (n = 159)</td>
<td>54%</td>
<td>18%</td>
<td>1986</td>
<td>9%</td>
<td>36%</td>
<td>28%</td>
<td>18%</td>
<td>11%</td>
<td>7%</td>
</tr>
<tr>
<td>51 to 55 (n = 213)</td>
<td>49%</td>
<td>13%</td>
<td>1981</td>
<td>7%</td>
<td>44%</td>
<td>25%</td>
<td>17%</td>
<td>10%</td>
<td>5%</td>
</tr>
<tr>
<td>56 to 60 (n = 168)</td>
<td>26%</td>
<td>15%</td>
<td>1976</td>
<td>4%</td>
<td>41%</td>
<td>25%</td>
<td>18%</td>
<td>9%</td>
<td>7%</td>
</tr>
<tr>
<td>61 to 65 (n = 106)</td>
<td>16%</td>
<td>9%</td>
<td>1971</td>
<td>9%</td>
<td>42%</td>
<td>24%</td>
<td>21%</td>
<td>9%</td>
<td>6%</td>
</tr>
<tr>
<td>66 to 70 (n = 65)</td>
<td>9%</td>
<td>9%</td>
<td>1965</td>
<td>2%</td>
<td>63%</td>
<td>26%</td>
<td>6%</td>
<td>3%</td>
<td>2%</td>
</tr>
<tr>
<td>Greater than 70 (n = 48)</td>
<td>6%</td>
<td>9%</td>
<td>1958</td>
<td>0%</td>
<td>71%</td>
<td>21%</td>
<td>6%</td>
<td>2%</td>
<td>0%</td>
</tr>
<tr>
<td>OVERALL (N = 1,188)</td>
<td>47%</td>
<td>26%</td>
<td>1983</td>
<td>9%</td>
<td>42%</td>
<td>25%</td>
<td>16%</td>
<td>12%</td>
<td>6%</td>
</tr>
</tbody>
</table>

\(X^2\) p < 0.001  
ANOVA p < 0.001  
\(X^2\) p < 0.001  
Chi-Square p < 0.001

N does not total 1,200 due to missing data.
# Table 4
Comparison of U.S. Pharmacist Year of Licensure Cohorts

<table>
<thead>
<tr>
<th>Year of Licensure Cohort (year of first licensure)</th>
<th>Female Gender</th>
<th>Age (years)</th>
<th>Hold PharmD Degree</th>
<th>Residency Training</th>
<th>% in Cluster 1 Medication Provider</th>
<th>% in Cluster 2 Medication Provider who also provides Patient Care</th>
<th>% in Cluster 3 Other Activity Pharmacist</th>
<th>% in Cluster 4 Patient Care Provider who also Provides Medication</th>
<th>% in Cluster 5 Patient Care Provider</th>
</tr>
</thead>
<tbody>
<tr>
<td>2005 to 2006 (n = 23)</td>
<td>70%</td>
<td>30.9</td>
<td>96%</td>
<td>30%</td>
<td>52%</td>
<td>4%</td>
<td>9%</td>
<td>13%</td>
<td>22%</td>
</tr>
<tr>
<td>2000 to 2004 (n = 101)</td>
<td>66%</td>
<td>33.7</td>
<td>75%</td>
<td>22%</td>
<td>33%</td>
<td>23%</td>
<td>18%</td>
<td>20%</td>
<td>7%</td>
</tr>
<tr>
<td>1995 to 1999 (n = 136)</td>
<td>67%</td>
<td>38.2</td>
<td>46%</td>
<td>13%</td>
<td>31%</td>
<td>27%</td>
<td>18%</td>
<td>19%</td>
<td>5%</td>
</tr>
<tr>
<td>1990 to 1994 (n = 142)</td>
<td>66%</td>
<td>42.0</td>
<td>30%</td>
<td>14%</td>
<td>44%</td>
<td>23%</td>
<td>12%</td>
<td>11%</td>
<td>10%</td>
</tr>
<tr>
<td>1985 to 1989 (n = 141)</td>
<td>58%</td>
<td>47.0</td>
<td>17%</td>
<td>6%</td>
<td>38%</td>
<td>26%</td>
<td>17%</td>
<td>15%</td>
<td>4%</td>
</tr>
<tr>
<td>1980 to 1984 (n =164)</td>
<td>50%</td>
<td>51.2</td>
<td>20%</td>
<td>7%</td>
<td>35%</td>
<td>29%</td>
<td>21%</td>
<td>9%</td>
<td>6%</td>
</tr>
<tr>
<td>1975 to 1979 (n = 188)</td>
<td>39%</td>
<td>55.6</td>
<td>12%</td>
<td>6%</td>
<td>47%</td>
<td>23%</td>
<td>16%</td>
<td>9%</td>
<td>5%</td>
</tr>
<tr>
<td>1970 to 1974 (n = 133)</td>
<td>22%</td>
<td>60.7</td>
<td>7%</td>
<td>3%</td>
<td>39%</td>
<td>30%</td>
<td>17%</td>
<td>8%</td>
<td>6%</td>
</tr>
<tr>
<td>1965 to 1969 (n = 74)</td>
<td>10%</td>
<td>65.4</td>
<td>5%</td>
<td>7%</td>
<td>47%</td>
<td>24%</td>
<td>18%</td>
<td>10%</td>
<td>1%</td>
</tr>
<tr>
<td>1960 to 1964 (n = 41)</td>
<td>10%</td>
<td>70.0</td>
<td>8%</td>
<td>3%</td>
<td>71%</td>
<td>20%</td>
<td>7%</td>
<td>2%</td>
<td>0%</td>
</tr>
<tr>
<td>Before 1960 (n = 33)</td>
<td>6%</td>
<td>77.1</td>
<td>9%</td>
<td>0%</td>
<td>73%</td>
<td>21%</td>
<td>6%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>OVERALL (N = 1,176)</td>
<td>47%</td>
<td>51.6</td>
<td>26%</td>
<td>9%</td>
<td>41%</td>
<td>25%</td>
<td>16%</td>
<td>12%</td>
<td>6%</td>
</tr>
</tbody>
</table>

χ² p < 0.001 ANOVA p < 0.001 χ² p < 0.001 χ² p < 0.001 χ² p < 0.001

Chi-Square, p < 0.001

N does not total 1,200 due to missing data.
Drug-risk communication to pharmacists: Assessing the impact of risk-minimization strategies on the practice of pharmacy

Lauren Y. Lee, Cindy M. Kortepeter, Mary E. Willy, and Parivash Nourjah

Abstract

Objectives: To gain insight on the knowledge, opinions, barriers, and practices of pharmacists regarding drug risk-minimization tools.

Design: Descriptive, nonexperimental, cross-sectional survey.


Participants: 2,052 randomly selected licensed pharmacists employed in a position requiring an active pharmacist license at the time of the survey and who responded to the survey.

Intervention: Participants completed a four-page survey regarding their experience with different types of risk-minimization tools.

Main outcome measure: Univariate distributions for each question were analyzed.

Results: 50% of survey recipients responded to the mailing; 88% of respondents had an active pharmacist license. Of respondents, 18% reported never having received a Dear Healthcare Professional letter and 29% stated that they were not familiar with Medication Guides. Patient package inserts were thought to be somewhat effective by 53% of respondents. Of pharmacists who dispensed a drug with programs for special stickers to be affixed on prescriptions to indicate that the labeled risk had been addressed by the prescriber, 41% reported receiving a prescription without a sticker; 45% dispensed the prescription when stickers were missing. Sixty percent of pharmacists stated that risk-minimization programs have a negative impact on the daily practice of pharmacy; nevertheless, many acknowledged that it was a necessary duty.

Conclusion: Pharmacists might benefit from additional training on risk-minimization strategies. The successful implementation and impact of risk-minimization programs on the practice of pharmacy should be carefully considered by drug manufacturers and regulators.

Keywords: Risk management, pharmacists, medication safety, Food and Drug Administration, adverse drug effects, black box warnings.


RESEARCH

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Ensuring the safe use of marketed drugs requires effective strategies to minimize known drug risks. The Food and Drug Administration (FDA) has worked to minimize drug risks by working with drug manufacturers to develop relevant labeling and patient information materials. Medication guides, which contain FDA-approved drug information directed to patients, have been required for certain drugs that may cause serious adverse events or when patient adherence to directions is deemed crucial to the effectiveness and/or safe use of the drug. Other risk-communication tools used in the past and present include (1) patient package inserts (PPIs), which are part of FDA-approved labeling and have been written by the manufacturer to provide drug information; (2) patient information leaflets (PILs) (also known as consumer medication information [CMI] leaflets), which are preprinted or often computer-generated non–FDA-approved drug information materials written by a vendor other than the drug manufacturer and dispensed to patients for educational purposes; and (3) Dear Pharmacist and Dear Healthcare Professional (DHCP) letters, which are distributed to relevant parties by the drug manufacturer to convey new safety information.

FDA has recently increased efforts beyond these established risk communication tools to minimize risks and maximize benefits of selected drugs with serious risks. As a result, Risk Minimization Action Plans (RiskMAPs) have become a component of certain new drug approval plans, often requiring changes in some prescribing practices by physicians and in the dispensing of prescriptions by pharmacists. These RiskMAPs generally include traditional risk communication along with additional risk-minimization efforts (e.g., restricted distribution of products or reminder systems such as physician/patient agreement forms and the use of prescription stickers). The levels of adherence to and impact of RiskMAP programs on pharmacy practice is largely unknown. For example, effective communication of drug risks is a critical component of risk minimization; however, the extent to which communication tools such as FDA-approved patient labeling (Medication Guides and PPIs) and DHCP letters are used by pharmacists is unknown. Likewise, the impact of risk-minimization tools such as sticker programs and restricted distribution of products on pharmacy practice is largely unknown.

**Objectives**

We sought to evaluate pharmacist knowledge of risk-minimization tools, to identify barriers to communication, and to assess pharmacist opinions regarding the impact of these tools on the practice of pharmacy.

**Methods**

U.S. state boards of pharmacy were contacted to obtain lists of registered pharmacists. Of the 50 states contacted, 20 provided a list of registered pharmacists for 2003. A total of 5,000 U.S. pharmacists (1,250 from each of the four geographic regions based on U.S. Census Bureau categories) were randomly selected to receive a survey. In fall 2004, survey participants were asked to complete an anonymous four-page survey (see Appendix 1 in the online version of this article at www.japha.org). The survey was sent via first-class mail with a cover letter and a prepaid, stamped return envelope. To ensure anonymity and confidentiality, no premarkings or numbering systems were recorded on the questionnaire or return envelope. Approximately 2 weeks later, a follow-up postcard was sent as a reminder to return the survey. Three weeks after the postcard mailings, a second duplicate survey was mailed with a letter asking those who had not previously responded to complete the survey.

Survey questions included topics on Dear Pharmacist and DHCP letters, Medication Guides, PPIs, and PILs. The survey defined Medication Guides and PPIs as drug information materials made available by drug manufacturers; PILs were defined as drug information materials that can be dispensed to patients for educational purposes but not written by the drug manufacturer.
Questions about special prescription stickers, special risk-minimization strategies (e.g., restricted distribution), and problems experienced while dispensing drugs with risk-minimization programs were also included.

