PUBLIC CITIZEN Health Letter

SIDNEY M. WOLFE, M.D., EDITOR OCTOBER 2013 – Vol. 29, No. 10

Public Citizen Report Highlights Crucial Generic Drug Labeling Concerns

The majority of prescriptions filled in the U.S. today are filled with generic drugs, making medication more affordable for patients. To ensure patient health, it is imperative that the labels for generic drugs include the most up-to-date safety information.

On June 20, Public Citizen issued a detailed report documenting that too often, a serious safety hazard is not identified until years after a prescription drug enters the market and that many drugs today are marketed only in generic form. These facts, combined with the Food and Drug Administration's (FDA's) regulations restricting the ability of generic drug manufacturers to update the labels of their products, create a gap with respect to the labeling of generic drugs that threatens patient health and safety.

About generic drugs

In 1984, the U.S. Congress passed a law, commonly referred to as the Hatch-Waxman Amendments, designed to promote the expansion of the generic drug market. Since the law passed, generic drug sales have grown dramatically, fundamentally reshaping the pharmaceutical market. The increased availability of generic drugs has made many prescription drugs more affordable for patients. In 2011, nearly 80 percent of prescriptions filled in the U.S. were filled with generic drugs.

Although generics now dominate the market for prescription drugs, current FDA regulations do not permit a generic drug manufacturer to alter its product's labeling, except to mimic a change made by the brand-name equivalent or ordered by the FDA. This restriction creates a safety gap for patients because generic manufacturers with a large stake — perhaps the largest stake — in the product have no responsibility for the adequacy of its labeling. This gap becomes even more troubling after the brand-name manufacturer stops selling the drug, as often happens within a few years after generics enter the market.

Also, in light of the generic manufacturer's lack of responsibility for product labeling, a patient injured because a generic manufacturer failed to warn of a serious risk — or provided unclear or misleading instructions for safe use — is unable to seek compensation from the manufacturer because of recent federal and U.S. Supreme Court decisions. This release from liability diminishes the incentive for generic drug companies to be vigilant about product hazards and eliminates the incentive to request labeling changes in response to new evidence.

Labeling changes

When the FDA approves a drug for marketing, it approves the drug's labeling as well. Even after approval, however, FDA regulations require drug labeling to include up-to-date information about hazards associated with a particular drug. Brand-name manufacturers may seek approval for revised labeling in one of two ways.

Under a procedure known as "changes-being-effected," a brand-name drug manufacturer may make certain changes to a product's labeling, including changes to strengthen warnings or contraindications and to clarify instructions for use, without first obtaining FDA approval for the changes. In this circumstance, the company must simultaneously notify the FDA of the label changes.

Brand-name manufacturers also can inform doctors and other health care professionals about newly discovered safety concerns by sending "Dear Health Care Professional" letters, which are considered part of drug labeling under federal regulations.

These options for labeling revision are *not* available to generic manufacturers under FDA regulations. Instead, generic drug companies can revise labeling only to mimic a change made by the brand-name manufacturer (which relies on that manufacturer to initiate the change) or as directed by the FDA.

Timing of warnings

Inadequacies in a drug's labeling, including those related to safety issues, often do not emerge until after the drug has been on the market for a long

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time. As one study found, "only half of newly discovered serious [adverse drug reactions] are detected and documented in the *Physician's Desk Reference* within 7 years after drug approval."

For especially serious risks, particularly those that may lead to death or serious injury, the FDA may require that the information be presented in a boxed warning at the top of the label. Sometimes called a black box warning, a boxed warning is reserved for the most serious drug contraindications (circumstances in which the drug should not be used) and warnings.

Public Citizen's report assessed the quantity of new boxed warnings added after the generic equivalent entered the market. (This research was limited to new boxed warnings added from January 2008 through March 2013.)

Public Citizen identified 53 drugs over the period analyzed for which a black box warning calling attention to serious or life-threatening risks was added after a generic version of the drug entered the market — and the list is likely incomplete. The report provides a list of these 53 drugs, including the generic and original brand names, the year of approval, current availability, and the year a new black box warning was added to the drug label. The data show that new safety issues commonly arise after generics have entered the market and underscore the public health imperative of maintaining an incentive for generic manufacturers to monitor safety concerns.

The following examples illustrate the severe risks set forth in boxed warnings that were added many years after approval of a drug and introduction of a generic equivalent onto the market:

- Promethazine hydrochloride, originally marketed under the brand name Phenergan, was approved by the FDA in tablet form in 1951, in injectable form in 1956 and in suppository form in 1960. It is approved for several uses, including treatment of motion sickness, nausea and some allergy symptoms. In 2000, the warning in the drug's label was strengthened to recommend against use in children younger than 2 years old, and in 2004, the FDA required a boxed warning instructing against such use. The boxed warning was added after the brand-name manufacturer reported cases of respiratory depression, including fatalities, in children under 2. Phenergan was later discontinued, but generic versions are still available. In 2009, the FDA required an additional boxed warning for injectable promethazine hydrochloride due to the risk of gangrene if the drug is injected into an artery.
- Metoclopramide hydrochloride, sold under the brand name Reglan and other names, was approved to treat gastrointestinal issues in three dosage forms: an injectable formulation approved in 1979, a tablet approved in 1980 and an oral solution approved in 1983. The drug received its first black box warning in 2009, 30 years after its first approval, when doctors discovered that its use could cause tardive dyskinesia in certain patients. Tardive dyskinesia is a serious, often irreversible movement disorder that causes involuntary, repetitive movements of the extremities, as well as lip smacking, grimacing, tongue protrusion and other uncontrollable facial movements. When the FDA announced the warning in 2009, the agency estimated that more than 2 million Americans were taking these products.
- Haloperidol is an antipsychotic drug approved by the FDA in 1967 as brand name Haldol. In 2007, the FDA announced that the drug company had updated the warning label due to reports of sudden death and heart-related side effects. In 2008, the FDA required manufacturers of haloperidol and many

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other antipsychotic drugs to add black box warnings following the release of several studies suggesting that the use of these types of drugs to treat elderly patients with dementia increased the risk of death among these patients.

