



**Statement of the
Pharmaceutical Research and Manufacturers of America
before the
Institute of Medicine
Committee on Conflict of Interest in Medical Research, Education, and Practice**

March 13, 2008

The Pharmaceutical Research and Manufacturers of America (PhRMA) appreciates the opportunity to offer testimony to the Institute of Medicine (IOM) Committee on Conflict of Interest in Medical Research, Education, and Practice. In 2007 PhRMA companies spent over \$44.5 billion in the search for new therapies and cures. Our companies' relationships with partners are two-fold: to develop new therapies that have a positive impact on public health and also to work with healthcare professionals to benefit patients and enhance the practice of medicine. PhRMA appreciates the effort that IOM is making to understand the nature of conflicts of interest in both the research enterprise and in post-approval interactions between and among healthcare professionals.

Introduction

Potential conflicts of interest are ubiquitous in research and medical practice and may arise not only in the context of financial funding of research or holdings by scientific and clinical investigators, but also in a variety of other interactions between industry and physicians. As discussed in Section I, industry, academia, practitioners, and the government each play important roles in managing conflicts of interest through transparency, disclosure, training and education, as well as enforcement of regulations.

Even as we strive to prevent conflicts, however, it is equally important to remember that interactions between industry and physicians/scientists in academia have been and will continue to be critical to medical advances that benefit the public health. Similarly, interactions between industry and physicians after medicines are approved provide benefits in the form of opportunities to exchange valuable information about the



appropriate use of medicines. Various industry-physician interactions are governed by scientific norms, peer review, laws, regulations and industry codes of conduct. Whatever benefits certain steps may arguably achieve in terms of reducing the risk of conflicts of interest should be weighed against the likelihood that arbitrary interference or undue restrictions of industry-physician interactions threatens to result in suboptimal treatment of patients and could ultimately compromise both patient safety and the search for life-saving and life-enhancing therapies. Society and history ultimately will judge both physicians and industry on our ability to serve the needs of patients, and this presents both challenges and opportunities as we work together to improve patient care.

Over the past seven years PhRMA has completed several projects leading to the publication of important guidances to our member companies in connection with both clinical and marketing activities.¹ These efforts demonstrate the serious commitment of America's pharmaceutical research companies to the responsible conduct of clinical research and post-approval interactions with healthcare professionals.

PhRMA's *Principles on Conduct of Clinical Trials and Communication of Clinical Trial Results* focus on four key areas:

1. Protection of research participants,
2. Conduct of clinical trials,
3. Objectivity in research, and
4. Appropriate disclosure of clinical trial results.

These principles reinforce industry's commitment to appropriate conduct – including the management of conflicts – in the research process.

The *PhRMA Code on Interactions with Healthcare Professionals* (PhRMA Code) addresses industry-practitioner interactions with respect to marketed products and related pre-launch activities. The Code was developed to help assure that company relationships

¹ See PhRMA Principles on Conduct of Clinical Trials and Communication of Clinical Trial Results (2002 and 2004) (attached as an appendix to this statement); PhRMA Code on Interactions with Healthcare Professionals (2002 and 2004) (attached as an appendix to this statement).



with healthcare professionals are focused on informing healthcare professionals about products, providing accurate scientific and educational information, and supporting medical education in appropriate ways. Pharmaceutical company educational efforts with healthcare professionals have important public health benefits, which are discussed in Section II.

PhRMA's testimony focuses on two principal areas, those associated with research issues, including regulatory submissions to the Food and Drug Administration (FDA) and secondly, activities that take place after a drug is approved for use in patients.

I. Research Issues

There is a long history of industry support for basic research in the sciences.² Industry, academia, and government have developed important mechanisms to preserve the integrity of sponsored research. Industry funding can take the form of support for graduate or post-graduate fellowships, unrestricted grants to universities, or sponsored research on either specific or broad areas of research interest.

A significant amount of clinical research into the development of new therapeutics and vaccines is sponsored by American pharmaceutical companies. This research takes place at medical school hospitals and community settings. The independence of both individual investigators and the institution is paramount. Typically, a pharmaceutical company provides the funding and clinical grade investigational product; the physician/investigator and parent institution share the responsibilities for the direct conduct of the research. This includes appropriate Institutional Review Board (IRB) review and approval and administration of informed consent to patients enrolling in the trial. *The Principles on Conduct of Clinical Trials and Communication of Clinical Trial*

² "Partners in the Research Enterprise," Alfred P. Fishman, Albert V. Glowasky, Sheldon Hackney, Thomas W. Langfitt, editors; University of Pennsylvania Press, 1983



Results discuss the importance of independent review as well as appropriate compensation to patients and clinical investigators for their service.