One of our objectives was to study pharmacist practices and opinions by region. Therefore, we attempted to have equal sample sizes for each of the four U.S. geographic regions. To calculate estimates for the 20 states for which pharmacist data were provided, each sample record in each region was weighted by the ratio of the number of pharmacists in its corresponding region in the 20 states over the number of pharmacists for the same region in the final sample. Univariate distributions were calculated using PROC FREQ in SAS (version 8.2; SAS Institute, Cary, NC).

Results

Of the 5,000 mailed surveys, 295 were returned without reaching the pharmacist (marked “return to sender”), leaving 4,705 surveys assumed to have reached the addressees. A total of 2,342 responses were received, a response rate of 50%. Approximately 88% of the respondents were employed in a position requiring an active pharmacist license; all analyses were restricted to these 2,052 pharmacists. Community pharmacies and inpatient hospitals were the most frequently reported pharmacy practice settings (Table 1). There were no observed differences in responses among the geographic regions.

DHCP letters

When asked if they had ever received a DHCP letter, 18% of pharmacists reported never receiving a DHCP letter. Of the 81% who received DHCP letters, 39% always read the letters, 32% often read the letter, and 6% rarely or never read the letters. Among those who always read the DHCP letters, 54% replied that the letter was very effective in communicating drug risks to pharmacists, whereas 8% of those who sometimes read the letters believed that the letter was very effective in communicating risks.

Medication Guides

Of respondents, 29% indicated that they were not familiar with the term Medication Guide. Overall, 25% of respondents stated that Medication Guides were very effective. Only 26% of the respondents correctly answered that Medication Guides are required to be dispensed with both new and refill prescriptions (Table 2). Among pharmacists who dispensed a medication requiring a Medication Guide, 23% reported patients complaining that the Medication Guide was not understandable. Thirty percent of pharmacist respondents always provided patient counseling with the dispensing of a Medication Guide, 26% always provided patient counseling with the dispensing of a PPI, and 32% always provided patient counseling with the dispensing of a PIL.

PPIs/drug package inserts

Of pharmacists, 20% believed that PPIs were very effective in communicating drug risks to patients, while 18% stated that

Table 1. Characteristics of pharmacist respondents to survey on impact of drug risk-minimization strategies

<table>
<thead>
<tr>
<th>Status</th>
<th>No. respondents (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respondents</td>
<td>2,342*</td>
</tr>
<tr>
<td>Employed in position requiring active pharmacist license</td>
<td>2,052 (88)</td>
</tr>
<tr>
<td>Employment setting b</td>
<td></td>
</tr>
<tr>
<td>Community pharmacy</td>
<td>1,207 (59)</td>
</tr>
<tr>
<td>Inpatient hospital</td>
<td>487 (24)</td>
</tr>
<tr>
<td>Clinic</td>
<td>146 (7)</td>
</tr>
<tr>
<td>Outpatient hospital</td>
<td>120 (6)</td>
</tr>
<tr>
<td>Long-term care</td>
<td>130 (6)</td>
</tr>
<tr>
<td>Academia</td>
<td>38 (2)</td>
</tr>
<tr>
<td>Returnedc</td>
<td>295 (6)</td>
</tr>
<tr>
<td>No response</td>
<td>2,363 (47)</td>
</tr>
</tbody>
</table>

*47% of total mailings; 50% of survey recipients.

bPersons may appear in more than one category.

cReturned surveys did not reach the pharmacists and came back “return to sender.”

Table 2. Pharmacist responses to Medication Guide questions

<table>
<thead>
<tr>
<th>Question</th>
<th>Response options</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>When should a Medication Guide be given to patients with the dispensing of a medication?</td>
<td>Required with new and refill prescription</td>
<td>26</td>
</tr>
<tr>
<td></td>
<td>Required with new prescription only</td>
<td>38</td>
</tr>
<tr>
<td></td>
<td>Required with refill prescription only</td>
<td>&lt;1</td>
</tr>
<tr>
<td></td>
<td>Always optional</td>
<td>21</td>
</tr>
<tr>
<td></td>
<td>Do not know/no response</td>
<td>15</td>
</tr>
<tr>
<td>How often do you counsel patients when you provide a Medication Guide?</td>
<td>Always</td>
<td>30</td>
</tr>
<tr>
<td></td>
<td>Often</td>
<td>28</td>
</tr>
<tr>
<td></td>
<td>Sometimes</td>
<td>17</td>
</tr>
<tr>
<td></td>
<td>Rarely</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>Never/no response</td>
<td>18</td>
</tr>
<tr>
<td>How effective are Medication Guides at communicating drug risks to patients?</td>
<td>Very effective</td>
<td>25</td>
</tr>
<tr>
<td></td>
<td>Somewhat effective</td>
<td>51</td>
</tr>
<tr>
<td></td>
<td>Not effective</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>Do not know/no response</td>
<td>18</td>
</tr>
</tbody>
</table>
PPIs were not effective (Table 3). Overall, 17% of pharmacist respondents were not aware that the contraindications, warnings, precautions, and adverse reactions sections of the product labeling intended for health care professionals could be revised to reflect changes in drug risks or adverse reactions.

**PILs**

PILs (i.e., drug information materials that can be dispensed to patients for educational purposes but are not written by the drug manufacturer) were reported by 30% of pharmacists to be very effective at communicating drug risks to patients.

**Special programs**

At the time of the survey, both Accutane (isotretinoin—Roche) and Lotronex (alosetron—Prometheus) had risk-minimization programs whereby a special sticker was affixed on prescriptions by the prescriber as a mechanism to notify the pharmacist that the safety risks have been addressed. Of pharmacists who dispensed at least one of the aforementioned drugs, 41% had received a prescription without the required sticker. When the sticker was missing, 55% of the pharmacists did not dispense the drug and 23% dispensed the drug only after calling the prescriber. However, 20% dispensed the drug after talking to the patient and 2% dispensed the drug after calling the drug manufacturer. Fifty percent of the pharmacists stated that the special sticker was a very effective tool for communication between physicians (prescribers) and pharmacists. Of pharmacists, 39% felt that the sticker was somewhat effective and 6% that it was ineffective.

Among the surveyed drugs with risk-minimization programs, those for Accutane and Clozaril (clozapine—Novartis) were the most recognized, as shown in Table 4. Of pharmacists, 44% believed that restricting drug dispensing to designated pharmacies was ineffective in reducing drug risks. Limiting the quantity of pills to be dispensed and writing an expiration date on the prescription were felt to be effective risk-minimization strategies by 72% and 74% of respondents, respectively. To reduce drug risks, 64% of respondents believed that physicians should issue written prescriptions only and not telephone or fax prescriptions for particular drugs (Table 5).

As shown in Table 6, pharmacists encountered complaints from prescribers and patients when dispensing drugs with risk-minimization programs. Prescribers telephoned or faxed prescriptions when only written prescriptions were allowed under the program. Prescribers also authorized refills for nonrefillable drugs under the plan and complained about limited day

---

### Table 3. Pharmacist responses to PPI questions

<table>
<thead>
<tr>
<th>Question</th>
<th>Response options</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Based on your understanding, please indicate when a PPI should be given to the patients with the dispensing of a medication?</td>
<td>Required with new and refill prescription</td>
<td>24</td>
</tr>
<tr>
<td></td>
<td>Required with new prescription only</td>
<td>30</td>
</tr>
<tr>
<td></td>
<td>Required with refill prescription only</td>
<td>&lt;1</td>
</tr>
<tr>
<td></td>
<td>Always optional</td>
<td>35</td>
</tr>
<tr>
<td></td>
<td>Do not know/no response</td>
<td>10</td>
</tr>
<tr>
<td>How often do you counsel patients when you provide a PPI?</td>
<td>Always</td>
<td>26</td>
</tr>
<tr>
<td></td>
<td>Often</td>
<td>27</td>
</tr>
<tr>
<td></td>
<td>Sometimes</td>
<td>21</td>
</tr>
<tr>
<td></td>
<td>Rarely</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>Never/no response</td>
<td>15</td>
</tr>
<tr>
<td>In your opinion how effective are PPIs in communicating drug risks to patients?</td>
<td>Very effective</td>
<td>20</td>
</tr>
<tr>
<td></td>
<td>Somewhat effective</td>
<td>53</td>
</tr>
<tr>
<td></td>
<td>Not effective</td>
<td>18</td>
</tr>
<tr>
<td></td>
<td>Do not know/no response</td>
<td>9</td>
</tr>
</tbody>
</table>

**Abbreviation used:** PPI, patient package insert.

---

### Table 4. Dispensing of specified drugs with risk-minimization programs by pharmacist respondents

<table>
<thead>
<tr>
<th>Drug</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Accutane (isotretinoin—Roche)</td>
<td>80</td>
</tr>
<tr>
<td>Actiq (fentanyl—Cephalon)</td>
<td>33</td>
</tr>
<tr>
<td>Clozaril (clozapine—Novartis)</td>
<td>64</td>
</tr>
<tr>
<td>Thalomid (thalidomide—Celgene)</td>
<td>37</td>
</tr>
<tr>
<td>Lotronex (alosetron—Prometheus)</td>
<td>36</td>
</tr>
<tr>
<td>Mifeprax (mifepristone—Danco)</td>
<td>4</td>
</tr>
<tr>
<td>Tikosyn (dofetilide—Pfizer)</td>
<td>12</td>
</tr>
<tr>
<td>Tracleer (bosentan—Actelion)</td>
<td>3</td>
</tr>
<tr>
<td>Xyrem (sodium oxybate—Jazz)</td>
<td>24</td>
</tr>
</tbody>
</table>
supply imposed by the risk-minimization programs. Similarly, pharmacists reported that patients complained about limited day supply, wanted refills for nonrefillable drugs, and indicated that Medication Guides were difficult to understand. Of pharmacists, 19% stated that they had difficulty obtaining Medication Guides and 38% described difficulty confirming that patients or prescribers were registered when required under the risk-minimization program. Overall, 61% of pharmacists stated that risk-minimization programs had a negative impact on the practice of pharmacy because the plans were confusing and required more time, personnel, and cost to pharmacies. Seven percent of respondents stated that risk-minimization programs have a positive impact on the daily practice of pharmacy.

The pharmacists were asked to provide free-text suggestions on how communication of drug risks between drug manufacturers and pharmacists could be improved; multiple answers were allowed. The top five recommendations to improve the communication of drug risks between manufacturers and pharmacists were disseminating information via e-mail/electronic mailing lists, providing brief and concise information, sending a manufacturer representative to the pharmacist, creating a drug counseling website, and distinguishing DHCP letters from advertisements. Free-text suggestions on how to improve the communication of drug risks between pharmacists and patients included smaller patient-to-pharmacist ratios, patient counseling by the pharmacist, compensating pharmacists for counseling, and improved auxiliary labels. Other suggestions included telephone/e-mail/Internet access to pharmacists, eliminating drive-through pharmacies, no direct-to-consumer advertisements, and patient counseling by physician before the pharmacy visit. Suggestions on how to improve communication of drug risks between prescribers and pharmacists included direct communication between the prescriber (i.e., not the prescriber’s agent) and pharmacist, universal computer/electronic communication (e.g., electronic prescribing), notation on prescriptions (e.g., indication for use), pharmacist access to patient information, communicating to the pharmacist that the patient has been counseled by the physician, educating physicians on drug risks and the role of pharmacists, and better handwriting on prescriptions.