Lack of alternatives

Competition from generics frequently leads a brand-name manufacturer to cease production of the brand-name drug. For those drugs, patients and physicians cannot rely on the brand-name manufacturer to monitor reports of adverse effects and update the labeling. In such situations, the limitation on generic drug companies' ability to update labeling to provide the most current warning information takes on added significance, particularly when the drug is known to pose serious risks.

The market withdrawals of Accutane and Serzone illustrate the point:

- Isotretinoin, originally marketed under the brand name Accutane, is used to treat a severe form of acne. It first received FDA approval in 1982. Accutane was linked to several severe side effects, including birth defects when taken by pregnant women, damage to the liver and other internal organs, and depression. In 2009, after nearly 30 years on the market, the brand-name manufacturer discontinued manufacturing and distributing Accutane, citing the cost of personal-injury lawsuits and the effect of generics on its market share. Generic versions of isotretinoin remain available.
- Nefazodone hydrochloride, an antidepressant approved in 1994 as brand-name Serzone, was removed from the market by the brand-name manufacturer in 2004. Although the drug had been withdrawn from the market in Canada for safety reasons and is associated with liver failure, the company purported to stop selling it in the U.S. due to economic considerations. Nefazodone hydrochloride remains on the market in the U.S. in generic form.

Using a publicly available FDA database, Public Citizen compiled a list of 434 approved prescription drug formulations for which the brand-name manufacturer has discontinued sales but a generic equivalent remains on the market. The complete list is provided in Public Citizen's report, available at www.citizen.org/hrg2138.

Public Citizen Petition

In August 2011, Public Citizen submitted a citizen petition to the FDA to request that the agency amend its regulations to allow generic drug manufacturers to take advantage of the same procedures for updating labeling that are currently available to brand-name manufacturers. The petition was intended to help address the existing regulatory gap that threatens patient health and safety.

Allowing generic drug manufacturers to provide updated safety information would have two benefits. First, in light of the large market share of generic drugs, it would help to ensure that drug labeling provides adequate warnings to patients based on information that comes to light after the drug is approved for marketing.

Second, because the U.S. Supreme Court held in *PLIVA, Inc. v. Mensing* in 2011 that a patient harmed by a generic drug that had inadequate labeling cannot sue the manufacturer for compensation for her injuries, revised regulations would correct the illogical disparity between the rights of patients injured by generic drugs and the rights of those injured by brand-name drugs.

The FDA has not responded substantively to the petition, although it recently signaled its intention to issue a proposed rule that may implement this change.

Conclusions

The data presented in Public Citizen's report demonstrate that new serious risks to patients are sometimes identified years after a drug enters the market, making a drug's longevity no guarantee of safety. In addition, hundreds of generic drugs are sold without a currently marketed brand-name equivalent. These facts make generic drug manufacturers' inability to update the labeling of their products under current regulations a threat to the safety of prescription drugs, and, accordingly, a source of unnecessary risks to patients.

Under the laws of many states, the brand-name company cannot be held liable for harm caused by inadequate labeling in cases where the injured patient took a generic form of the drug. When more than 75 percent of all prescriptions are filled by generic versions, this legal reality further diminishes the brand-name manufacturer's incentive to be vigilant and to take the time and expense to submit an application to the FDA to update a drug label.

These developments, among others cited in Public Citizen's report, collectively give rise to a safety problem: As generic market share increases, the brand-name manufacturer loses incentive to invest resources in post-approval safety monitoring, while generic manufacturers face no concomitant increase in incentive and have no authority to update labeling. Given that the FDA cannot monitor all post-approval data by itself, drug safety is threatened when the regulatory and legal incentives designed to motivate manufacturer diligence weaken with shifting control of market share.

Regulatory revisions are needed to bring post-market regulation in line with the realities of the pharmaceutical market and to help ensure that drug labeling provides adequate warnings to patients based on information that comes to light after the drug is approved for marketing. ✦

Uncovering Quality Concerns In Nursing Homes

It was January 2011, and Maria Watterson* was concerned about her mother Myra, who was staying in the Trussville, Ala., Golden Living Center, a long-term skilled nursing facility. She had just learned that Myra had experienced dramatic weight loss in August, falling from almost 140 pounds to less than 120 pounds over the course of a few weeks. The nursing home staff had never mentioned this to Maria; she learned the news from a government inspector during a visit to the home five months later. She also learned that her mother, who has difficulty moving on her own, had suffered a bedsore that had healed by October and was now dealing with a second one. Maria knew that her mother had to be repositioned every two hours to allow the sore to heal, but no one came to turn her mother during Maria's 3½ hour visit with Myra. Maria finally went out and found a nursing home employee to intervene and reposition Myra properly.