Human clinical trials that evaluate safety and efficacy are the most critical step in the drug development process, and consequently, the FDA is closely involved in clinical trial design and review of data. Extensive discussions are held with the FDA leading to agreements on clinical trial design and the type of data that will be required to support licensure. Clinical trials on a specific drug are conducted at multiple research sites, many of these major American medical schools. Multi-center clinical trials markedly reduce the potential for bias from a single clinical investigator. Most drug development today takes place over multiple geographical regions, employing numerous clinical investigators. The involvement of the FDA, as well as many different medical centers and IRBs helps to manage conflicts of interest in such trials.

Transparency and disclosure are cornerstones of PhRMA's clinical trial guidelines and FDA regulation and policy. FDA regulations require that clinical investigators disclose relevant financial holdings, if the holdings exceed a certain minimal threshold, and then report them to the FDA when the license application is submitted.³ In addition, company sponsors utilize quality assurance units that are separate and independent from the clinical research group to audit trial sites. Sites are typically visited every 6-8 weeks to assure good clinical practice (GCP) compliance, check on data quality and help to assure that relevant procedures regarding the conduct of the trial are being followed. It is not uncommon for academic investigators to question the need for such frequent audits, but when so much is at stake, data quality is paramount. In addition, clinical data and trial sites are subject to audit by the FDA.⁴ PhRMA has sponsored workshops on fraud detection, inviting FDA to participate in sessions on how companies can better uncover fraudulent investigators.

³ See 21 C.F.R. part 54.

⁴ See 21 C.F.R. 312.58; 21 C.F.R. 312.68.



In addition, FDA's regulations attempt to manage potential conflicts of interest in FDA's own review process.⁵ The Agency's over 2,500 talented and highly dedicated drug review employees involved in drug product reviews cannot have any financial interests in companies that the FDA regulates.

Frequently FDA utilizes expert advisory committees consisting of leading practitioners and academics to provide scientific input on products that are or have been reviewed by the Agency. These committees also are used to assist in the development of various guidance documents designed to facilitate drug development. Members of advisory committees have long been subject to a number of conflict of interest laws.⁶ In 1997 section 505(n)(4) of the Food and Drug Modernization Act (FDAMA) introduced new administrative conflict of interest and associated waiver considerations. Specifically, absent a waiver, a committee member may not vote on any matter regarding the clinical investigation or approval for marketing of a drug if the member or the member's immediate family could gain financially from the committee's recommendations. These provisions are set forth in an FDA Guidance to Industry.⁷ The Agency is also finalizing a Guidance on disclosure of conflicts of interest.⁸ Advisory committee deliberations and voting are open and a matter of public record. Regardless of what the advisory committee may recommend, the final decision on whether to approve a drug and the precise language of the product label rest with the FDA.

Another method of managing the risk of conflicts of interest in research activities is to establish a transparent clinical trial process that extends from registration of clinical trials to the appropriate disclosure of trial results.⁹ In 2002, PhRMA noted the critical importance of timely communication of meaningful results of controlled clinical trials of

⁵ 21 C.F.R. part 19.

⁶ *See, e.g.*, 18 U.S.C. 208

⁷ Guidance to Industry – Advisory Committees: Implementing Section 120 of the Food and Drug Modernization Act, accessed at: <http://www.fda.gov/cder/guidance/2117fnl.pdf>

⁸ Draft Guidance on Disclosure of Conflicts of Interest for Special Government Employees Participating in FDA Product Specific Advisory Committees, accessed at: http://www.fda.gov/OHRMS/DOCKETS/98fr/02d-0049_gdl0001.pdf

⁹ Alan Goldhammer, "Transparency and Validity of Pharmaceutical Research," in *Clinical Trial Registries: A Practical Guide for Sponsors and Researchers of Medicinal Products*, Mary Ann Foot, ed; Birkhäuser, 2006



marketed products or investigational products that are approved for marketing regardless of outcome. In 2004, PhRMA established a website, www.clinicalstudyresults.com, where pharmaceutical companies could post information on marketed products. This information includes the most current FDA-approved drug labeling, a bibliography of relevant peer-reviewed publications, and summaries of all unpublished studies. Since opening the site in October 2004, companies have posted information on almost 500 drugs, demonstrating PhRMA companies' commitment to transparency for patients and healthcare providers. This activity was initiated three years prior to the recent Food and Drug Administration Amendments Act of 2007, which now mandates that the National Library of Medicine establish a government-run clinical trial results website.