Discussion

Efforts to minimize known drug risks often involve pharmacists. These efforts are particularly important because pharmacists, along with physicians, have been reported to be the preferred source of drug information. 3 To minimize patient drug risk, pharmacists must be given risk-minimization tools that are convenient and effective. Pharmacists themselves must be informed and educated on drug risks and the tools used to minimize patient risk. 4

DHCP letters are used to communicate newly realized drug risks and/or additional findings on preexisting drug risks to pharmacists and other health care providers. The effectiveness of these letters has been studied 4,5 and found to be variable; publicity and direct intervention with dispensing pharmacies may be needed for these letters to be effective. One recent study analyzed 36 Dear Doctor letters and concluded that many of the letters did not communicate drug risk information clearly or effectively. 6 The response from our surveyed pharmacists provides additional insight into some of the limitations of this

Table 5. Pharmacist responses regarding effectiveness of drug risk-minimization strategies

<table>
<thead>
<tr>
<th>Risk-minimization strategy</th>
<th>Effective (%)</th>
<th>Not effective (%)</th>
<th>No opinion (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Restricting the dispensing of the drug to a specific designated pharmacy</td>
<td>46</td>
<td>44</td>
<td>7</td>
</tr>
<tr>
<td>Limiting the quantity of pills to be dispensed</td>
<td>72</td>
<td>21</td>
<td>5</td>
</tr>
<tr>
<td>Physicians writing an expiration date on the prescription</td>
<td>74</td>
<td>18</td>
<td>6</td>
</tr>
<tr>
<td>Physicians allowed to issue only written prescriptions and no phone or fax option</td>
<td>64</td>
<td>28</td>
<td>5</td>
</tr>
</tbody>
</table>

Table 6. Pharmacist responses to barriers encountered with drug risk minimization tools

<table>
<thead>
<tr>
<th>Barrier</th>
<th>Encountered barrier (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prescriber wishes to phone in the prescription to a pharmacy even though only written prescriptions can be filled</td>
<td>37</td>
</tr>
<tr>
<td>Prescriber wishes to fax in the prescription to a pharmacy even though only written prescriptions can be filled</td>
<td>36</td>
</tr>
<tr>
<td>Prescriber wants to authorize refills even though refills cannot be prescribed</td>
<td>42</td>
</tr>
<tr>
<td>Prescriber wishes to exceed the limited number of pills</td>
<td>26</td>
</tr>
<tr>
<td>Patient complains about not being able to receive drug quantities that exceed the limited day supply</td>
<td>51</td>
</tr>
<tr>
<td>Patient wants a refill even though refills cannot be prescribed</td>
<td>60</td>
</tr>
<tr>
<td>Difficulty obtaining Medication Guide</td>
<td>19</td>
</tr>
<tr>
<td>Patient indicates Medication Guide difficult to understand</td>
<td>23</td>
</tr>
<tr>
<td>Difficulty confirming that the patient or prescriber is registered</td>
<td>38</td>
</tr>
</tbody>
</table>
tool. Our survey revealed that nearly 20% of pharmacists have never received DHCP letters. Among those who always read the letters, only one-half felt that DHCP letters were a very effective tool in communicating drug risks to pharmacists. Those who read the DHCP letter less frequently had lower effectiveness ratings, suggesting a positive correlation between reading the DHCP letters and the rating of their effectiveness in communicating drug risks to pharmacists (i.e., those who read DHCP letters more often felt that they were more effective). Survey pharmacists suggested that communication from drug manufacturers could be improved by maximizing use of computerized/electronic information technologies and minimizing use of lengthy “futile” information (e.g., advertisements); both measures would allow for more efficient use of the pharmacist’s time.

As described above, Medication Guides are FDA-approved drug information directed to patients and are required to conform to specifications noted in the Code of Federal Regulations (CFR). The CFR specifies that each authorized dispenser (a pharmacist, for the purpose of this article) of a prescription drug product for which a Medication Guide is required will provide a Medication Guide directly to each patient (or to the patient’s agent) when the product is dispensed, unless an exemption applies. Of concern, nearly 30% of pharmacists responding to our survey were not familiar with the term “Medication Guide.” Confusion seems to exist regarding the knowledge and understanding of dispensing requirements for Medication Guides among the pharmacists surveyed. Although the majority of pharmacists knew that Medication Guides were dispensed with new prescriptions, notably only approximately 25% of respondents correctly answered that Medication Guides are required to be dispensed with both new and refill prescriptions (for products that require a Medication Guide). Pharmacists who have dispensed a medication requiring a Medication Guide reported that they have encountered difficulty obtaining Medication Guides, and pharmacists have encountered patients who complained that the Medication Guide was difficult to understand.

PPIs and PILs are two other forms of written communication materials intended for patients. Although PPIs are part of approved labeling and are written by the drug manufacturer, not all drugs have PPIs and dispensing of PPIs is left to the discretion of the pharmacist, unless state laws instruct them otherwise. The majority of pharmacists surveyed felt that PPIs were at least somewhat effective in communicating drug risks to patients. However, of note, 16% of pharmacist respondents were not aware that the contraindications, warnings, precautions, and adverse reactions sections of the drug package insert can be revised to reflect new information or findings in drug risks or adverse reactions. These changes, if appropriate, are also reflected in the PPIs, and because not all pharmacists surveyed knew that labeling is often updated and modified, they may not be communicating new safety information to patients when dispensing refills.

PILs, the preprinted and often computer-generated drug information materials for patients, are written by a vendor other than the drug manufacturer. They are sometimes more general in nature and may cover a class of agents rather than a specific drug. PILs are also referred to as CMI leaflets and are not reviewed or approved by FDA. PILs were reported by pharmacists to be very effective in communicating drug risks to patients by 30% of responders—slightly higher perceived effectiveness than PPIs and Medication Guides. It is possible that since many pharmacies have technologies allowing for these computer-generated leaflets to be printed along with prescription labels, the mere convenience of these leaflets for all drugs possibly make them a favorable written communication tool for pharmacists to dispense to patients. A study by Svarstad et al. suggested that these leaflets may be popular drug information choices with high rates of patient leaflet distribution (89%) in a study of 384 community pharmacies, but many leaflets were abbreviated (≤70 words), were hard to read, or provided non-specific information.

When the pharmacists were asked how often patient counseling was provided with a Medication Guide, PPI, and PILs, the results were similar despite the fact that pharmacist distribution of Medication Guides to patients (or the patient’s agent) is required and that PPIs and PILs have no such requirement (unless the pharmacist is using these tools to fulfill their state-mandated counseling requirement). In terms of counseling, Medication Guides were not treated differently compared with PPIs and PILs; however, some confusion appeared to exist in the knowledge and understanding of dispensing requirements of Medication Guides, PPIs, and PILs among the pharmacists surveyed.

A special sticker is a tool used to facilitate communication between a prescriber and a pharmacist. At the time of the survey, both Accutane and Lotronex had a program whereby a special sticker was affixed on prescriptions by the prescriber as a method to inform the pharmacist that the specific safety risk had been addressed. An overwhelming majority (89%) of pharmacists believed that sticker programs were a very or somewhat effective communication tool between prescribers and pharmacists. However, 40% of those respondents who dispensed Accutane and/or Lotronex had encountered missing stickers and more than one-half of these pharmacists did not dispense the drug for this reason. In addition, nearly 25% of pharmacists dispensed the drug only after calling the prescriber when the sticker was missing. Many would agree that unintended consequences with missing stickers were problematic and burdensome, and our survey revealed that missing stickers was not uncommon. Of note, after the study time frame, only Lotronex was continuing the sticker program.

Educating physicians, pharmacists, and patients about the proper use and risks of medications is an essential step toward minimizing the risk. This survey shows that pharmacists were not receiving educational material on all drugs with risk-mini-
mization programs. In addition to the problem of accessing drug information (e.g., Medication Guide, DCHIP letter), pharmacists cited difficulties with implementing risk-minimization programs because of the barriers in verifying patient/physician registries, physicians not following risk-minimization procedures (i.e., noncompliance with a special sticker, prescribing quantities exceeding the limited day supply), and patients complaining of risk-minimization procedures (i.e., requesting refills when not allowed, difficulty understanding Medication Guides). With growing numbers of new risk-minimization programs being launched on the market, it is concerning that 61% of pharmacists in this study stated that risk-minimization programs have a negative impact on the daily practice of pharmacy, primarily because the plans are confusing and require more time, personnel, and costs to pharmacies. Only 7% of pharmacists stated that risk-minimization programs have a positive impact on the daily practice of pharmacy; however, even among those who stated a negative impact, many acknowledged that these risk-minimization strategies were necessary for the safe use of drugs by their patients and that it was their professional responsibility as pharmacists to implement them. Although minimizing drug risks is an important objective in risk-minimization programs, its effect on the practice of pharmacy, both direct and indirect (e.g., from physicians and patients) should be carefully considered by drug manufacturers and regulators.

Limitations

This study has certain limitations that must be considered when reviewing the findings. First, we included the 20 states that provided data about their licensed pharmacists; we do not have any information about the remaining states or the proportion of practicing pharmacists that our study represents. Therefore, our results may not be representative of the entire United States. The results may be biased if the opinions of those who did not return their survey differed from the responders. Another limitation is the possibility of confusion by respondents about the different tools: Medication Guides, PPIs, and PILs. Although the definitions of each of the tools were provided, the analysis of the Medication Guide section was restricted to those respondents who indicated that they were familiar with Medication Guides. The survey results are based on the responses that were received at the time of the survey and may not be reflective of current practice.

Conclusion

This survey is the first reported comprehensive study of pharmacists’ perceptions and implementation of a number of risk-minimization tools. This study suggests that pharmacists do not always use or have access to available risk-minimization tools and that certain risk-minimization strategies are not fully implemented by some pharmacists. Improving communication of drug risks between drug manufacturers and pharmacists or between prescribers and pharmacists is an important aspect of risk minimization. Pharmacists might benefit from additional training and/or education about risk-minimization strategies. Consideration should be made by regulators of the problems encountered when implementing the programs at the level of the physician, pharmacist, and/or patient.

Pharmacists can currently access clinically important medical product safety alerts, as well as up-to-date information about drugs, by visiting FDA Medwatch at www.fda.gov/medwatch and selecting the “Join the E-list” option.

References

8. U.S. Food and Drug Administration, Department of Health and Human Services. 21 C.F.R. 208.3(a): defines an authorized dispenser as an individual licensed, registered, or otherwise permitted by the jurisdiction in which the individual practices to provide drug products on prescriptions in the course of professional practice. 2006.
Attachment 3
White paper on designing a risk evaluation and mitigation strategies (REMS) system to optimize the balance of patient access, medication safety, and impact on the health care system

American Pharmacists Association

Abstract

Objective: To convene a group of expert stakeholders to develop recommendations for standardizing systems for the implementation of risk evaluation and mitigation strategies (REMS).