In another patient's room, the inspector noticed another problem: A nurse was improperly cleaning a resident who had experienced an accidental bowel movement, putting the resident at risk for urinary tract infections.

Just miles down the road, at the Hueytown, Ala., Golden Living Center, conditions were very different. Inspectors visited the facility in February that year and found no unhappy family members, improperly treated bedsores or hygiene concerns. The only issues noted were fish filets served at lunch that were smaller than planned and two bottles of insulin that were used a few days past their expiration dates.

The Hueytown and Trussville Golden Living Centers are both run by the same national chain, and they are both Medicare/Medicaid-certified, employ licensed nurses and offer multiple types of skilled care. Yet weight loss is a common problem at the Trussville location, where 14.5 percent of long-stay residents (nearly twice the national average of 7.5 percent) lose too much weight, according to government inspection reports. By contrast, weight loss at the Hueytown facility is lower than the national average. Hueytown also has about half the number of patients with pressure ulcers as Trussville and about one-third as many patients with urinary tract infections. Even more striking, though the Hueytown facility is ranked highly by federal inspectors on quality measures, the Trussville facility has been identified for special focus by the Medicare program for its history of persistent poor quality of care and could have its Medicare provider status revoked if conditions do not improve.

Until just a few years ago, families like the Wattersons had no way of accessing any of this information, which was collected by government inspectors but not made easily accessible to patients and their families. Over the past five years, the federal government has been making public more information describing the quality of nursing home facilities across the country.

You can use new government tools to examine nursing home quality and uncover information about observations at nursing homes in your area. You also can learn how to protect yourself and your family from poor nursing home practices by understanding your legal rights and finding out how to seek government assistance when these rights are violated.

Comparing nursing home quality

When they chose the Trussville Golden Living Center, Myra and Maria Watterson probably did not know that in December 2008, the Centers for Medicare and Medicaid Services (CMS) had begun publishing quality ratings for nursing homes using a simple five-star rating system (see the text box on this page.) The rating system relies on information collected by state and federal agencies during inspections, as

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National Rating System

The Centers for Medicare and Medicaid Services (CMS) publishes nursing home quality rating information and lets you compare up to three nursing homes side by side. The rating system is available at www.medicare.gov/nursinghomecompare.

The rating system is based on the relative quality of nursing homes within the same state: The top 10 percent of nursing homes receive a five-star rating, regardless of how they compare in quality with other states. So if you are trying to decide whether you would rather be near your son in Texas or your sister in Connecticut, the CMS rating system will not be able to answer which of these nursing homes has better performance on quality measures.

Don't have access to the Internet? You can ask for help at your local library or senior center or call the Medicare 24-hour help hotline at 1-800-MEDICARE (1-800-633-4227). You can use the hotline to help look up star ratings for nursing homes in your area, access inspection reports and identify other useful resources. Ask the representative to mail you their booklet entitled "Your Guide to Choosing a Nursing Home" for more information on how to research nursing homes in your area.

Fictional patient and family member names have been created for a case anonymized to protect patient privacy.

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well as quality measures and staffing levels reported to the government by the nursing homes themselves.

CMS also now provides online access to detailed health inspection reports describing specific violations observed by government inspectors during their visits to facilities. Inspectors typically visit a home about once a year to ensure compliance with the regulations put in place to protect patients. Inspectors make observations about residents' care, interview residents and families, ask how the staff talks to and treats the residents, look at records, and examine the condition of resident rooms and common areas. Observations made during the visit are written up in the reports that CMS makes available online. (Officials remove private information that could be used to identify residents and staff before posting the reports.)

Recognizing problems

Learning about a home's quality rating is just one way to identify problems at nursing homes. Another excellent way to find a quality nursing home is to visit the facility yourself. Talk to staff and residents about their daily experiences and speak with other families and visitors. Be observant: Do the staff respect residents by, for example, knocking on doors before entering resident rooms, referring to residents by name, and talking to them before touching them or helping them with something? Are residents clean, well groomed and appropriately dressed for the season or time of day? Do you notice any unpleasant smells?

Another thing to look for is the extent to which a nursing home relies on chemical restraints (such as antipsychotic drugs) or physical restraints (such as bedside rails) to control residents' behavior. Overuse of restraints can endanger residents (see text box at right), and nursing homes are legally prohibited from relying on such restraints for the convenience of the staff or to discipline residents for bad behavior. (Drugs or bedside rails can justifiably be used to address a medical condition, such as schizophrenia, or to mitigate the risk of falling.) When you visit the nursing home, ask about the circumstances in which physical and chemical restraints are used in the facility and what steps the home has taken to reduce their use.

Nursing homes often have a resident council or family council, allowing residents and family members to meet to address concerns and improve the quality of care and life for residents. Find out if the nursing home has a council and ask if you can attend the next meeting. This is a great way to find out what concerns are important to residents and whether their needs are being appropriately addressed.

Before you make a final choice to enter a nursing home, it's a good idea to visit at least twice, on a different day of the week and time than your initial visit.