PhRMA has also been active on issues related to registration of clinical trials. In 1997 when FDAMA was passed, PhRMA supported section 113 of the legislation that resulted in the information program on clinical trials for serious or life-threatening diseases. This important initiative provides patients and healthcare providers with important information on clinical trials of interest.¹⁰ Although FDAMA section 113 only called for the registration of a limited number of clinical trials, there was emerging consensus that all hypothesis testing trials regardless of indication should be registered. The first editorial on this subject appeared under the auspices of the International Committee of Medical Journal Editors (ICMJE) in 2004.¹¹ In 2005, PhRMA proactively suggested that member companies register all hypothesis testing trials, going beyond the FDAMA requirements.¹²

II. Post-Approval Activities

¹⁰ Information is readily available at the website: <http://clinicaltrials.gov/> that is run by the National Library of Medicine.

¹¹ Accessed on February 19 at: http://www.icmje.org/clin_trial.pdf Three subsequent updates (2004, 2005 & 2007) to the ICMJE policy are at: <http://www.icmje.org/>

¹² http://www.phrma.org/publications/policy_papers/phrma_clinical_trial_registry_proposal/ accessed on February 20, 2008



Just as pharmaceutical companies, government, and healthcare professionals work in various ways to manage the risk of conflicts of interest in the clinical setting, they also strive to manage potential conflicts that may arise in interactions that follow the FDA's approval of a new medicine or a new indication for a previously approved medicine. Pharmaceutical companies devote substantial efforts to providing health care professionals with up-to-date, accurate information regarding prescription medicines, which play a significant role in healthcare. Direct communication with healthcare professionals allows pharmaceutical manufacturers to inform healthcare professionals about the benefits and risks of their products, provide scientific and educational information, support medical education, and obtain information and advice about their products through consultation with medical experts. Ethical relationships between healthcare professionals and prescription drug manufacturers are critical to the pharmaceutical industry's mission of developing and bringing to patients medicines that allow for longer, healthier, and more productive lives.

PhRMA Code on Interactions with Healthcare Professionals

PhRMA's member companies are committed to following the highest ethical standards as well as all legal requirements in their interactions with healthcare professionals. An expanded version of the PhRMA Code was adopted in 2002 to demonstrate member companies' intention of interacting with healthcare professionals for the benefit of patients and to enhance the practice of medicine. The Code starts with the fundamental principle that a healthcare professional's care of patients should be based, and should be perceived as being based, solely on each patient's medical needs and the healthcare professional's medical knowledge and experience.

The PhRMA Code sets out concrete standards that apply in particular situations. The Code, for example, states clearly that it is inappropriate for companies to provide to a healthcare professional entertainment or recreational activities, such as golf or theater tickets. Companies may provide modest meals in connection with presentations by pharmaceuticals representatives or other speakers, if the meal is conducive to the exchange of information. Similarly, companies may offer healthcare professionals



educational gifts that are primarily for the benefit of patients and are not of substantial value. The Code does not condone offering items that are of only personal benefit to healthcare professionals.

The Code allows a company to engage healthcare professionals for bona fide consulting services, provided that the company has a legitimate need for the services and compensation is based on the fair market value of those services. In certain circumstances, a company may also provide financial support for conferences and professional meetings and for scholarships that permit medical students, residents, and others in training to attend these conferences. The Code provides that a grant, consulting arrangement, contract, gift, or other benefit may never be offered to a healthcare professional in exchange for agreeing to prescribe a product.

PhRMA Code Cited by the Office of the Inspector General of the Department of Health and Human Services

Although adherence to the PhRMA Code is voluntary, the Office of the Inspector General (OIG) of the Department of Health and Human Services (HHS) has noted the Code as a positive step in a key document that provides guidance for manufacturers concerning the legal requirements that govern pharmaceutical marketing practices.¹³ The OIG is the agency within HHS that is responsible for protecting the integrity of government programs and for enforcing federal fraud and abuse laws that apply to the provision of goods and services to the government. In its Compliance Program Guidance for Pharmaceutical Manufacturers, the OIG provided its views on fundamental elements of pharmaceutical manufacturer compliance programs and principles that pharmaceutical manufacturers should consider when developing and implementing an effective compliance program. The OIG stated that compliance with the PhRMA Code is not an absolute safe harbor, but noted that compliance would “substantially reduce the risk of

¹³ See OIG Compliance Program Guidance for Pharmaceutical Manufacturers, 68 Fed. Reg. 23731 (May 5, 2003).



fraud and abuse and help demonstrate a good faith effort to comply with the applicable federal health care program requirements.”¹⁴