Data sources: On July 15, 2009, the American Pharmacists Association convened an expert panel of stakeholders to explore standardized solutions to REMS development and implementation. Meeting participants included pharmacists from various practice settings, physicians, researchers, patient advocates, and a nursing delegate, and the meeting was observed by a U.S. Food and Drug Administration representative. The stakeholders’ recommendations were combined with themes arising from discussion of their experiences with existing REMS, and a review of the literature on REMS and risk management was performed by the author.

Summary: A systematic, standardized REMS process that balances the need to control the risks of medications with the need to minimize the impact on patient access is required. A standardized REMS system could address various aspects of development and implementation, including the creation of specific REMS “levels,” centralized systems for data management and program structure, public education, individualized patient education, provider education, access to medications, pilot testing, outcomes monitoring, and quality of care.

Conclusion: Several strategies to streamline the development and implementation of a REMS system are feasible. Incorporating such strategies is necessary to manage the rapidly growing number of individual and diverse REMS programs that patients and health care providers must navigate. Furthermore, a standardized REMS system could be used to improve quality of care and support patient education and empowerment.

Keywords: Food and Drug Administration, health care administration, health care providers, patient accountability, patient education, pharmacists, provider education, quality of care, REMS, risk evaluation and mitigation strategies, risk management, workflow.

Evolution of risk management programs

Medications have the potential to considerably improve the health and well-being of patients, but medication use is not without risk. The U.S. Food and Drug Administration (FDA) uses several tools, which have evolved over time, to detect, evaluate, prevent, and mitigate adverse events associated with medications as part of the Agency’s mission to protect and promote public health.

A few decades ago, FDA’s drug safety and risk management activities focused primarily on data from a medication’s clinical trials to assess whether identified risks were outweighed by benefits and to determine whether that medication should be approved. However, societal awareness of postmarket medication safety issues has increased and tolerance for adverse events by patients and the public has decreased. In addition, some safety issues do not surface until after a medication has been marketed and used by a broader population. To address these concerns, FDA has increased its efforts to focus on postmarket safety issues associated with medications.

FDA postmarket surveillance seeks to identify problems that were not observed or recognized before drug approval. Tools used for postmarket surveillance include the Adverse Event Reporting System (AERS) and MedWatch. AERS is a database of adverse event reports that supports FDA’s postmarket safety surveillance program for all approved drugs and therapeutic biologics. MedWatch includes a voluntary adverse event reporting program for both health care providers and patients, and it provides communications about risks. These safety announcements include early communications about ongoing safety reviews, public health advisories, and other information for health care professionals. Additional communication activities, such as letters to health care professionals (e.g., Dear Doctor letters) and labeling revisions (e.g., addition of black box warnings) are coordinated with manufacturers.1

Despite increasing risk mitigation activities and risk communications from FDA, several medications with known, preventable risks were withdrawn from the market or placed on restricted distribution because of a lack of appropriate patient monitoring or because medications continued to be inappropriately prescribed to patients who had contraindications to the product’s use.

For example, cisapride (Propulsid) was approved in 1993 for treating gastroesophageal reflux disease and was widely prescribed. During the postmarketing period, cisapride was found to be associated with serious cardiac dysrhythmias including ventricular tachycardia, ventricular fibrillation, torsades de pointes, and QT prolongation when prescribed to patients who had specific known risk factors or were on certain other medications that interact with cisapride. Several risk communication tools were used to prevent the use of cisapride in such patients, including the use of a black box warning, Dear-Health Care Professional letters, an FDA Talk Paper, and information on FDA’s website. (FDA Talk Papers are used to disseminate detailed, accurate information to the media and to guide FDA staff in responding to questions from the public on specific topics of interest.) These efforts did not appear to alter prescribing practices, and cisapride was withdrawn from the general market in 2000. It continues to be available to a small number of patients through a restricted distribution program (i.e., Propulsid Limited Access Program).2

At a Glance

**Synopsis:** The Food and Drug Administration Amendments Act of 2007 (PL 110-85) authorized the U.S. Food and Drug Administration (FDA) to require risk evaluation and mitigation strategies (REMS) for medications or medication classes with known serious risks. The law gives FDA the authority to determine whether a REMS is necessary to ensure that the benefits of a drug or biological product outweigh the risks associated with the drug. FDA has the authority to require a REMS as part of the approval process or during the postapproval period. As of July 2009, approximately 50 different REMS programs were required by FDA, as well as indications that the Agency intends to expand REMS. The increasing number and diversity of programs creates a considerable burden on the health care system. A systematic, standardized process is needed to facilitate implementation of REMS, minimize the impact on patient access, and limit the administrative burden and impact on the health care system. To help address this need, the American Pharmacists Association convened a group of stakeholders in July 2009 to develop recommendations for creating such a process.

**Analysis:** Stakeholder meeting participants agreed that the lack of a systematic, standardized, efficient REMS system causes confusion, burdens the health care system, and creates barriers to patient access. Recommendations for moving forward with building a standardized, system-based set of solutions for REMS include creating different levels of intensity founded on the risks the REMS is designed to mitigate, developing a public education campaign, using face-to-face education with health care providers to convey important educational and accountability messages to patients, designing provider education to accommodate the needs of busy health care professionals, creating a REMS data management system that is interoperable with current health information technology systems, ensuring that monitoring of REMS outcomes measures and effectiveness address both the risks the REMS is designed to mitigate any unintended consequences, and requiring a pilot program to assess the effectiveness and impact of any new REMS system before implementation. Participants emphasized that these features would be necessary for creating a system that enhances patient safety, promotes quality of care, and is feasible for the health care system.
Likewise, alosetron (Lotronex) was approved in February 2000 for treating diarrhea-predominant irritable bowel syndrome in women. Within a few months, FDA had received reports of serious adverse events, including death, associated with use of alosetron. As these reports began to emerge, the manufacturer worked with FDA to develop a Medication Guide (MedGuide) to communicate the risks to patients and educate them to prevent serious harm. (MedGuides are FDA-approved patient information leaflets that must be distributed at the point of medication dispensing. They are deemed necessary when FDA determines that patients require certain information to support the safe and/or effective use of the medication.) Professional labeling was revised, and Dear Health Care Practitioner and Dear Pharmacist letters were issued to convey this new safety information.

Despite these communication activities, serious adverse events associated with alosetron use continued to be reported, including three deaths. Alosetron was withdrawn from the market in November 2000 and reintroduced in June 2002 under a restricted distribution program that included a MedGuide, a prescriber agreement, and a patient-physician agreement. (The use of the term “prescriber” throughout this document means physicians, physician assistants, nurse practitioners, certain pharmacists authorized to prescribe under specified conditions in their state based on collaborative practice agreements, and other health care providers authorized to prescribe prescription medications.)

As these cases illustrate, risk communication alone does not ensure appropriate prescribing practices. These experiences, in conjunction with an increase in the number of medications that have both important benefits and serious risks, led FDA to begin exploring more restrictive risk management programs in the late 1990s. These programs varied in restrictiveness; some required MedGuides for patient education, while other more intensive programs used restricted distribution programs. Examples of more intensive programs include the Clozaril Patient Management System (developed in the 1980s), the thalidomide (Thalomid) STEPS program (System for Thalidomide Education and Prescribing Safety; developed in 1998), and the isotretinoin (Accutane) iPLEDGE program (developed in 2006).

Clozapine (Clozaril), first introduced in the late 1980s for treating schizophrenia, is associated with an increased risk for agranulocytosis, which can be fatal. Close monitoring of white blood cell (WBC) counts can identify the development of this adverse event early enough for prompt discontinuation of therapy, resulting in considerable reductions in the morbidity and mortality associated with clozapine use.

A tightly controlled system of mandatory patient, prescriber, and pharmacist registration that requires adherence to a weekly WBC count was developed to support safe use of clozapine. Under this system, patients receive 1 week’s supply of clozapine at a time and WBC counts must be obtained before each refill (prescribers may write prescriptions that include refills). The frequency of WBC counts can be reduced if the patient is maintained on clozapine for more than 6 months without a need for treatment interruption or increased monitoring.) In addition, the system allows for a one-time emergency supply of medication without WBC monitoring.

Risk management programs also have been designed to prevent prenatal exposure to a medication. For example, the thalidomide and isotretinoin risk management programs (STEPS and iPLEDGE, respectively) are designed to prevent pregnancy in women using these known teratogens.

Thalidomide was originally marketed outside the United States from 1957 to 1961 as a sedative, tranquilizer, and antiemetic for treating morning sickness. It was removed from the market after it was found to cause serious congenital abnormalities. However, before it was removed, approximately 10,000 children were born with thalidomide-related malformations. Shortly after, in 1965, thalidomide was noted to be effective for treating erythema nodosum leprosum (an inflammatory condition that affects patients with leprosy). However, as a result of concerns about teratogenicity, it was not until the late 1990s that thalidomide was introduced in the United States with a strict system intended to prevent prenatal exposure.

Today, thalidomide is approved in the United States for treating multiple myeloma, erythema nodosum leprosum, and HIV wasting disease. The STEPS program includes restricted distribution; a national registry for prescribers, patients, and pharmacists, central authorization of prescriptions, a patient informed consent form and required phone survey, and required pregnancy testing in female patients of childbearing potential.

Isotretinoin, which is approved for treating severe recalcitrant nodular acne, is more widely used than thalidomide. The evolution of risk management programs to prevent pregnancy in patients using isotretinoin (including the Pregnancy Prevention Program, the System to Manage Accutane Related Teratogenicity [SMART], and iPLEDGE) provides an example of the use of progressively more restrictive strategies and the impact of these practices on pregnancy rates (Table 1). In 2005, the Accutane brand of isotretinoin was withdrawn from the market by the manufacturer, but generic versions remain available.

In recent years, a substantial increase has occurred in the number of medications that have risk management programs. The programs, previously called Risk Minimization Action Plans (RiskMAPs) by a 2005 FDA guidance, varied in restrictiveness; some required restricted distribution programs, while others were limited to MedGuides. As of February 2007, 30 products had RiskMAPs.

**REMS: A new approach to managing risk**

Under the RiskMAP system, FDA had the authority to require postmarketing commitments from manufacturers prior to drug approval but could not enforce the commitments after approval. Several concerns were raised that this system did not...
provide adequate safety controls and led to calls for greater
FDA authority over the postmarketing period.12 On September
27, 2007, the Food and Drug Administration Amendments Act
of 2007 (FDAAA; PL 110-85) was signed into law.13 One goal of
this law was to improve drug safety by providing FDA with post-
marketing authority over drugs and biological products through
new risk identification and communication strategies.

FDAAA includes provisions authorizing FDA to require risk
evaluation and mitigation strategies (REMS) for medications
or medication classes with known serious risks. The law gives
FDA the authority to determine whether a REMS is necessary
to ensure that the benefits of a drug or biological product out-
weigh its risks. FDA has the authority to require a REMS as part
of the approval process or during the postapproval period if the
Agency becomes aware of new safety information about serious
risks associated with the use of the medication. FDAAA directs
FDA to be very explicit about why a REMS would be necessary
to manage the risks of a medication or class of medications.