Knowing your rights

Under federal law, nursing home residents staying in Medicare- or Medicaid-certified facilities have a right to care

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Chemical, Physical Restraints Overused in Nursing Homes

Many nursing homes rely on physical restraints (such as bedside rails) and chemical restraints (such as antipsychotic drugs) to control residents who become agitated or cause problems. Bedside rails used to prevent people from getting out of bed pose unnecessary risk, because elderly or disabled people may fall while attempting to climb over the rails or may slip between the bedside rail and the bed and become trapped, leading to strangulation and death. The Consumer Product Safety Commission reported in 2012 that portable bedside rails have been associated with at least 155 fatalities, mostly from strangulation incidents in which an elderly victim became stuck, wedged or trapped between the mattress and the rail.

Chemical restraints, including antipsychotic drugs, also put patients at risk. The Food and Drug Administration has placed a black box warning on atypical antipsychotic drugs stating that elderly patients with dementia-related psychosis were at more than 50 percent increased risk of death compared to those who received a placebo in randomized trials. There also is some evidence that conventional antipsychotics carry increased risk of death, but randomized trials have not been conducted on these drugs, which are older and therefore more likely to be off-patent.

The use of chemical and physical restraints can be reduced through better personal care by nursing home staff. A study published on the *British Medical Journal's* website on March 23, 2006, showed that antipsychotic drug use in nursing homes could be decreased by close to 20 percent if staff were trained on alternatives to drugs for managing agitated behavior in dementia patients. Other studies have indicated that institutions can prevent serious injuries and reduce the use of bedside rails as restraints by implementing programs to address the risk of falls in other ways.

Assessing quality at nursing homes can be a daunting task, but by doing your research, paying attention and using the available resources, you can avoid being caught in a nursing home that puts health and safety at risk.

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that meets certain quality standards. (See text box at right.)

Myra Watterson's right to have her family notified of major medical changes was violated when the nursing home failed to tell her daughter about Myra's bedsores and weight loss. Her right to be free of neglect was violated when the nursing home staff failed to turn her at proper intervals to allow her bedsore to heal and prevent new sores.

Avoid becoming a victim of similar quality-of-care problems. Learn your rights and know how to seek help when your nursing home fails to respect them.

The first way to address such a problem is to go to the head of the nursing home. All Medicare/Medicaid-certified nursing homes must have a grievance procedure for complaints. If your issue cannot be resolved informally, ask about filing a formal grievance through this process. You also can go to the resident council or family council to get extra assistance.

If your concerns are not resolved promptly, you can contact your local long-term care ombudsman or State Survey Agency. State Survey Agencies are organizations that oversee health care facilities participating in Medicare or Medicaid programs. These organizations inspect health care facilities and investigate complaints to ensure that health and safety standards are met. They can help with questions or complaints about the quality of care in nursing homes. Find out how to contact your local State Survey Agency by calling 1-800-MEDICARE (1-800-633-4227).

Assessing quality at nursing homes can be a daunting task, but by doing your research, paying attention and using the available resources, you can avoid being caught in a nursing home that puts health and safety at risk. ✦

Rights for Nursing Home Residents

Nursing home residents have many rights under federal law, including the right to:

- Be treated with respect: This includes making your own schedule, including when you get up and go to bed, and when you eat your meals.
- Participate in activities: You have the right to participate in activities that are designed to meet your needs and the needs of other residents.
- Be free from discrimination: A nursing home cannot discriminate based on race, color, national origin, age, disability, or religion.
- Be free from abuse and neglect: A nursing home cannot mistreat you (abuse) or fail to meet your needs (neglect).
- Be free from restraints: Nursing homes can't use any physical restraints (like side rails) or chemical restraints (like drugs) to discipline you for the staff's own convenience.
- Make complaints: You have the right to complain without fear of punishment, and the nursing home must address the issue promptly.
- Participate in medical decisions: You have the right to be informed and participate in decisions about choice of doctor, medications, and other decisions affecting your care.
- Have your representative notified: The nursing home must notify your doctor and legal representative or family member if you are involved in an accident or your medical condition changes significantly, or if you are transferred or discharged from the nursing home.
- Manage your money: You have the right to manage your own money or choose someone you trust to do this. If you choose the nursing home to manage your money, they must allow you access to your bank accounts, cash and financial records. The nursing home must manage your money responsibly.
- Get proper privacy, property, and living arrangements: You have the right to keep and use personal belongings as long as it doesn't interfere with the rights, health, or safety of others, and the nursing home should protect your property from theft. You also have the right to private visits, private phone calls, and private mail and e-mail. The nursing home should allow you to share a room with your spouse if you request it.
- Have your family and friends involved: Family and friends are allowed to contact the nursing home and help make sure you get good quality care. They can visit and get to know the staff and nursing home's rules. They can help with your medical care, with your permission.

Adapted from information available at:
http://downloads.cms.gov/medicare/Your_Resident_Rights_and_Protections_section.pdf

Health Advocacy Organizations: Patients' Voices or Corporate Front Groups?

If you or a loved one has ever been diagnosed with a severe disease, such as cancer, it is likely that one of your first responses was to seek out a support group or other organization of patients with the same condition. Some of these patient groups, known as health advocacy organizations (HAOs), are among the most visible public voices influencing health policy in this country. HAOs are a diverse collection of nonprofit groups covering a wide range of diseases and agendas, which give a human face to disease-related advocacy. They range in size from small teams of a few full-time staff focused on rare diseases (such as the Trisomy 18 Foundation) to influential national organizations with millions of volunteers and supporters (such as the American Heart Association and American Cancer Society).