Lewis Morris, OIG’s General Counsel, has explained that adherence to the PhRMA Code can serve as an indicator of a company’s commitment to compliance.¹⁵ According to Morris, conduct inconsistent with the Code “indicates something about how that manufacturer is approaching its relationship to our programs and consumers.”¹⁶

The PhRMA Code also has received praise from individual federal prosecutors responsible for enforcing the fraud and abuse laws. James Sheehan, an Assistant U.S. Attorney in Philadelphia, stated at the time the current version of the Code was issued: “If people comply with this code as it is currently drafted, we are going to see, in my view, a major difference in how this industry operates, and I think a major difference in how it is perceived by consumers and physicians.”¹⁷

PhRMA Code Similar to Codes of Other Health Care Associations

The PhRMA Code is similar in many ways to the American Medical Association’s ethical opinion on “Gifts to Physicians From Industry,” which was revised just before publication of the Code.

Subsequent to the issuance of the PhRMA Code, a number of other industry associations released similar documents. AdvaMed, whose member companies develop medical devices, diagnostic products, and health information systems, issued its “Code of Ethics for Interaction with Health Care Professionals”¹⁸ in September of 2003. The AdvaMed Code incorporates many of the same principles and limitations as the PhRMA Code. A year later, the Accreditation Council for Continuing Medical Education (ACCME)

¹⁴ Id.

¹⁵ “IG Rx Compliance Guide Sets PhRMA Marketing Code as Minimum Threshold,” *The Pink Sheet*, Oct. 7, 2003.

¹⁶ Id.

¹⁷ “PhRMA Marketing Code Should Cover Preceptorships, Surveys,” *The Pink Sheet*, June 10, 2002.

¹⁸ Available at: http://www.advamed.org/NR/rdonlyres/FA437A5F-4C75-43B2-A900-C9470BA8DFA7/0/coe_with_faqs_41505.pdf.



adopted the “Updated Standards for Commercial Support,”¹⁹ which provides guidelines for providers of continuing medical education in the same spirit as the PhRMA Code. (Recent changes in the ACCME guidelines are discussed further below).

The PhRMA Code has therefore become a de facto benchmark for industry practices among both member and non-member companies. A 2003 survey found that 96 percent of industry promotional meetings and events were compliant with the Code.²⁰ Today it is common practice for pharmaceutical companies to incorporate the provisions of the PhRMA Code into their compliance programs and standard operating procedures, and often explicitly refer to the Code in these materials. Lawyers rely on the Code when advising their clients on compliance matters. In addition, the OIG requires pharmaceutical companies to have a compliance officer who reports directly to the president or CEO of the company. These compliance officers look to the PhRMA Code as a baseline in overseeing their companies’ compliance efforts.

Managing Risks of Accredited Medical Education

Pharmaceutical companies, academic institutions, and practitioners each share an interest in promoting high caliber continuing medical education that presents up-to-date, factual information about new medicines and appropriate standards of care. Likewise, all of these entities share the responsibility for managing risk of conflict of interest in the provision of accredited continuing medical education (CME) utilized by healthcare professionals to improve medical care for patients. The ACCME Standards for Commercial Support are focused on ensuring that CME providers make key decisions about their course offerings without being influenced by the commercial interest of entities that may provide funding for the course. Specifically, ACCME standards provide that the CME provider maintains strict control of matters including identification of CME needs; determination of educational objectives; selection and presentation of content; selection of all persons and organizations that will be in a position to control the content

¹⁹ Available at: http://www.accme.org/dir_docs/doc_upload/68b2902a-fb73-44d1-8725-80a1504e520c_uploaddocument.pdf

²⁰ Herman R. and Schonbachler D., *PhRMA Code: New Rules, Same Game*, Med. Educ. Meetings. Aug. 2004, at 8, 10.



of the CME; selection of educational methods; and evaluation of the activity.²¹ In addition, the ACCME standards require that CME presentations must give a balanced view of therapeutic options, including use of generic names.²² PhRMA is supportive of the ACCME's mechanisms for helping to assure the integrity and independence of CME.

III. Value of Pharmaceutical Education of Health Care Providers

Discussion about pharmaceutical company educational efforts often seems to begin with an assumption that such activities are the sole influence on prescribing decisions and dictate the medicines that are prescribed to patients. This is not the case. Generic medicines now represent 67 percent of all prescriptions filled, according to IMS Health.²³—a pattern that is not consistent with the thesis that marketing and promotion dictate prescribing decisions. Moreover, this percentage has grown rapidly—just 8 years ago, it was 47 percent. The U.S. “generic fill” rate is one of the highest in the world. In most European countries, where pharmaceutical company educational efforts are substantially curtailed by legal restrictions, the percentage of prescriptions that are generic is much lower. This clearly demonstrates that influences other than pharmaceutical company activities play powerful roles in determining which medicines patients receive, and the need to consider such activities in a broader context.