As defined in FDAAA, a REMS must include a communica-
tion plan and may include a MedGuide, patient package insert,
and other elements to ensure safe use; may include an imple-
mentation system; and generally, innovator and generic spon-
sors shall use a single, shared system. The components used in
a specific REMS can vary. Elements to ensure safe use, which
must include goals to mitigate a specific serious risk listed in
the labeling of the drug, may include the following require-
ments13:

- Health care providers who prescribe the drug have particu-
lar training or experience or are specially certified.
- Pharmacies, practitioners, or health care settings that dis-
pense the drug are specially trained and/or certified.
- The drug is dispensed to patients only in certain health care
settings, such as hospitals (i.e., through a restricted distri-
bution program).
- The drug is dispensed to patients with evidence or other
documentation of safe use conditions, such as laboratory
test results.
- Each patient using the drug is subject to certain monitor-
ing.
- Each patient using the drug is enrolled in a registry.
- Physicians who prescribe and/or pharmacists who dis-
pense the drug are enrolled in a registry.

Table 1. Overview of isotretinoin risk management approaches

<table>
<thead>
<tr>
<th>Risk management strategies</th>
<th>Data on pregnancy rates</th>
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<tbody>
<tr>
<td><strong>1982 original warning</strong> Warning on label</td>
<td>Manufacturer receives multiple reports of fetal malformations</td>
</tr>
<tr>
<td><strong>1983 revised warning</strong> Added:</td>
<td>Reports of fetal malformations continued</td>
</tr>
<tr>
<td>Red label stickers to pharmacies</td>
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<tr>
<td><strong>1988 Pregnancy Prevention Program (PPP)</strong> Added:</td>
<td>2.8 to 3.4 pregnancies per 1,000 courses of treatment</td>
</tr>
<tr>
<td>“Avoid pregnancy” icon and black box warning on package insert</td>
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<tr>
<td>Patient consent form</td>
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<tr>
<td>Package insert noted a requirement for a pregnancy test prior to starting treatment</td>
<td></td>
</tr>
<tr>
<td>Package insert stated that two forms of birth control must be used</td>
<td></td>
</tr>
<tr>
<td><strong>2001 System to Manage Accutane® Related Teratogenicity (SMART)</strong> Added:</td>
<td>2.1 to 2.3 pregnancies per 1,000 courses of treatment</td>
</tr>
<tr>
<td>Package insert required two pregnancy tests prior to starting treatment</td>
<td></td>
</tr>
<tr>
<td>Package insert required the use of yellow qualification stickers by registered prescribers</td>
<td></td>
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<tr>
<td>Pharmacists required to give Medication Guide with prescription</td>
<td></td>
</tr>
<tr>
<td><strong>2006 Isotretinoin Pregnancy Risk Management Program (iPLEDGE)</strong> Added:</td>
<td>1.3 pregnancies per 1,000 female users of the program</td>
</tr>
<tr>
<td>Single, centralized program for all isotretinoin products</td>
<td></td>
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<tr>
<td>Required registration in database by patients, prescribers, pharmacies, and wholesalers</td>
<td></td>
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<tr>
<td>Mandatory monthly pregnancy tests before authorization of each prescription</td>
<td></td>
</tr>
<tr>
<td>Mandatory monthly education for patients</td>
<td></td>
</tr>
<tr>
<td>Centralized pregnancy registry</td>
<td></td>
</tr>
<tr>
<td>Removed: Use of yellow qualification stickers by registered providers</td>
<td></td>
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</tbody>
</table>

*Accutane is a brand of the generic isotretinoin.
Source: References 9 and 10.
If FDA deems that a REMS is necessary, the Agency directs manufacturers to create a REMS with specific elements and the manufacturers are required to comply. Manufacturers are responsible for implementing the system and working with FDA to assess and monitor outcomes of the system. On March 27, 2008, FDA clarified that certain medications with a previous RiskMAP were deemed to have a REMS after appropriately requirements were met. As of July 2009, approximately 50 different REMS programs were required by FDA.

Because each REMS is created independently by the affected medication’s manufacturer, REMS lack standardization in program design and implementation. (However, generic versions of a medication use the same REMS as the branded product.) The resulting growing number of disparate programs leads to administrative, logistical, and workflow challenges for the health care system. The inconsistency that results from such “silo” programs leads to provider confusion, administrative inefficiencies in implementation, workflow inefficiencies, and burdens on the health care system. This burden on the health care system has the potential to reduce patient access to medications because it may limit provider participation.

Participants noted that independent development of each REMS has resulted in limited opportunities for stakeholders, such as health care providers and patients, to provide recommendations regarding how to design and implement existing REMS early in the process and prior to the announcement of a REMS. The creation of a standardized system of REMS tools could facilitate opportunities for stakeholder input earlier in the REMS design and development process, help streamline implementation for stakeholders, and reduce the burden on the health care system.

FDA’s increased REMS activity since enactment of FDAAA in 2007 could affect a much broader patient population and thus have a greater impact on the health care system. This recent activity has stimulated discussion of broad-based solutions for developing a standardized system for REMS. Standardization, consistency, and program efficiency and design must be addressed to streamline the implementation and logistics of REMS programs and support achievement of intended outcomes while minimizing potential negative effects on the health care system.

In addition to the economic cost for patients and health care providers, all restrictive measures have the potential to reduce patient access owing to a lack of provider participation in a REMS because of the program’s impact. Limited provider participation could contribute to patients being excluded from therapy for other reasons than safety issues. Therefore, the group agreed that the most restrictive REMS measure (i.e., restricted distribution) should be reserved for only those situations in which the measure would be critical for risk reduction to ensure patient safety.

Participants discussed their experiences with a variety of specific risk management tools used by existing REMS (some were previously categorized as RiskMAPs) and provided their recommendations for modifying such tools and overall risk management programs.
Medication guides

Medication guides (MedGuides) are one of the most common risk management tools used by many current REMS. For a REMS, MedGuides are often combined with Dear Health Care Provider letters. Although MedGuides are a frequently used tool, they are not without challenges. MedGuides create administrative burdens, workflow inefficiencies, and supply challenges for pharmacists; they also generate extra costs (e.g., paper and ink for printing), lack a balance of risk and benefit information, and have format inconsistencies. Meeting participants noted that MedGuides are generally ineffective at communicating risk information to patients.

Participants agreed that patients often do not read MedGuides, and those who do struggle to understand them. The participants felt that current MedGuides are written at a very high reading level and are challenging from a health literacy perspective. MedGuides tend to provide very lengthy technical information but do not summarize the most important points for patients or provide a list of actionable items so patients know how to apply the information, participants remarked. In addition, MedGuides lack information about the balance of benefit and risk and may contain information that is inconsistent with other written patient materials. Furthermore, existing MedGuides do not take into account patient diversity, such as cultural issues, and are often not available in languages other than English.

Additional research supports the meeting participant’s experiences with MedGuides as risk communication tools. For example, in one survey, many pharmacists reported receiving complaints from their patients that they did not understand the MedGuides. Furthermore, this survey revealed pharmacist confusion about the use of MedGuides—only 26% of pharmacists correctly responded that the MedGuides should be provided with both initial prescriptions and refills.

Another challenge that participants reported is the growing number of MedGuides and the need to keep track of which medications require a MedGuide. Concern was raised that rather than being available from one centralized location, MedGuides must be ordered from each manufacturer when the pharmacy’s supply runs out, or MedGuides may not be included with the delivery of the medication order. Therefore, participants commented that it can be difficult to ensure that the pharmacy has a supply of the most recent set of MedGuides for all covered medications, particularly when MedGuides are revised or new ones are issued. Although manufacturers are required to provide MedGuides to the pharmacy, participants noted that currently, many of the costs associated with identifying, storing, and dispensing MedGuides are borne by pharmacies (e.g., printing costs for pharmacies that have voluntarily chosen to print MedGuides to improve identification and dispensing processes). To avoid further confusion and burdens on pharmacies, participants recommended that the MedGuide system be addressed before additional MedGuides are required.

Participants discussed the need for an easy-to-read, patient-friendly version of each MedGuide that could be supplemented by a comprehensive MedGuide for patients who wanted more detailed information. The patient-friendly component could explicitly state which symptoms should be of concern to patients and when to contact the health care provider. Participants also recommended that important educational messages be provided in a face-to-face encounter with a health professional, and written material should be used as a supplement to the personal interactions. Participants noted that, ideally, the information that the patient receives from the pharmacist will reinforce what they already received from the prescriber.

Participants acknowledged that FDA and FDA’s Risk Communication Advisory Committee (RCAC) have recognized the need to improve written information that patients receive at the pharmacy, such as MedGuides, and have engaged in ongoing activity with stakeholders to address this issue. For example, the RCAC developed recommendations for better dissemination of information following a February 2009 committee meeting. In addition, FDA’s Office of the Commissioner hosted a public workshop on providing effective information to patients in September 2009 that focused on MedGuides, Consumer Medication Information, and patient package inserts.

Informed consent forms

Informed consent forms, or patient agreement forms, are generally used to ensure that patients are aware of the risks posed by a medication and acknowledge acceptance of those risks when they receive a treatment. Participants expressed concern that, in current practice, these forms are sometimes used for liability reasons rather than as a tool for patient education and empowerment. They speculated that lack of provider compensation for time spent discussing the informed consent documents may contribute to this issue. Participants believed that informed consent forms could be a tool to promote communication, empower the patient to work with health care providers, and assist in the patient education process. If informed consent forms are used as a REMS tool, a streamlined and consistent process should be used for implementation.

Participants also discussed medication therapy management (MTM), which is a patient-centered interaction and functions as a collaborative process among the patient, pharmacist, and health care team. Currently, compensation for providing MTM services is provided through several sources, including Medicare Part D, several state Medicaid programs, numerous self-insured employers, and others. More information about MTM services is provided through several sources, including the website of the American Society for Pharmacy. Participants discussed designating an MTM visit with a pharmacist or other health care provider as a REMS tool to review the informed consent forms and ensure that patients understand their medications’ benefits and risk, patient accountability requirements, and terms of the agreements. Follow-up could take place at later visits, telephonically, or through e-mail, text, or other forms of electronic communication. Participants also noted that, if MTM is used as a mechanism for implementing REMS tools, compensation to providers will be necessary.

Laboratory monitoring for effective and safe use

Assessments of clinical indicators for monitoring safety are used by several existing REMS programs. Such requirements,
including those for clozapine and isotretinoin, often create strict limits on windows of opportunity for completing tasks (e.g., a laboratory test) and dispensing a medication. Although such programs can support conditions for safe use of the medications, they do not completely eliminate undesirable events and they create barriers to access. For example, participants reported that prescribers of isotretinoin struggle with barriers that include working within a system that does not allow for exceptions, such as a vacation supply or specific dosing regimens outside the normal parameters.

