



founded 1881

May 7, 2012

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

Re: Using Innovative Technologies and other Conditions of Safe Use to Expand Which Drug Products Can Be Considered Nonprescription, 77 Fed. Reg. 12059 (February 28, 2012) [Docket No. FDA-2012-N-0171]

Dear Sir or Madam:

Founded in 1881, the Consumer Healthcare Products Association represents companies that develop, manufacture, and market over-the-counter, or OTC, medicines and dietary supplements, including those medicines that have been introduced through the prescription-to-nonprescription switch process. As such, we have an interest in the subject of the Federal Register notice referenced above. These comments supplement our March 22, 2012, presentation at FDA's public meeting on the subject.

Access to appropriate medicines without a prescription empowers consumers to take greater control over their health and provides tremendous public health benefits. Fueled in part by innovations in prescription-to-nonprescription switch, the U.S. market for OTC medicines is strong, providing consumers with accessible, affordable, and trusted self-care options available 24 hours a day, seven days a week in a wide range of retail outlets, including pharmacies, supermarkets, convenience stores, and other access points. A regulatory framework that accommodates greater use of tools and technologies in innovative switches can further increase access to medicines.

Summary

Americans today have a growing ability to access a greater depth and breadth of information than ever before, and they are doing so through a widening array of means. This includes the healthcare setting. This has significant implications for our industry and may assist in enhancing the safe use of OTC medicines.

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Prescription-to-nonprescription switches have evolved over decades, as have the types of evidence and studies to support them. Switches have moved beyond the common conception that OTC medicines are for self-diagnosed symptoms, or for a limited duration of use. Nicotine replacement therapy and orlistat to aid in weight loss, for example, have indefinite durations of use.

Ultimately, we envision a future where innovative switches are made possible by a regulatory framework that accommodates greater use of tools and technologies. Conditions of safe use or special conditions of use specific to the drug product would have a role in this future framework. Application of technologies on a case-by-case basis, supported by data, can provide a means to achieve novel, future switches in exceptional cases where reliance on the Drug Facts label alone might be insufficient to assure proper consumer selection and use. It may also be possible that, based on data, conditions of safe use could be eased or removed over time as more is known about the product's use.

But we believe the concept of conditions of safe use can be applied without changing the existing clear distinction between prescription and nonprescription drugs – the Durham-Humphrey drug definition. Our two-class system – prescription and nonprescription – works and has served the nation well. If a medicine can be safely and effectively used as an OTC, then it should be sold as an OTC.

Looking ahead, if some future prescription-to-OTC switches require fresh interpretations of existing policies on authority or enforceability, we support that effort and are committed to working with the Food and Drug Administration to identify and resolve issues, and to finding an appropriate legal and regulatory path.

We turn to the specific questions FDA raises in the Federal Register notice. We note that many of the questions in FDA's meeting notice speak to pharmacist dispensing of prescription medicines, including refills. This speaks to the practice of medicine and pharmacy and falls outside of our expertise and our comments. We have omitted questions outside of CHPA's expertise, but maintained the sequence and numbering of FDA's notice.

A. Types of Technology and Conditions of Safe Use

1. Can you suggest specific medical conditions or diseases for which consumers may benefit if the treatment drug were available as a nonprescription product with conditions of safe use?

CHPA supports a science-based, data-driven process to determine if conditions for safe use would be necessary to support appropriate consumer behavior in selecting and using a nonprescription medicine. While we would not expect conditions for safe use to be the norm, they should be considered, on a case-by-case basis, when it becomes clear that a product label alone is not sufficient to support a correct selection decision for the safe use of the nonprescription medicine. Self-selection decision criteria are in turn identified a priori between a switch sponsor and the agency. Conditions for safe use should not automatically be seen as

required for a specific list of diseases or conditions. Most important is the consumer's ability to choose the appropriate treatment.

2. What types of technologies (e.g. kiosks, computer algorithms) are currently in development that could assist in allowing drugs to be used safely and effectively in the nonprescription setting?