Published research has looked at whether physicians see value in pharmaceutical educational efforts. One survey found that over 90 percent of physicians surveyed said that the education provided by pharmaceutical representatives about specific drug therapies was either “somewhat valuable” (53 percent) or “very valuable” (38 percent).²⁴ Another survey found that the “sources of greatest importance (to physicians) were those

²¹ ACCME Standards for Commercial Support § 1.1 (2007).

²² Id. at § 5.2.

²³ IMS Data through 3rd Quarter of 2007.

²⁴ 2002 BCG Proprietary Physician Survey (400 respondents), 2002, as reported in “Pharmaceutical Marketing and Promotion, Creating Access to Innovation,” *Economic Realities in Health Care Policy*, Pfizer, 2003: 3(1):11.



involving the transfer of information through the medium of personal contact.”²⁵ This kind of contact comes mostly in the form of pharmaceutical representatives and industry-sponsored educational events.

While some critics have questioned the reliability of information provided by pharmaceutical companies in their marketing to healthcare providers, the reality is that there are state and federal government regulations that govern the marketing of products and serious consequences exist for non-compliance. Only a product’s scientifically proven capabilities, verified by the FDA, can be used in its marketing. Furthermore, pharmaceutical representatives depend on good, long-term relationships with physicians, relationships that are built on trust. If a medical representative provides information that a physician believes to be or later learns to be false, significant damage is done to that relationship, and the physician is less likely to rely on information from that representative or company again. Finally, there is competition among sellers of medical products, so it is unlikely that incorrect information would go unchallenged for very long.

Helping Translate New Technologies and Therapies into Practice

Pharmaceutical educational efforts play a valuable role in the healthcare system by delivering the newest information regarding pharmaceutical therapies to physicians and helping to bridge this gap and translate new technologies into practice. An Institute of Medicine report issued in 2001 noted that medical science and technology have advanced at an unprecedented rate during the past half-century. In tandem, the complexity of healthcare has grown.²⁶ Faced with these rapid changes, our healthcare delivery system has fallen short in its ability to translate knowledge into practice and to apply new technology safely and appropriately. In fact, the report noted that it now takes an average of 17 years for new knowledge to be incorporated into practice, and even then the application is highly uneven. Research suggests that without the information provided by

²⁵ McGettingan P. et al., “Prescribers Prefer People: The Sources of Information Used by Doctors for Prescribing Suggest that the Medium is More Important than the Message,” *British Journal of Clinical Pharmacology*, 51:184-189.

²⁶ “Crossing the Quality Chasm: A New Health System for the 21st Century,” Institute of Medicine, March 2001.



pharmaceutical representatives, utilization of valuable medical innovation would decrease significantly.

In fact, according to an article in *Health Affairs*, variations in prescribing patterns from location to location are not nearly as severe as variations in diagnostics and surgical procedures. The authors suggest one explanation may have to do with the valuable role pharmaceutical representatives play in informing doctors. “Drug firms’ efforts may truly educate consumers and providers and lead to greater uniformity of practice.”²⁷

Similarly, pharmaceutical marketing and promotion has played a valuable role in raising physician awareness of the most recent clinical practice guidelines, and thus improving health outcomes. According to an article in the *Journal of the American Medical Association (JAMA)*²⁸, “physician adherence to practice guidelines is critical in translating recommendations into improved outcomes. [The guidelines] successful implementation should improve quality of care by decreasing inappropriate variation and expediting the application of effective advances to everyday practice.” However, “a variety of barriers undermine this process,” such as physicians’ lack of awareness and/or lack of familiarity with a guideline. In the case of high cholesterol, for example, in May of 2001, the National Institutes of Health updated their National Cholesterol Education Program [NCEP] guidelines. These guidelines called for greater numbers of individuals to be treated for high cholesterol. According to October 2002 article in the *American Journal of Managed Care*, “[c]oncurrent public and private efforts aimed at physicians and consumers were related to increased diagnosis and treatment. Physician-directed initiatives have included pharmaceutical industry marketing, continuing medical education programs, and promotion of NCEP guidelines. Consumer-directed initiatives have included direct-to-consumer advertisements sponsored by various pharmaceutical companies and patient education programs....”²⁹

²⁷ Dubois R. W., Batchlor E. and Wade S., “Geographic Variation in the Use of Medications: Is Uniformity Good News or Bad?” *Health Affairs*, January/February 2002: 21(1): 240-250.