Participants noted that such REMS programs contribute substantially to the costs associated with covered medications. These costs included those for the actual testing, as well as time required to implement the program and ensure that all program requirements are met. Participants anecdotally reported that the number of isotretinoin prescribers shrank dramatically when the iPLEDGE program was implemented, in part because of the uncompensated time spent ensuring that testing was completed and components of the REMS had been met.

**Restricted distribution**

Restricted distribution programs, such as those for alos-teron and cisapride, can help prevent the use of a medication by inappropriate patients, but they also may create barriers to access for appropriate patients. Furthermore, participants noticed that these programs can lead to fragmentation of care, particularly if patients are required to obtain one of their prescriptions from a centralized pharmacy and these records are not communicated to the patient’s regular pharmacy. Other restricted distribution options include requiring patients to select a single prescriber (or practice) and single pharmacy of their choosing to fill all prescriptions for the medication covered by the REMS.

Greater use of restricted distribution strategies would require enhanced communication of electronic prescription records to ensure that all prescribers and dispensers have access to complete records. Participants also suggested that national pharmacy data systems, such as those used by the Department of Health and Human Services (via the Centers for Medicare & Medicaid Services) during natural disasters (e.g., Katrina Health), could serve as a model strategy for allowing the review of prescription fill histories without limiting patients to a single location. If such a system is used for restricted distribution, attention to database design would be needed to ensure that all REMS medications, including those that are paid for in cash rather than through a third-party insurer, are captured by the system.

Participants commented that restricted distribution strategies should include options to accommodate patients who live in multiple locations throughout the year and patients who travel. The system also would need to accommodate individuals who move across practice settings (e.g., community, hospital, nursing home, assisted living). Finally, the participants emphasized that the use of restricted distribution as a REMS tool would need to be limited to cases involving only the most serious risks.

**Specialized training**

Several existing REMS programs require health care providers to undergo specialized training before prescribing or dispensing a medication. Participants noted that many providers do not participate in the additional training required by these REMS, which results in barriers to access for patients who have difficulty finding providers participating in a specific REMS program.

Finding a provider who participates in the REMS can be particularly problematic for patients whose insurance coverage has a specific network of providers. Furthermore, patients in rural areas may live several hours away from prescribers who have participated in required REMS training. In more densely populated areas, patients may live in closer proximity to participating prescribers but may have difficulty scheduling appointments.

Specialized training issues also can cause problems in pharmacies because all pharmacists in a participating pharmacy may not have received the training. Additionally, pharmacists who work in multiple locations or are not permanent staff in a participating pharmacy may not have received the REMS training. These situations could result in dispensing delays when the activities required are above the common set of dispensing procedures for a pharmacy. Pharmacists also may face administrative and logistical challenges because various pharmacies may have different operating systems, procedures for accessing REMS programs (e.g., specific login codes), and processes for handling other features of the programs. Physician group practices may experience similar issues.

**Specific ordering/inventory procedures**

In some current risk management programs, community pharmacies must use specific ordering procedures to obtain medications for patients. For example, pharmacies that dispense thalidomide must individually order the medication for a specific patient. If that patient discontinues the medication, it must be returned to the distributor rather than kept in stock for a future patient.

Drawbacks to such procedures include the time-consuming nature of handling a patient-specific medication and the requirement for additional training and administrative oversight. The associated costs can reduce pharmacy participation, resulting in fewer options for patient access.

These policies also may result in inconsistent compliance with procedures, in the event that a pharmacy inadvertently has an incorrect process in place. Individuals who may not know the procedure or who do not perform it on a regular basis have an increased potential to experience challenges complying with the program, face administrative and logistical burdens, and require additional support. Pharmacies incur additional costs for administrative oversight to ensure that processes are implemented and maintained correctly. Thus, these factors may ultimately result in delayed patient care.

Participants urged that any requirements for specific ordering should be standardized so pharmacies would not need to learn and accommodate an ever-expanding number of differing policies and procedures.
Patient registries

Patient registries require all patients who receive a particular medication to participate in a central registry that tracks the safety of the product. Participants noted that registering all patients when the medication is used by a small population is feasible, but as numbers increase, systems become unwieldy and difficult to manage unless a streamlined, efficient system to enroll patients is developed. Even with a small patient population, registries can cause delays in treatment, particularly if a patient or provider inadvertently fails to complete a step in the process.

Participants reported that providers are sometimes unaware of appropriate processes for using a registry in current practices. Furthermore, many patient registries require duplicate entry of information, leading to inefficient use of providers’ time. Health care providers are not compensated for their time dedicated to the administrative requirements of the registry, which acts as a deterrent to participating in such REMS, particularly if the process is cumbersome.

Well-designed patient registries could support high-quality patient care, according to participants. In some instances, health care providers have supported the use of state prescription drug monitoring programs, which are used by many states to track patient prescriptions for controlled substances. Providers anecdotally reported that such systems, when used appropriately, could be beneficial because they provide a useful tool to support safe and appropriate practice and they do not require providers to spend large amounts of uncompensated time managing the system. Participants recommended exploring opportunities for coordination with existing state tools and programs; however, FDAAA does not specifically grant authority to do so.

Participants expressed that a desired feature for a patient registry is access to the registry at the point of care. They reasoned that this design would make the process more efficient and decrease the likelihood that important steps in the process would be overlooked. For example, if the provider forgets to ask the patient a question for the registry, it becomes much more difficult and time consuming to go back and get the information from the patient than it would be if the provider had worked through any questions at the point of care. Furthermore, participants recommended that patient registry systems be interoperable with other patient data systems.

Finally, participants cautioned against a system that is only accessible to patients via the Internet. Many patients lack reliable Internet access or may not be computer literate.

Prescription stickers

Stickers placed on written prescriptions by prescribers to communicate information to pharmacists have been used for various programs including one version of the risk management system for isotretinoin. In this case, stickers were placed on written or hardcopy prescriptions by the prescriber to indicate to the pharmacy that the conditions required for prescribing isotretinoin had been met. However, stickers posed administrative challenges for prescribers; for example, providers were unable to issue a prescription if they ran out of the stickers.

Looking to the future, participants recognized that electronic prescribing (e-prescribing) cannot accommodate stickers. As an alternative, they recommended a system that allows electronic communication between prescriber and pharmacy to indicate when aspects of the REMS program have been satisfied. (A physical back-up option could be used in situations where e-prescribing is not viable.)

Recommended strategies for standardizing REMS

Participants explored various aspects of programs that could be applied systematically to all REMS to reduce the variation of systems and processes. Although each medication or class of medications requiring a REMS will have unique safety issues, participants agreed that it would be possible to create a common framework so REMS programs have some universal similarities that could guide manufacturers as they develop individual programs and facilitate implementation of the programs by the health care system. This proposed framework will be particularly critical given that the number of medications requiring a REMS will likely continue to rise. The increasing use of REMS is expected to come from both new safety information about currently available medications and the potential that many medications in development could require a REMS.

Participants generally agreed that strategies deemed appropriate for medications with limited uses in a small group of patients would be unmanageable if applied to medications with broader uses in larger populations. This concern was particularly evident for REMS that are time consuming to implement. Wide-scale use of such programs could impede the health care system and create numerous barriers to care, which could extend beyond the medications covered by the REMS. Participants recommended involving front-line providers early in the process of developing a REMS to support creation of pragmatic, feasible systems. Streamlining the infrastructure of the REMS, including centralizing REMS functions and data management, could reduce overall costs by eliminating duplication of similar functions by multiple entities and reducing training and oversight costs.

Creation of REMS levels

Participants supported the concept of creating different levels or tiers of REMS, analogous to the Schedule I through V system used for controlled substances. The level would be based on the required intensity needed to mitigate the risk for which the REMS is designed and would automatically communicate the required REMS components to the health care provider. Participants discussed various options for defining REMS levels.

One option would create different categories based on the severity of risks that the REMS is designed to prevent. Standard REMS components could then be selectively used based on the required intensity of the REMS. For example, the lowest level of the system could include REMS that are composed of a MedGuide and Dear Health Care Provider letter, whereas use of restricted distribution programs would be reserved for only
the most intensive REMS level (i.e., REMS designed to mitigate the most serious medication risks). Such a system may help support the goal of ensuring that the most restrictive elements, which create the greatest barriers, are limited to only absolutely necessary cases.

Another option discussed by the group would be to structure REMS programs according to the type of event the program is designed to mitigate. For example, specific systems could be designed for REMS intended to minimize prenatal exposure to a medication. All REMS designed to manage a medication with known teratogenic risks would be designed to use similar processes.

The group explored options for modifying REMS elements for different patient populations (e.g., institutionalized patients in long-term care settings, hospitals, or other practice settings). For example, REMS tools designed to mitigate risks for individuals to whom the medication was not originally prescribed could be modified to use less stringent requirements for institutionalized patients because these risks may be lower in such settings. Furthermore, the REMS system should have strategies in place to meet the needs of patients who have cognitive impairment or are otherwise incapable of providing informed consent or complying with other REMS requirements.

REMS data management

Participants recommended the creation of a standardized, system-based process for managing REMS data. They stressed the need for seamless interoperability of systems that are user-friendly, automatic, workable at the point of care, and capable of being integrated into the existing workflow for prescribers and pharmacists with minimal impact on efficiency. Furthermore, system standardization should reduce the training and administrative oversight investments that are currently required of each prescriber and pharmacy to ensure compliance with diverse systems.

The design of REMS data management systems should include interoperability with the health information technology (HIT) infrastructures currently used by pharmacy and medical practices, recommended participants. For example, a preferred system for REMS would allow data fields to be populated automatically from existing HIT records to avoid redundant data entry. Participants reported that some current software and systems can automatically retrieve appropriate patient information (e.g., patient identifiers, diagnosis codes, current medications) from a practice’s existing electronic records.

Participants noted that electronic aspects of the REMS system could be designed to support provider compliance with the logistical procedures to prescribe or dispense the medication. However, it would need to be readily accessible by all involved parties, including prescribers, pharmacists, and patients. Participants observed that the REMS system could potentially be integrated with the system for third-party claims adjudication at the pharmacy, which currently manages limited patient and prescription information electronically. Participants expected that use of such systems could improve workflow efficiencies and limit barriers to provider participation.

With national HIT standards for managing data, e-prescribing, and electronic health record (EHR) systems still evolving, the participants envisioned the evolution of an EHR system that would allow prescribers and pharmacists access to input and read data related to a REMS and to other health care issues. Current systems may need to be upgraded or revised but could potentially be used for building a new REMS system. Conversely, the REMS system will need to be flexible and interoperable with evolving HIT systems. However, participants noted that even in the future, a REMS system should not solely rely on HIT systems. A paper-based option must be available for any health care providers who have not adopted the necessary electronic technology. Finally, participants cautioned against excessive use of system alerts to support REMS requirements. They noted that providers may not closely read every alert owing to overuse of alerts causing “alert fatigue” in the use of existing systems for e-prescribing, EHR, and prescription processing.

Participants also stressed that incorporation of any REMS program requirements into existing systems must allow the REMS to be managed as part of routine prescription processing. This structure would avoid requirements for pharmacists to check REMS prescriptions through multiple unique and/or proprietary systems that are independent of the typical workflow for prescription processing. (Use of multiple unique systems poses an administrative burden, is inefficient and inconsistent, can lead to compliance challenges and inadvertently overlooking REMS requirements, disrupts workflow, and requires substantially more administrative oversight to ensure compliance.)