A significant number of technologies have been developed and are in use in today's marketplace in a variety of industries. These technologies could be easily reapplied to the nonprescription medicine setting. Examples include an expansion of the current Drug Facts label to include video or audio (talking) technology, online or in store questionnaires; 2D bar codes that can be scanned with a smart phone or with an in store scanner to allow access to much more information about the product; in store diagnostic testing such as blood pressure or glucose measurement; in store availability of educational material at the shelf or via an informational kiosk; kiosks that can administer a questionnaire, read data on a smart card, or control access to the product; or age, gender, or subpopulation restrictions controlled at check-out via scanning technology. Portable electronic medical records are another means to support safe use of medicines.

3. What other types of conditions of safe use (e.g., pharmacy monitoring or counseling) could be used to help ensure the safe and effective use of certain drug products as nonprescription products?

CHPA supports a definition of conditions of safe use that includes the type of technologies described above, where no pharmacist or other intermediary is needed. We see pharmacist or other intermediary (such as a nurse practitioner) involvement in the selection and safe use of a nonprescription product as an additional type of condition of safe use. The choice of the type of condition of safe should be driven by the switch sponsor. In the case of a sponsor electing to use a pharmacist or other intermediary for a specific purpose, as with any condition of safe use, this would be based on sponsor-generated criteria or data. Criteria on the pharmacist's value would be identified a priori between a switch sponsor and the agency. As to roles, the pharmacist or other intermediary could, as examples, perform diagnostic tests, interpret data presented on a smart card, or interpret data from a questionnaire. Another type of condition of safe use is a toll-free telephone number used, for example, to interact with consumers post-purchase to reinforce safe use, educate about appropriate use, or answer questions.

5. What data or other information exist on the use of conditions of safe use, including novel technologies, and on their effects on health care, access to medication, and/or disease and treatment education or awareness?

There are already instances with either nonprescription medicines or health conditions in general, where novel technologies have been applied to improve access, awareness, or outcomes. For instance, the use of a web-based tailored behavioral support program for smoking cessation

found significantly higher continuance abstinence rates compared to participants in a non-tailored support program.¹ The study showed how an algorithm allowing tailoring (assessment of characteristics relevant to smoking cessation, algorithms using the assessment data to target specific needs of the user, and a feedback protocol) improved outcomes for the specific therapy. The authors also noted the web-based, tailored program held the promise of combining benefits of high-reach media interventions with individually oriented clinics or self-help programs, and in a more cost-efficient manner.²

As another example in home-based healthcare, text messaging was more effective than printed material in improving knowledge, attitudes, and practices of mothers in taking care of their preschool children's oral health.³

Well beyond current nonprescription medicines, novel technologies show promise in increasing awareness in areas such as rapid HIV screening and patient knowledge, self-monitoring by patients at risk of heart failure in reducing hospitalization, and beyond.⁴

The larger point of referencing HIV or heart failure is not to suggest the conditions are candidates for nonprescription drugs under conditions of safe use, but rather to point out that novel technologies are growing in their usefulness and acceptance, and that there is growing recognition that use of technologies directly by consumers can assist them in managing their own health – be it in the form of products, services, or both. A literature review by Or, et al., for example, noted consumer health information technologies can empower patients to participate in information sharing and decision making, which enables them to be in more control and contribute to quality healthcare.⁵

Novel technologies are also growing in use and acceptance as the penetration of mobile devices and internet access continues to increase. There are now more wireless connections than there are people in the U.S. Just five years ago, that number equated to only 72% of the population.⁶ Internet penetration in the U.S. was 78% as of the end of 2011.⁷ More specific to health, health-

¹ Strecher, et al., "Randomized controlled trial of a web-based computer-tailored smoking cessation program as a supplement to nicotine patch therapy," *Addiction* 100: 682-688 (2005).

² Id.

³ Sharma, et al., "Mobile-phone text messaging (SMS) for providing oral health education to mothers of preschool children in Belgaum City," *Journal of Telemedicine and Telecare* 17: 432-436 (2011).

⁴ See, for example, Kurtz, et al., "Automated home telephone self-monitoring reduces hospitalization in patients with advanced heart failure," *Journal of Telemedicine and Telecare* 17: 298-302 (2011); Saifu, et al., "Impact of a kiosk educational module on HIV screening rates and patient knowledge," *Journal of Telemedicine and Telecare* 17: 446-450 (2011).