²⁸ Cabana M., MD, MPH et al., “Why Don’t Physicians Follow Clinical Practice Guidelines? A Framework for Improvement,” *JAMA*, October 22, 1999: 282(15).

²⁹ Dubois R. W. et al., “Growth in Use of Lipid-Lowering Therapies: Are we Targeting the Right Patients,” *The American Journal of Managed Care*, October 2002: 8(10).



Pharmaceutical marketing and promotion has also been credited with helping to improve treatment of mental illness. According to a study by David Cutler and Mark McClellan, through promotional activities, “manufacturers of SSRIs [medications used to treat depression] encouraged doctors to watch for depression and the reduced stigma afforded by the new medications induced patients to seek help.” As a result, diagnosis and treatment doubled over the 1990s.³⁰

Helping Patients Find the Right Medicine

Another important role that pharmaceutical educational efforts play is providing samples to physicians. Potential conflict of interest risks involving provision of samples to prescribers are managed by FDA regulations.³¹ Doctors may distribute samples to patients for several reasons – for instance, to get patients started on therapy right away, to help patients who might not be able to afford medicines on their own or to optimize dosing or choice of drug before committing to a particular course of treatment. These samples can allow the patient and physician to work together to determine what medicine is best for the patient. A poll of physicians reported that over 90 percent found product samples “valuable” or “extremely valuable” in their practices.³²

Researchers have examined physicians’ decisions to distribute free samples to their patients: one study, funded by the U.S. Agency for Health Care Policy and Research, examined the use of samples in primary care practices. According to the study, samples were used in about 20 percent of all patient interactions across a wide range of diseases and conditions. The study concluded that with regard to the impact of pharmaceutical company representatives, patients “...profited in a spectrum of ways. While samples represented tangible cost savings, immediate relief and convenience to the individual

³⁰ Cutler D. and McClellan M., “Is Technological Change in Medicine Worth It?” *Health Affairs* September/October 2001: (20)5:11-29.

³¹ See 21 C.F.R. part 203.

³² Boston Consulting Group, Physician Poll, 2002, as reported in “Pharmaceutical Marketing and Promotion, Creating Access to Innovation,” *Economic Realities in Health Care Policy*, Pfizer, 2003: 3(1).



patient....patient education materials facilitated further understanding of their diagnosis, potentially leading to a higher degree of satisfaction with their health care.”³³

Value of Pharmaceutical Company Educational Efforts in Encouraging Prevention and Treatment of Chronic Disease

As the U.S. population ages, its health care needs continue to expand. Diseases that affect the elderly, such as Alzheimer’s, and chronic conditions, such as diabetes, are becoming increasingly prevalent. According to the Centers for Disease Control and Prevention, chronic conditions account for 75 percent of total health care spending today.³⁴ Public health officials have shown growing concern over the increasing incidence of diabetes, obesity, depression, asthma, hypertension and many other conditions.

Today, many patients with these conditions are not treated at all or are not treated according to recommended guidelines. As the data demonstrate, wide-scale underdiagnosis and undertreatment of many common, chronic diseases remains an issue:

- In a landmark study RAND researcher Elizabeth McGlynn and colleagues reported that underuse was the principal quality of care problem associated with use of medicines in seven of nine diseases studied and 83 of 103 individual quality measures.³⁵
- A study published in the *Annals of Internal Medicine* on quality problems in medication management has identified underuse of needed medicines as

³³ Backer E. et al., “The Value of Pharmaceutical Representative Visits and Medication Samples in Community-Based Family Practices,” *Journal of Family Practice*, September 2000: 49(9): 811-816.

³⁴ Centers for Disease Control and Prevention, Chronic Disease Overview, <http://www.cdc.gov/nccdphp/overview.htm>

³⁵ McGlynn E.A., “The Quality of Health Care Delivered to Adults in the United States,” *New England Journal of Medicine*, June 26, 2003: 348(26): 2635-2645.



accounting for 50 percent of all quality problems while overuse accounted for only 3 percent.³⁶

- A study in California – using claims data from 3 of the 10 largest health plans to determine the appropriateness of prescription medication use based upon widely accepted treatment guidelines – found that “effective medication appears to be underused.”³⁷ Of the four therapeutic areas examined in the study – asthma, congestive heart failure (CHF), depression, and common cold or upper respiratory tract infections – asthma, CHF and depression were undertreated.
- A study by Medco researchers found that increased compliance or adherence to prescription drug treatment regimens can result in reduction of medical costs.³⁸ For diabetes, the average incremental drug cost for a 20 percent increase in drug utilization was \$177 and the associated disease related medical cost reduction was \$1251, for a net savings of \$1074 per patient (an average ROI of 7.1:1). For cardiovascular conditions, the average ROI for a 20 percent increase in drug utilization was 4.0:1 (hypertension) and 5.1:1 (hypercholesterolemia).
- Recent press reports explain that leading-edge employers are taking steps, such as reducing copays for both brand and generic drugs, to increase use of medicines by employees with conditions such as diabetes, in an effort to achieve better health outcomes and lower overall costs.³⁹