The necessity for strategies to manage blocks in the system to accommodate individual patient needs (e.g., a vacation occurring at the same time as a required laboratory test) or emergency situations also was discussed. Participants stressed that the system should be able to accommodate various patient situations where access to a medication may be significantly delayed because REMS requirements are not being met. A follow-up process for emergency prescriptions should be in place to record and track the causes of the occurrence and to allow for subsequent contact with other health care providers and the patient as appropriate.

Participants discussed the possibility of using a patient card program that could link into a REMS system as an option for managing data related to the REMS. If a card system were used, using a standardized system so all such cards would be managed in the same manner would be essential. Participants remarked that challenges regarding the cards include issues associated with both prescriber management of the cards (e.g., inventory issues) and patient management (e.g., lost cards).

The REMS system could include a central data repository for information that allows access and input across multiple practice settings by prescribers and pharmacists. For example, if a REMS requires laboratory monitoring, the REMS system could interface with the EHR from the laboratory with the prescriber’s office and the pharmacy.

Participants also called for centralized availability of information related to a REMS, so all users of the system (i.e., patients and health care providers) would know where to locate
such information. FDA currently maintains a website listing all medications that have a REMS and the elements of those REMS at [www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm111350.htm](http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm111350.htm).

Meeting participants suggested improvements that could be made to the existing FDA REMS webpage to make it more user friendly, such as including links to all of the program elements (e.g., access to printable MedGuides for REMS that require them) and providing details about the specific steps required for a health care provider to prescribe or dispense the medication. The National Cancer Institute clinical trials website ([www.cancer.gov/clinicaltrials](http://www.cancer.gov/clinicaltrials)) was suggested as a model of a central repository of information from diverse sources. Furthermore, awareness among providers of the existing FDA REMS webpage is limited. Participants suggested that FDA consider setting up a dedicated website such as “www.REMS.gov” and work with stakeholders to create an educational campaign to support awareness of FDA’s resources.

**User identification.** Current REMS systems often require health care providers and patients to have different personal identifiers for each system they use. Participants discussed strategies for identifying unique users (patients, prescribers, and pharmacists or pharmacies) that could be standardized for all REMS. Such a system is needed to differentiate among individuals for cases when multiple patients with the same name (e.g., John Smith) use a medication that is covered by a REMS. Similar issues exist for health care providers, who also may have identical names and require a strategy for unique identification.

The concept of developing national unique patient identifiers was discussed but was considered impractical by the group. Many current systems designed for identifying patients rely on combining patients’ names with their dates of birth or social security numbers, which are potential options for a REMS.

For providers, participants supported building on the existing identification infrastructure and using the National Provider Identifier (NPI) numbers to track provider education and eligibility to participate in REMS programs if required. The development or use of an existing process (e.g., NPIs) for user identification within a REMS system will need to take into account how to manage students, residents, and health care providers who work in more than one location.

The provider identification system will need to consider whether to use identifiers for individuals (e.g., NPIs) or to assign identifiers at the group practice or pharmacy level. Participants mentioned that in busy office practices, prescribers often instruct nurses or front desk personnel to login to manage REMS systems. Allowable uses of user identification by office staff will need to be clarified to make implementation more feasible.

**Risk management education**

Participants explored several areas of education surrounding risk management and REMS. These areas included the need to (1) address societal perceptions about medications and risk, (2) educate individual patients about appropriate use of medications covered by REMS, and (3) educate health care providers to support appropriate use of covered medications and compliance with risk management programs.

**Public education campaign.** Participants expressed concern that the public lacks adequate general knowledge about balancing the benefits and risks of medications and that this situation presents a serious, broad societal issue that needs to be addressed. They noted that many patients have a low tolerance for medication-related risks and/or assume that medications are “safe” because they have FDA approval. Additionally, patients may have limited opportunities to discuss the risks and benefits of each of their medications with a health care provider (or may not realize that they should be discussing these issues with their health care provider), which can contribute to poor general understanding of appropriate medication use. Patient-specific risk communication may be limited because it can be time consuming and is often uncompensated.

Because conversations with health care professionals about medications and risk may be limited, participants noted that patients often seek information from other sources (e.g., the media) that tend to feature risks of medications without addressing the importance of balancing risk with benefit. In addition, participants commented that patients are increasingly obtaining information about their medications and disease states from Internet sources, including social networking sites and blogs, rather than more credible, authoritative sources. As a result, patients are often accessing information of questionable accuracy, which may lead to poorly informed decision making about available health care options.

Participants recommended a national public education campaign to discuss issues surrounding the balance between benefit and risk of medications and to explain how REMS can be used to influence this balance. They suggested that stakeholders, including FDA, work with the Centers for Disease Control and Prevention (CDC) or other national organizations involved in health promotion to spearhead such a campaign. Participants strongly urged that public education campaigns be continually reinforced (e.g., through individualized patient education) to produce a widespread change in patient perceptions.

In addition, participants recommended that if a REMS is added to a product already available on the market, the associated public education campaign could be designed to make patients aware of impending requirements to change their behavior and manage expectations accordingly. Such communications will be important to help frame public perceptions of REMS as risk management programs to improve patient care and safety.

**Individual patient education.** Participants stated that even though individualized discussions about the different risks and benefits of medications are limited in current practice, these discussions are often necessary to support patient understanding. Participants agreed that face-to-face patient education is the most effective method for educating individual patients about their medications and is preferred to relying on written education for communicating information to patients.
Ideally, patient education would be provided by the prescriber at the point of prescribing and reinforced by the pharmacist at the point of dispensing. Alternatively, the education could be delivered in a medical home model in which a pharmacist works in a prescriber’s office or in collaboration with the office to provide education in conjunction with the prescriber. A pharmacist-provided MTM service consultation was supported as an option for providing REMS-related patient education. Participants stressed that, if a specific patient education component is required by a REMS, compensating providers for their time required to deliver the education will be critical.

Participants commented that face-to-face education helps to establish a trusting relationship between the patient and the health care provider, which can facilitate ongoing monitoring and follow-up and improve the quality of care. Face-to-face education also allows the opportunity to address any patient misperceptions and allows the pharmacist or other health care provider to tailor the education to the patient’s level of understanding and use strategies to assess and support patient comprehension. When such processes are in place, serious adverse events can be averted, resulting in cost savings. Education could be telephonic if a face-to-face visit is not practical. (The option of telephonic consultation may be needed for patients who receive REMS medications from mail order pharmacies or have limited mobility.)

Participants recommended that patient education should include discussion of medication safety issues, strategies for optimizing therapy, and patient responsibilities for complying with the REMS. The education should be individualized to meet the patient’s unique needs and care plan and provide the patient with information necessary for complying with the care plan. Patients should receive a list of specific action items, including where to go for more information and when to contact their health care team.

Furthermore, noted participants, if patients will be held accountable for complying with various aspects of the REMS, clearly communicating these requirements to them will be crucial. Patient requirements should be provided to them in an action plan during face-to-face education. For example, if patients are expected to store their medications in a certain manner, this must be clearly communicated. Education about patient responsibilities must be provided carefully to ensure that patients do not feel burdened by the process; rather, education should empower patients and help them feel that they are active partners in their own care.

Patient education and other REMS requirements should also consider issues for patients who have multiple residences and those who may transition among community, hospital, assisted living, and other institutional settings. As with provider education, a standardized, system-based approach could track patient receipt of required education and allow review of this information by providers. Furthermore, a strategy that allows modification of educational requirements should be developed for patients who have cognitive impairments or other barriers to full participation in their health care (e.g., patients residing in skilled nursing homes).

Participants suggested that education about a REMS for a newly approved medication might be implemented differently than one for a medication that had previously been on the market without a REMS. In the latter situation, the introduction of a REMS requires patients and providers to change established behaviors, whereas for a new medication, no one has an expectation based on experience of how the medication should be accessed. If a patient is well controlled on a medication, a process for maintaining the patient while the REMS is phased in could be implemented. Otherwise, patients may arrive at the pharmacy to have their prescriptions filled only to be denied the medication and experience therapy interruptions that could be detrimental to their health.

Compensation to providers for their time delivering the service is an important aspect for the face-to-face component of a REMS to be feasible, stressed participants. Participants universally agreed that face-to-face educational strategies are currently underused because no financial incentive to provide them exists. Furthermore, failure to appropriately value the time health care providers spend administering REMS programs will lead to low provider participation and barriers to patient access. Participants noted that because manufacturers are responsible for creating and maintaining the REMS, compensation for services provided by health care providers to implement the REMS could potentially be provided by the manufacturers and facilitated through user fees to a centralized entity.

**Provider education.** Participants underscored that health care provider training will be an essential component of new REMS systems. Recommendations for the content included a REMS program overview (including the risks to be mitigated), details about how to implement the required elements of the REMS, patient care plans and education strategies, and responsibilities of the prescriber, pharmacist, and patient. Overarching concepts in disease management could be included, not as a thorough disease state review but as a means for addressing the risk or outcomes the REMS is designed to mitigate and for explaining how the REMS could be used to support improved quality of care. Higher-level clinical and therapeutic content could be required by specific REMS, whereas education for other REMS could primarily focus on program logistics.

Content could be tailored to individual practitioner needs. A set of core elements could be developed, with flexibility to add sections to accommodate special populations, noted participants. For example, long-term care providers could elect to participate in a section of training devoted to incorporating the REMS in institutionalized settings, but primary care providers would not be required to participate in that section of training.

The design of educational components of REMS will need to account for aspects of implementation in teaching hospitals and other educational health care systems, noted participants. The process in these settings will need to accommodate prescribers (including medical students and residents who may be involved in the prescribing process) to ensure that the system works for patients in the institution or transitioning between settings.
Education about REMS should be provided in a manner that supports participation and minimizes the burden on busy health care practitioners. Participants urged that provider education required by a REMS should be accessible online, on demand, and allow users to complete the education in small segments. Adult learning strategies, including active learning and self-assessment tools, could be incorporated throughout so users could assess their own knowledge before taking the formal program assessment. The system should allow for interactivity with experts (e.g., live webinars, chats, question-and-answer boards). Educational components would need to be designed to accommodate quick updates in the event of a REMS system change, new safety information, or new medications added (for REMS designed to affect a drug class).

Participants also suggested that required REMS educational programs be linked to the proposed central REMS information repository to facilitate accessibility to potential users. Tracking of completion of educational requirements and any other REMS requirements for certification could be conducted through the repository by individual providers.

Although participants discussed the option of requiring education for license renewal as a mechanism to support widespread participation and reduce the impact on patient access, they voiced opposition to this idea. Their concerns surrounded the possibility of setting a precedent that could lead to the creation of dozens of new education requirements, which could be overly burdensome for providers and the license renewal process. If a REMS is developed for a medication used by a large population, education and/or certification should be available to any willing provider. Restrictive measures should be considered only for medications used to treat small, unique, specialized populations.