Many HAOs play a vital role in promoting public health through raising disease awareness, holding mass screenings, funding research and advocating for public policy in the perceived best interest of their members. However, a series of recent studies have found that HAOs often accept large sums of money from the drug industry and that a glaring lack of transparency characterizes most of these financial ties. Such relationships inevitably raise questions about potential conflicts of interest at play in the operations and policy positions of these highly influential, trusted organizations.

Can HAOs be trusted to provide fair and balanced information?

Lack of transparency

In 2011, Dr. Sheila Rothman and colleagues at Columbia University and New York University analyzed the financial records of Eli Lilly, one of the world's largest pharmaceutical companies, to tabulate the number of HAOs to which the company had given a grant, as well as the extent to which the HAOs disclosed these ties. The researchers found that during the first six months of 2007, Eli Lilly had given grants to a total of 188 HAOs, primarily to organizations that worked in diseases related to its bestselling products. A total of 94 percent of the grants went to HAOs working in the three therapeutic areas (neurosciences, oncology and endocrinology) that generated 87 percent of Eli Lilly's U.S. sales at the time.

This was not surprising given Eli Lilly's stipulation in its guiding principles for grant-making that it expects to "build long term relationships [with grantees] … based on mutual support," while offering the disclaimer that those receiving grants are not "obligated or directed to use these funds in a manner that benefits the company or its products."

Although the financial ties were pervasive, in most cases they were not disclosed anywhere on the HAOs' websites. Of the 161 HAOs for whom the researchers had found a website, only 25 percent disclosed that they had received grant money from Eli Lilly, including only 18 percent of HAOs working in the neurosciences, Eli Lilly's most lucrative therapeutic area. None of the 161 HAOs disclosed on their websites the exact amounts received from the company.

Extensive industry-HAO relationships are not unique to the U.S. In 2010, the nonprofit group Health Action International-Europe (HAI-Europe) surveyed the 23 patient groups (itself included) eligible to participate in the European Medicines Agency's (EMA's) Patient and Consumer work group, which advises and makes policy-related recommendations to the agency. HAI reviewed the organizations' annual financial statements to determine the share of their funding from health care companies from 2006 to 2008. Fifteen of the 23 organizations (65 percent) received funding from health care companies. Over the three-year period studied, corporate funding made up an increasing proportion of the organizations' annual budgets, rising from 47 percent in 2006 to 57 percent by 2008.

As with the Rothman study of U.S. HAOs, a lack of full transparency also was apparent. Fewer than half of all the European organizations (including HAI-Europe, though the organization accepts no corporate money) disclosed their financial data in the format mandated by the EMA, which requires names of individual donors and the corresponding contributions relative to the organization's annual budget. The European Union's (EU's) Executive Agency for Health and Consumers (EAHC), a research-funding arm of the EU, gives grants only to organizations that receive less than 20 percent of their funding from industry. However, HAI-Europe noted that while the EAHC has created guidelines requiring financial transparency, it did not stipulate any mechanisms for holding organizations accountable for noncompliance with the guidelines, presenting an enforcement challenge.

Corporate funding and public policy

Though it is self-evident that companies would not continue to give money to HAOs unless they perceived some financial benefit from the arrangement, it is difficult to prove empirically whether HAOs respond to funding by changing their advocacy approach. However, in 2011, HAI-Europe attempted to do just that. The group examined whether organizations' industry ties correlated with their positions on key policies affecting patients (and the drug industry). HAI-Europe surveyed the same European HAOs (this time excluding itself) it had earlier studied, eliciting their views on pending EU legislation (since approved) that

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would expand the type of drug-specific information that pharmaceutical companies could communicate directly to European consumers (though the law purportedly preserves the European ban on pharmaceutical direct-to-consumer advertising, which is legal in the U.S.).

Among the organizations that responded, a striking correlation was seen between their views of the proposed legislation and their financial connections with drug companies. All six of the organizations that received money from the drug industry were in favor of allowing companies to distribute more information to the public, while none of the five companies without industry backing supported such a move.

Anecdotally, such bias also is reflected in public debates concerning important health regulatory decisions. Public Citizen's Health Research Group (HRG) routinely testifies at Food and Drug Administration advisory committees on important matters before the agency, such as new drug approvals or serious safety issues concerning a drug or class of drugs. Usually during the public hearings, HRG is the lone voice warning of the dangers of a new and often ineffective medicine. And many of those speaking in favor of the drugs are patients or other representatives of industry-funded HAOs, whose travel expenses are paid for by the drug manufacturer and who give harrowing testimony about their conditions, imploring the committee to vote in favor of the drug in question.

These patients' stories are true, and their concerns are entirely understandable. Anyone who has ever been diagnosed, or has known someone diagnosed, with a debilitating or life-threatening condition can empathize with these stories and identify with the desperation for any treatment that promises to alleviate their condition. Yet it also is true that the patients' and HAOs' wishes for more treatment options happen to coincide with the financial interests of drug companies. And all too often, the patients are only able to tell their stories because of the financial largesse of those same companies eager to present a compelling case to the committees on whom the fate of their lucrative medicines hinge.

Are these patients therefore being co-opted, or is underwriting the patients' presentations a legitimate and necessary means that justify the ends of more life-saving therapies for these patients and others?