Undertreatment exacts a cost – for example, one study found that untreated depression costs employers over \$30 billion per year.⁴⁰ Another study found that if all patients with high blood pressure were treated with medicines according to recognized guidelines, 89,000 lives could be saved and 420,000 hospitalizations avoided annually—on top of the

³⁶ Higashi, T., P. G. Shekelle, et al. (2004). "The quality of pharmacologic care for vulnerable older patients." *Ann Intern Med* 140(9): 714-20.

³⁷ Gilberg K. et al., “Analysis of Medication Use Patterns: Apparent Overuse of Antibiotics and Underuse of Prescription Drugs for Asthma, Depression and CHF,” *Journal of Managed Care Pharmacy*, 2003: 9(3): 232-237.

³⁸ Sokol M. et al., “Impact of Medication Adherence on Hospitalization Risk and Healthcare Cost,” *Medical Care*, 2005: 43(6): 521-530.

³⁹ Freudenheim M., “To Save Later, Some Employers are Offering Free Drugs,” *New York Times*, February 21, 2007; Freudenheim M., “New Urgency in Debating Health Care,” *New York Times*, April 6, 2007; and Aetna, “New Preventive and Chronic Medications Option,” August 2005.

⁴⁰ Finkelstein J.B., “Mental Health Parity Extended Another Year,” *Am News*, December 2, 2002.



86,000 lives saved and 833,000 hospitalizations avoided by those using antihypertensive medicines.⁴¹ As discussed above, pharmaceutical marketing and promotion plays a role in increasing treatment rates, improving the quality of life for patients and lowering overall costs.

New medicines and vaccines play a role in helping to prevent disease, lengthen lives, avert surgeries and trips to the ER, prevent disability, and improve patients' quality of life. For instance:

- In a 2006 monograph on “Research and Development in the Pharmaceutical Industry,” the Congressional Budget Office observed: “Many examples exist of major therapeutic gains achieved by the industry in recent years ... anecdotal and statistical evidence suggests that the rapid increases that have been observed in drug-related R&D spending have been accompanied by major therapeutic gains in available treatments.”⁴²
- Likewise, in 2006 the Centers for Disease Control and Prevention noted, “Factors contributing to the decline in heart disease and stroke mortality include better control of risk factors, improved access to early detection, and better treatment and care, including new drugs and expanded uses for existing drugs.”
- In 2007, Chia and colleagues, examining metastatic breast cancer survival, stated, “This improvement in survival appeared to be caused by the availability and use of newer, more effective systemic agents for the treatment of metastatic breast cancer.”⁴³

⁴¹ Cutler D. et al., “The Value of Antihypertensive Drugs: A Perspective on Medical Innovation,” *Health Affairs*, January/February 2007: 26(1): 97-110.

⁴² Congressional Budget Office, “Research and Development in the Pharmaceutical Industry,” October 2006.

⁴³ SK Chia et. al, “The Impact of New Chemotherapeutic and Hormone Agents on Survival in a Population-Based Cohort of Women with Metastatic Breast Cancer,” *Cancer* 2007; 110.



- A Columbia University researcher reports that new medicines generated 40 percent of the two-year gain in life expectancy achieved in 52 countries between 1986 and 2000.⁴⁴

New medicines also make it possible to reduce costly hospitalizations and invasive surgery. Between 1980 and 2000, the number of days Americans spent in the hospital fell by 56 percent. As a result, Americans avoided 206 million days of hospital care in 2000 alone.⁴⁵ New medicines clearly were one important factor in this improvement.

Innovative medicines can also make life better for patients, reducing the severity of illness and disability, while allowing for greater productivity. For example:

- One study found that inner-city children who had asthma, but were enrolled in a comprehensive disease management program that included appropriate medications, experienced significant quality of life improvements. As their symptoms decreased and their capacity for activity rose, they reported greater emotional well-being.⁴⁶
- With benefit design improvements designed to increase adherence to physician-prescribed medicines for the treatment of rheumatoid arthritis, the incidence and duration of disability among workers dropped, yielding a 26% reduction in lost productivity costs.⁴⁷
- Another study reported that 50 percent of workers receiving a drug injection for a migraine attack returned to work within two hours, compared to only 9 percent of workers who received a placebo.⁴⁸

⁴⁴ Lichtenberg F.R., "The Impact of New Drug Launches on Longevity: Evidence from Longitudinal, Disease-Level Data from 52 Countries, 1982-2001," National Bureau of Economic Research, Working Paper No. 9754 (Cambridge, MA: NBER, June 2003).