Participants recommended that verification of education requirements could be tracked on the provider level using NPI numbers. As an alternative for pharmacists who are not required to have NPIs, the tracking could occur on a pharmacy level using the pharmacy NPI. Tracking should use a standardized system that includes training requirements for all REMS programs. Such a centralized system could track which training components were completed, if required, and which still need to be addressed for each unique user.

The group recommended that training programs be created and provided by accredited organizations that offer continuing professional education to health care providers. They recommended that various requirements could be centrally established for the REMS education to allow for consistency. Providers of continuing education (e.g., continuing medical education, continuing pharmacy education) could choose to create training programs that meet those requirements. The overall educational content, as well as specific training programs, should be evaluated by a variety of stakeholders who will be affected by the REMS. Requirements for program review also should be determined collaboratively.

Pilot testing of REMS systems

Participants acknowledged that limited data are available to guide the development of new REMS systems, regarding both the effectiveness of existing programs at preventing risks and their unintended consequences. Therefore, they supported the suggestion that new REMS strategies be pilot tested before implementation on a national scale.

A pilot program could be implemented in a selected market segment, with predefined outcomes to be monitored, to determine real-world effectiveness of the planned REMS system. Ideally, the pilot should assess whether the REMS achieves the desired outcomes and whether it produces unintended consequences and burdens on the health care system. Participants also noted that it would be essential to have practicing pharmacists, prescribers, and patient advocates involved during development and evaluation of the pilot process.

Participants generally agreed that questions remain regarding funding for REMS pilot programs. However, they suggested that manufacturers could potentially fund the pilot indirectly through user fees to a central entity. Participants recommended consideration of user fees to FDA to pilot test REMS and expressed that a reliable source of funding must be established to ensure ongoing monitoring occurs.

Identifying outcomes of the REMS system

Although there will be differences in the specific outcomes that will be tracked by individual REMS, several issues can be addressed in a systematic fashion. Participants stated that it is essential to prospectively identify the specific risks each REMS is designed to mitigate, the associated outcomes to be measured, and the strategies for measurement. Participants agreed that stakeholders from multiple constituencies should be involved in assessing why a component of a REMS was or was not successful in mitigating risk.

Participants stressed that outcomes must be achievable and acknowledged that REMS systems cannot eliminate 100% of the risk associated with a medication. Furthermore, some REMS are designed to mitigate adverse events that could potentially occur for a number of reasons, particularly in patients with multiple disease states. Thus, some occurrence of adverse events among patients using the medication should be expected regardless of any REMS system. Ideally, baseline data would be established before the REMS is implemented to accurately evaluate the impact of the REMS.

Monitored outcomes may include both those that affect the patient and those that impact other individuals. If the REMS is designed to minimize the incidence of a single serious adverse event associated with the use of a medication, tracking the impact of the REMS on the incidence of that event is relatively straightforward; however, determining which components of the REMS were responsible for the impact may not be possible. On the other hand, if a REMS is designed to address behaviors of individuals other than the patient or risks based on population-level data, accurately determining the overall impact of the REMS or the effectiveness of individual REMS tools to mitigate such risks is much more difficult.
Participants remarked that a well-designed REMS could not only reduce specific adverse events but also improve other aspects of quality of care. They recommended use of systems to assess and report on both positive and negative outcomes of a REMS. They suggested use of quality-reporting measures that would be linked to REMS development and implementation to support quality of patient care and lead to more educated, empowered patients. Monitoring for unintended consequences of the REMS was also considered crucial by participants. Such consequences could include shifts in prescribing patterns that result in greater use of non-REMS medications that may not be as therapeutically appropriate and changes in pharmacy stocking of medications covered by the REMS. To monitor for such outcomes, planned evaluations could track the rates of prescribing and adverse events associated with other medications that may be used as alternatives to medications covered by the REMS. In addition, patient attempts to access medications outside legitimate distribution channels should be monitored.

Finally, participants concurred that evaluation of REMS that require health care provider certification and training should include an assessment of the proportion of eligible providers who participate in the training and prescribe or dispense the medication.

**Table 2. Recommendations for creating a standardized REMS system**

<table>
<thead>
<tr>
<th>Topic</th>
<th>Recommendation</th>
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<tbody>
<tr>
<td>Balance</td>
<td>The need to control medication risks must be balanced against the need to maintain access and affordability.</td>
</tr>
<tr>
<td>Standardization</td>
<td>REMS should have a standardized, system-based process that is user-friendly, seamless, and integrated into the workflow of prescribers and pharmacists (ideally as a software function that operates in the background). The system could include a central information repository that allows access and input by prescribers and pharmacists.</td>
</tr>
<tr>
<td>REMS levels</td>
<td>The REMS system could use various levels or tiers based on degree of intensity and the types of risks being targeted (e.g., REMS level 1 would be the most restrictive, whereas REMS level 5 would be the least restrictive). Products placed on more restrictive tiers would require more REMS components or education.</td>
</tr>
<tr>
<td>Public education</td>
<td>A public relations campaign should be implemented to educate the public about REMS and the balance between medication risks and benefits.</td>
</tr>
<tr>
<td>Individual patient education</td>
<td>When required by a REMS, patient education should ideally be provided face to face or could be provided telephonically. Education should occur both at the point of prescribing and at the pharmacy where the pharmacist (the medication expert) would reinforce the education that the patient should have already received from the prescriber. A pharmacist-provided medication therapy management service consultation could be used as a mechanism to provide this patient education. Written educational materials can be used to supplement the education, but should not be the only form of education. Face-to-face education and additional administrative time dedicated to managing the REMS must be compensated for any system to be practical.</td>
</tr>
<tr>
<td>Provider education</td>
<td>Provider education should be accessible to any willing provider and accommodate the needs of practitioners in all practice settings. It should focus on the REMS and the event(s) the REMS is designed to mitigate. REMS education for providers should also include program logistics and requirements for prescribing and dispensing the medications. General education about the disease state treated by the medication should be limited to a brief overview and not be the focus. Participants recommended that the education be provided by accredited providers of continuing education.</td>
</tr>
<tr>
<td>Pilot testing</td>
<td>Before implementation, a pilot program of a REMS that measures real-world effectiveness, not just theoretical efficacy, should be performed. In addition, practicing prescriber and pharmacist input should be used early on during the design of any REMS program.</td>
</tr>
<tr>
<td>Data management</td>
<td>The system for managing REMS data should be user-friendly, seamless, automatic, and integrated into health care providers’ existing workflow to support efficiency and compliance. Ideally, the system would interface with health information technology infrastructures used by pharmacy and medical practices.</td>
</tr>
<tr>
<td>Outcomes monitoring</td>
<td>Outcomes of REMS must be prospectively defined and monitored for effectiveness at mitigating the identified risk(s); an independent organization could be considered for such a role in collaboration with FDA and drug manufacturers. Monitoring needs to include potential unintended consequences of REMS (e.g., limiting patient access because of prescriber/pharmacists lack of participation in a REMS program, shifting prescribing patterns to non-REMS medications that may be less therapeutically appropriate). Outcomes should also capture reasons why a REMS was or was not successful.</td>
</tr>
<tr>
<td>Quality of care</td>
<td>A cross section possibly exists between REMS and quality measures. Systems should be designed in a manner that supports improved quality of care. Outcome monitoring should be designed to support this goal.</td>
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</table>

Abbreviation used: FDA, Food and Drug Administration; REMS, risk evaluation and mitigation strategies.
Participants agreed that pilot testing the effect of the REMS on desired outcomes would be essential. However, despite efforts to design the best system possible at the outset, data should be collected on an ongoing basis to allow for continuous quality improvement. Such monitoring also can be used to support program modification if evidence of unintended consequences arises.

Data sources for outcomes monitoring

Participants noted that REMS systems could use several existing data sources, including the AERS and MedWatch systems, to assess program outcomes. In addition, FDA’s Sentinel Initiative is an active surveillance system for monitoring drugs, using electronic data from multiple sources. This system, which draws on existing data to actively monitor the safety of medical products continuously and in real time, could be used to assess REMS outcomes.

Exploring opportunities to involve the Reagan-Udall Foundation in REMS outcome monitoring was another option suggested by participants. (The Reagan-Udall Foundation is a nonprofit organization created by FDAAA to identify and address unmet scientific needs in the development, manufacture, and evaluation of the safety and effectiveness of FDA-regulated products, including postmarket evaluation.) This organization could independently pool resources of stakeholders to examine the impact of REMS. Participants also recommended exploring options to have outcomes monitoring performed by the Agency for Healthcare Research and Quality (AHRQ). AHRQ aims to improve the quality, safety, efficiency, and effectiveness of health care.

Large national surveys could be useful for outcomes monitoring. Existing options discussed by participants include the CDC’s Behavioral Risk Factor Surveillance System, which is the world’s largest ongoing annual telephone health survey system. A second option is the National Health and Nutrition Examination Survey, which is a study designed to assess the health and nutritional status of adults and children in the United States. This survey is unique in that it combines interviews and physical examinations. Such surveys could be used to look for more global impacts of REMS systems.

Insurance companies could also be involved in tracking outcomes data. They maintain extensive databases of health care use and have a stake in promoting improved outcomes. In addition, various national organizations could enter into public/private partnerships to conduct surveys targeted to specific outcomes both before and after REMS implementation. Other national systems that track event data should be explored.

Additional potential data sources for outcomes monitoring suggested by participants include pharmacy and practice-based research networks. (These networks are groups of practices, devoted principally to the care of patients, that also are committed to partnering with academicians to conduct research in practice.)

Finally, participants cautioned that although national data can be a useful tool, performing subpopulation analyses to assess the impact on various groups will be important. For example, a REMS could impact patient access differently in rural and urban areas.

Concluding recommendations

Consensus on several themes emerged during the stakeholder meeting on designing a well-balanced REMS system. Participants observed that the lack of a system-based, standardized, efficient REMS system creates confusion, burdens the health care system, and creates barriers to patient access to medications. These burdens are likely to worsen as more REMS are developed in coming years and may impede the health care system’s ability to use medications appropriately.

Participants agreed that development and implementation of a systematic, standardized process for REMS programs is essential to minimizing the impact on patient access and the impact on the health care system and, ultimately, to improving the quality of care. Recommendations for moving forward included creating various REMS levels, using a public education campaign, providing face-to-face individualized patient education when needed, streamlining processes and requirements for provider education, creating a data management system that is interoperable with current systems, developing a robust system for outcomes monitoring, and pilot testing REMS programs and seeking early input from health care providers to support real-world effectiveness. Participants’ recommendations are summarized in Table 2. Participants advised that these features would be necessary for creating a system that enhances patient safety, promotes quality of care, and is feasible for the health care system.

Appendix. Participants in the APha Stakeholder Meeting on Risk Evaluation and Mitigation Strategies

<table>
<thead>
<tr>
<th>Name</th>
<th>Affiliation</th>
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<tbody>
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<td>Tom Clark, BPharm, MHS, CGP</td>
<td>American Society of Consultant Pharmacists Foundation</td>
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<td>Leslie Greenberg, RN, MSN, OCN</td>
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<tr>
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<td>Anita Martinez, BPharm, CDE</td>
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References