Shareholder versus patient interests

HAOs that accept drug industry money understandably cry foul at suggestions that the money influences their actions in any way. Such was the case in 2011, when a public spat between the French nonprofit pharmaceutical information publication *Prescrire* and the French Diabetic Association highlighted the arguments at the heart of this debate. The row concerned a French law that allowed pharmaceutical companies to underwrite "therapeutic education programs" and "patient assistance" initiatives, as long as patient groups and health care professionals designed and managed the programs.

A *Prescrire* editorial in 2009 criticized French HAOs that supported the law and took money from the drug industry rather than lobby more strongly for public money to fund their activities, citing the French Diabetic Association as an example. In a combative open letter responding to the allegation, the French Diabetic Association maintained that patient groups play a vital role in educating the general public about health issues. The association also alluded to the limited financial resources of some HAOs, such as itself, as a reason why so many feel compelled to turn to industry funding, and it insisted that corporate money had not compromised its mission or positions on the issues affecting its members.

The *Prescrire* editors countered that the nature of the influence of donor companies on HAOs is much more subtle than the image of a nefarious *quid pro quo* relationship evoked by the French Diabetic Association. Accepting money from a drug company does not result in night-and-day differences in the policies and actions of the organizations, they argued. Rather, a company only gives to organizations that it perceives as favorable to its products and, in turn, the organizations may slowly, over time, adapt their operations due to "subtle feelings of gratitude for receiving a benefit rather than to blatant corruption."

This is not to say that HAOs do not do good work. There is no shortage of HAOs that do not accept money from corporate interests, and many HAOs play a crucial role in raising awareness of, and directing crucial research money to, devastating diseases that affect millions of people. Dr. Rothman opened a critique of HAOs published in the *Journal of the American Medical Association* with the following observation: "Strong and *independent* [emphasis added] not-for-profit advocacy organizations are vital to a democratic society. At their best, they stand apart from the interests of the marketplace and the government, helping to promote diverse public concerns."

But creeping corporate influence — in the form of financial ties — can compromise this core mission of the organizations and, in subtle but real ways, direct their energies toward strengthening the bottom lines of large pharmaceutical companies rather than enhancing the health of the patients whose interests they claim to represent. In other words, such ties serve only to corrupt HAOs' otherwise laudable and often life-saving activities.

In the original editorial that triggered the confrontation with the French Diabetic Association, *Prescrire* reminded its readers of the simple, overarching truism that governs corporate-HAO relationships: "One thing is certain: drug company shareholders will only tolerate spending on patient education if it increases profits. To lose sight of this fact would be naive, hypocritical or cynical." ✦

Health Letter Editor Role Changes Hands

Beginning with the November 2013 issue, *Health Letter* will be edited by the new Director of Public Citizen's Health Research Group (HRG), Dr. Michael Carome. Readers of *Public Citizen News* may recall reading that Dr. Sidney Wolfe, who started HRG in 1971 and has served as editor of *Health Letter* since its inception in 1985, is turning over the reins to Carome, even while Wolfe continues his work as HRG Founder and Senior Advisor.

Carome, who became HRG director in June, is an expert in the ethics of human subjects research, having served as associate director for regulatory affairs at the U.S. Office for Human Research Protections.

In his role as HRG director, and as editor of *Health Letter*, Carome plans to continue the scope and range of issues that Wolfe started working on 42 years ago, including drug and device safety, research ethics, medical board oversight of doctors, health care delivery, and more.

HRG Works for You!

Our latest work involves informed-consent policy, a new unethical study involving premature infants and a drug safety petition

The work of Public Citizen's Health Research Group (HRG) doesn't end with its *Health Letter* and *Worst Pills, Best Pills News* publications. HRG uses our own research, current academic research, government data and information from whistle-blowers to advocate for consumers by:

- petitioning the government to remove unsafe drugs or medical devices from the market, and to require warnings of dangerous side effects on other drugs;
- testifying before government committees and arguing against approval of unsafe/ineffective drugs and devices;
- writing letters to government agencies about the adverse effects of drugs and medical devices; and
- urging Congress to strengthen the regulatory oversight of drugs and medical devices.

Our latest research-based consumer advocacy includes:

- **Testimony Before HHS Panel on Informed Consent for Human Subjects Research — 8/28/2013 —** In light of recent, high-profile instances of serious ethical breaches in clinical trials involving infants, HRG Director Michael Carome and Founder Sidney Wolfe testified before the Department of Health and Human Services regarding the risks of research testing "standard of care" interventions in human subjects.
- **Letter to HHS Secretary Sebelius on a New NIH-Funded Premature Infant Study Lacking Compliance With Ethical Consent Standards — 8/22/2013 —** Only months after exposing an unethical, federally funded experiment conducted on premature infants, Public Citizen has learned of a new trial with similar informed-consent problems. The new study is designed to determine which of two different strategies for treating anemia with blood transfusions is more likely to result in death or neurologic injury in premature babies. In the letter, Public Citizen urges the halting of recruitment for the trial, which started only recently, and states that the parents of babies enrolled should be contacted regarding the consent-form deficiencies.
- **Public Citizen Petition to FDA to Warn Against Prolonged Use of Clopidogrel (Plavix) in Cardiac-Stent Patients Because of Lethal Side Effects, No Benefit — 8/21/2013 —** Public Citizen petitions the Food and Drug Administration to warn patients and doctors that taking clopidogrel (Plavix) for more than a year after having a drug-eluting stent implanted can lead to potentially fatal bleeding without providing further benefits.

Visit www.citizen.org/hrgpublications to read full reports and testimonies as HRG fights for government and industry accountability in the interest of the public's health.