⁴⁵ MEDTAP International Inc., "The Value of Investment in Health Care: Better Care, Better Lives," (Bethesda, MD: MEDTAP, 2003).

⁴⁶ Munzenberger P.J. and Vinuya R. Z., "Impact of an Asthma Program on the Quality of Life of Children in an Urban Setting," *Pharmacotherapy*, 2002: 22(8): 1055-1062.

⁴⁷ Integrated Benefits Institute, *A Broader Reach for Pharmacy Plan Design*, May 2007.

⁴⁸ Cady R.C. et al., "Sumatriptan Injection Reduces Productivity Loss During a Migraine Attack: Results of a Double-Blind, Placebo-Controlled Trial," *Archives of Internal Medicine*, May 11, 1998: 158:1013-1018.



The Cost of Pharmaceutical Company Educational Efforts Compared to Research and Development Activities

Debates about pharmaceutical company activities often suggest that educational activities, including marketing efforts, have little or no value and come at the expense of investment in R&D of new medicines. The facts do not support this view. In the preceding section we have discussed why pharmaceutical company educational efforts have value. Here, we discuss the comparison of spending on such efforts to R&D investment.

It is important to recognize the extraordinary magnitude of the biopharmaceutical research enterprise. In 2007, the biopharmaceutical industry invested an estimated \$58.8 billion in total R&D spending, according to Burrill & Company. PhRMA members alone spent \$44.5 billion on R&D in 2007.⁴⁹ As the Congressional Budget Office recently reported, “The pharmaceutical industry is one of the most research-intensive industries in the United States. Pharmaceutical firms invest as much as five times more in research and development, relative to their sales, than the average U.S. manufacturing firm.”⁵⁰ At the same time, as discussed above, marketing and promotion play an important role in informing physicians and patients about the fruits of this investment—new medicines that improve and save lives.

Uwe Reinhardt of Princeton University has explained how educational and promotion costs often are inaccurately characterized in policy debates. According to Reinhardt, “...the [selling, general and administration or SGA] category represents many expenses other than selling expenses and should not be seen as an estimate purely of outlays on marketing, as the industry’s critics occasionally do.”⁵¹ Moreover, Harvard economist Joseph Newhouse has written, “One sometimes hears it said that the industry would have

⁴⁹ Pharmaceutical Research and Manufacturers of America, *Annual Member Survey 2008* (Washington, D.C.: PhRMA, 2008).

⁵⁰ Congressional Budget Office, “Research and Development in the Pharmaceutical Industry,” October 2006.

⁵¹ Reinhardt U.E., “Perspectives on the Pharmaceutical Industry,” *Health Affairs*, September/October 2001: 20(5): 136-149.



more money for R&D if it would cut down its marketing costs. This comment reflects misunderstanding of the economics of the industry. If a firm did so, it would be less profitable and have would attract less capital for R&D or would have fewer internally generated funds to invest.”⁵²

Conclusion

Industry, academia, practitioners, and the government each play important roles in managing conflicts of interest in pharmaceutical research and development as well as after medicines are approved. These risks are effectively managed through transparency, disclosure, training and education, as well as enforcement of regulations. Arbitrary interference with such interactions may adversely impact the public health by limiting research in important disease areas. In addition, pharmaceutical company educational efforts after drug approval provide value to physicians by allowing pharmaceutical research companies to inform healthcare providers about the benefits and risks of new medicines in accordance with FDA regulation, provide educational and scientific information, support medical research and education, and obtain information and insight about medicines through consultation with medical experts. Published research has reinforced the value physicians see in promotional and marketing efforts. The establishment of the PhRMA Code confirms our commitment to interact with healthcare professionals for the benefit of the patient and to enhance the practice of medicine.

⁵² Additionally, the Federal Trade Commission has stated that direct to consumer (DTC) advertising does not significantly affect prescription drug prices: “[DTC advertising] can empower consumers to manage their own health care by providing information that will help them, with the assistance of their doctors, to make better informed decisions about treatment options...Consumers receive these benefits from DTC advertising with little, if any, evidence that such advertising increases prescription drug prices. DTC accounts for a relatively small proportion of the total cost of drugs, which reinforces the view that such advertising would have a limited, if any, effect on price.”