Product Recalls

August 7, 2013 – August 20, 2013

This section includes recalls from the Food and Drug Administration (FDA) Enforcement Report for drugs and dietary supplements (www.fda.gov/Safety/Recalls/EnforcementReports/default.htm), and Consumer Product Safety Commission (CPSC) recalls of consumer products.

DRUGS AND DIETARY SUPPLEMENTS

Recalls and Field Corrections: Drugs – Class I

Indicates a problem that may cause serious injury or death

Lightning Rod Capsules, 500 mg/capsule, packaged in 3-count and 12-count bottles. Volume of product in commerce: unknown. No lot information provided. Marketed without an approved NDA/ANDA: Lightning Rod capsules are being recalled because FDA analysis found it to contain an undeclared analogue of sildenafil. Sildenafil is the active ingredient in an FDA-approved product indicated for the treatment of male erectile dysfunction (ED), making this product an unapproved new drug. Chang Kwung Products.

Night Bullet Capsules, 1-count packets. Volume of product in commerce: 429,619 capsules. Lot #: B43N032, expiration date 10/2015. Marketed without an approved NDA/ANDA: Product contains analogues of sildenafil and tadalafil, which are active pharmaceutical ingredients in FDA-approved drugs used to treat erectile dysfunction (ED), making this product an unapproved new drug. Green Planet Inc.

Reumofan Plus, 30 tablets per bottle. Volume of product in commerce: 586 bottles. Lot #: 99515, expiration date 09/2016. Marketed without an approved NDA/ANDA: Product may contain undeclared active pharmaceutical ingredients diclofenac sodium, dexamethasone and methocarbamol. Reumofan Plus USA.

Warfarin Sodium Tablets, USP 2 mg. Volume of product in commerce: 960 bottles. Lot #: MM5767, no expiration date provided. Failed tablet/capsule specifications: A product complaint was received from a pharmacist who discovered that 3 tablets in a 1,000-count bottle were oversized. Zydus Pharmaceuticals USA Inc.

Recalls and Field Corrections: Drugs – Class II

Indicates a problem that may cause temporary or reversible health effects; unlikely to cause serious injury or death

Enablex (darifenacin) Extended Release Tablet, 15 mg per tablet. Volume of product in commerce: 188,680 capsules. Lot #: F1002, expiration date 12/2013. Failed impurities/degradation specifications: Unspecified degradation product. Warner Chilcott US LLC.

Ethambutol Hydrochloride Tablets, USP 400 mg, 60 tablets. Volume of product in commerce: 118 bottles. Lot #: 69968B, expiration date 03/2014. Discoloration: Out-of-specification result for description testing for a surface defect of ink. West-Ward Pharmaceutical Corp.

Excedrin Extra Strength (acetaminophen 250 mg,aspirin (NSAID) 250 mg and caffeine 65 mg), a) 2-count tablets in pouches, b) boxes of 50/2-count package. Multiple lots, multiple expiration dates. Defective container: Products are packaged in pouches that may not have been fully sealed. Novartis Consumer Health.

Excedrin Migraine (Acetaminophen 250 mg, Aspirin (NSAID) 250 mg and Caffeine 65 mg), 2-count tablets packaged in pouches. Multiple lots, multiple expiration dates. Defective container: products are packaged in pouches that may not have been fully sealed. Novartis Consumer Health.

Lisinopril Tablets, USP 2.5 mg. Volume of product in commerce: 51,704 bottles. Multiple lots, multiple expiration dates. Failed impurities/degradation specifications: Out-of-specification results for individual other unknown related Compounds were obtained at the 48 month time-point. West-Ward Pharmaceutical Corp.

Methylphenidate Hydrochloride Extended-Release Capsules (LA), 20 mg, 30 mg and 40 mg, 100-count bottle. Volume of product in commerce: unknown. Multiple lots, multiple expiration dates. Failed dissolution specifications: Product is being recalled due to out of specification dissolution results obtained during routine stability testing. Teva Pharmaceuticals USA, Inc.

No Doz, Max Strength (200 mg caffeine) caplets, 2-count caplets per pouch. Volume of product in commerce: 4,422,000 pouches. Multiple lots, multiple expiration dates. Defective container: Products are packaged in pouches that may not have been fully sealed. Novartis Consumer Health.

Olanzapine Tablets, USP, 10 mg. Volume of product in commerce: 18,721 bottles. Lot #: BS392004A, expiration date 09/2014. Defective container: This action is being taken as a precautionary measure due to the product being re-packaged in the U.S. using a filler material that removes or blocks less moisture than what is approved in the application. Torrent Pharma Inc.

DRUGS AND DIETARY SUPPLEMENTS (CONTINUED)

Parsel Plus (reference U.S. product: Excedrin Tension Headache) (acetaminophen 500 mg and caffeine 65 mg), packaged in 2-count pouches. Volume of product in commerce: 472,000 pouches. Lot #: 10121996, expiration date 07/2013. Defective container: Products are packaged in pouches which may not have been fully sealed. Novartis Consumer Health.

Terazosin Hydrochloride Capsules,10 mg, 100-count bottle. Volume of product in commerce: 6,267 bottles. Lot #: N07321, expiration date 06/2014. Label error on declared strength: Unopened, sealed bottle of terazosin hydrochloride (HCl) 10 mg capsules contained terazosin HCl 5 mg capsules. Teva Pharmaceuticals USA, Inc.

Zolpidem Tartrate Tablets, 5 mg, 10 tablets per blister, 10 blisters per carton, 100 cartons per box. Volume of product in commerce: 48,230 carton units. Multiple lots, multiple expiration dates. Unit dose mispackaging: This recall event is due to a random undetected packaging issue that could increase the potential for a small number of individual unit dose blisters to be packed with more than one tablet. American Health Packaging.

CONSUMER PRODUCTS

Contact the Consumer Product Safety Commission (CPSC) for specific instructions or return the item to the place of purchase for a refund. For additional information from the CPSC, call its hotline at (800) 638-2772. The CPSC website is www.cpsc.gov. Visit www.recalls.gov for information about FDA recalls and recalls issued by other government agencies.

Name of Product; Problem; Recall Information

Black & Decker® Spacemaker™ 12-Cup Programmable Under-the-Cabinet Coffeemakers. The coffee pot handle can break, causing cuts and burns to the consumer. Applica Consumer Products at (866) 708-7846 or www.aprecall.com.

Char-Broil® Gas Patio Bistro® Grills. The electronic ignition on the grill can ignite unexpectedly, posing a burn hazard. Char-Broil at (866) 671-7988 or www.charbroil.com.

Children's Pajamas and Nightgowns. The pajamas fail to meet federal flammability standards for children's sleepwear, posing a risk of burn injuries to children. Klever Kids at (855) 553-8375 or www.shopkleverkids.com.

Endura and Ambient LED Dimmable Light Bulbs. A lead wire in the bulb's housing can have an improper fitting, which can electrify the entire lamp and pose a shock hazard. Philips Lighting Co. at (800) 295-5147 or www.recall.philips.com.

Giant Bicycle XtC Bicycles and Seatposts. The bicycle seatposts on the affected bicycles and the after-market seatposts can crack, posing a fall hazard. Giant Bicycle Inc. at (866) 458-2555 or www.giant-bicycles.com-en-us/.

Holgate Toys Playmat Sets. The wheels on the wooden vehicles can detach, posing a choking hazard to young children. Holgate Toys at (855) 344-7488 or www.holgatetoy.com.

Husqvarna Closed Course/Competition Off-Road Motorcycles. The motorcycle's throttle cable can malfunction so the rider loses speed control, posing a crash hazard. Husqvarna Motorcycles at (888) 985-6090 or www.husqvarna-motorcyclesna.com.

Ikea Kritter and Sniglar Junior Beds. The metal rod connecting the guard rail to the bed frame can break in use, posing a laceration hazard. IKEA at (888) 966-4532 or www.ikea-usa.com.

Light-Up Toy Frogs and Ducks. The metal conductor pin on the bottom of the toys can come out, posing a choking hazard. Toysmith at (800) 356-0474 or www.toysmith.com.

Sleepharmony Metal Youth Beds. The surface paint on the pink-colored youth beds contains levels of lead that exceed the limits allowed by law. Glideaway at (800) 428-5222 or www.glideaway.com/recall/.

Sulley Character Stuffed Animal. The stuffed animal's eye can detach, posing a choking hazard to young children. Build-A-Bear at (866) 236-5683 or www.buildabear.com.

Tabletop Torches. Once lit, the glass citronella table torches can flare up and emit burning lamp oil onto consumers and property, posing fire and burn hazards. Big Lots at (866) 244-5687 or www.biglots.com.

PUBLICCITIZEN Health Letter

Outrage of the Month: Preventable Death and Lack of Insurance

Last month, the federal Centers for Disease Control and Prevention (CDC) published for the first time an analysis of changing patterns of preventable deaths from heart disease, stroke and hypertension. CDC found more than 200,000 avoidable deaths in 2010 — about one-fourth of the 800,000 annual deaths from these diseases. These preventable deaths disproportionately occurred among non-Hispanic blacks and residents of the South.

The *good news* was that between 2001 and 2010, the number of preventable deaths due to heart disease and stroke declined in people aged 65 to 74 years. "This may well be because they have access to health insurance and preventive screenings and treatment through their Medicare coverage," CDC Director Dr. Thomas Frieden said.

The *bad news* was that preventable deaths have fallen more slowly in those under age 65. More than half (56 percent) of preventable heart disease and stroke deaths occurred in this younger age group.

One important facet of the study is vastly different access to health care, dependent on age. The report stated:

> Whereas the percentage of adults aged 18–64 years with no health insurance increased from 17% in 2001 to 22% in 2010, it remained at less than 2% among adults aged 65 years or older (because of Medicare coverage in this population)…. The increase in percentage without insurance among the younger age groups might have limited their access to preventive screenings and early treatment of high blood pressure and elevated cholesterol….

The report also noted that "compared with persons aged 60 years or older, during 2009–2010, adults aged 18–39 years with high blood pressure experienced much lower rates of treatment and control and saw no improvements in those rates from 2001 to 2010."

The effects of going without health insurance are deadly for the 48 million people uninsured in this country. Unlike most developed countries, health care is not a basic right here. Although there will be some modest improvement with the Affordable Care Act, an estimated 20 to 30 million people will still be uninsured and therefore at increased risk of death, even after the law is implemented. This is why we and a growing number of people strongly prefer a single payer health care system, also known as improved Medicare for All. ✦

PUBLICCITIZEN
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