⁵ Or and Karsh, "A systematic review of patient acceptance of consumer health information technology," *Journal of the American Medical Association* 16: 550-560 (2009).

⁶ CTIA industry survey at http://files.ctia.org/pdf/CTIA_Survey_Year_End_2011_Graphics.pdf, access March 15, 2012. A separate research report from 2010 estimates 86% of people in the U.S. have a mobile device, or which 91% are SMS-enabled (i.e., can receive and send text messages), totaling more than 240 million individuals. Nielsen Mobile, Nielsen telecom practice group report on text messaging, 2010.

⁷ Miniwatts Marketing Group at <http://www.internetworldstats.com/>, accessed March 15, 2012.

related applications are among the highest three mobile or tablet applications of interest to employees, according to a survey by incentaHEALTH. The group pointed to a “more active push model that leverages technology employees are already using” to improve access to information and wellness programs.⁸ And consumers use technology, including mobile devices, for information on nonprescription medicines: One CHPA member reports that approximately two in five of the visits to their website in the first quarter of 2012 for a particular OTC medicine are from mobile devices. This is double what it was in the first half of 2011.

More specific to internet search for existing nonprescription medicines, Google reports that search queries for cold and flu medicines increased by 114% from January 2009 to January 2012.⁹ Pain management queries increased 110% over the same period.¹⁰

In sum, evidence exists that information technologies can lead to either better health outcomes or improve awareness. The use of novel technologies continues to expand, and consumers seek out technologies and, more importantly, information from them. There is no reason to think that nonprescription drugs should not be involved in these developments.

6. Are there data on how expanded access to medication or increased consumer education or awareness could affect patient or consumer behavior (e.g., by promoting patient compliance with a medication dosage regimen) or on health outcomes generally that would be relevant to the discussion of expanding the availability of nonprescription medications with conditions of safe use?

A number of studies have looked at the benefits of expanded access as seen through specific prescription-to-nonprescription switches, categories of switches, or through access to nonprescription medicines as a whole. Expanding the availability of nonprescription medicines holds out the promise of gaining greater value through more direct access.

For instance, the importance of access was captured in a study by Keeler on the increase in attempts to quit smoking following the switch of nicotine replacement therapy gum (a 178% to 180% increase in quit attempts in the year following the switch to nonprescription status) and nicotine replacement therapy patches (78% to 93% increase in quit attempts).¹¹ The authors also note survey data, consistent with published clinical studies, found no evidence of significant health costs from harm or injury from misuse due to a lack of a doctor’s supervision.¹²

In mild upper respiratory infections, through nonprescription access to symptomatic treatment, authors concluded their “study suggests that when adults use OTC medications to treat their

⁸ Davis, “Health info one of top 3 subjects employees look for when using apps,” *Employee Benefit News*: March 8, 2012.

⁹ Google presentation, March 2012. Copy on file at CHPA.

¹⁰ Id.

¹¹ Keeler, et al., “The benefits of switching smoking cessation drugs to over-the-counter status,” *Health Economics* 11: 389 (2002). See also Shiffman, et al., “Public health benefit of over-the-counter nicotine medications,” *Tobacco Control* 6: 306 (1997).

¹² Id.

symptoms, not only is there a symptom benefit, but there appears to be a substantial cost savings to the healthcare system and the economy alike.”¹³

When examined in reverse, utilization of pseudoephedrine-containing medicines for cold or allergy symptoms was reduced by 83% in states which moved these products to prescription status, leaving consumers in those states to either seek substitute medicine, suffer from congestion symptoms, or, for the remaining 17%, seek a doctor’s prescription for those medicines.¹⁴

In a study on the benefits of OTC heartburn medicines, the authors found both high patient satisfaction with available treatments, and savings to both consumers (from reduced drug and office visit costs) and the healthcare system (from fewer office visits) for heartburn.¹⁵

An increase in utilization of heartburn medicines was also found following the switch of proton pump inhibitors in a state employee health plan program involving formulary use of a pharmacy-adjudicated nonprescription PPI for a prescription indication in the state’s plan.¹⁶

More broadly, access to medicines through nonprescription status already provides value to Americans and the U.S. healthcare system. In 2011, CHPA commissioned Booz & Company to estimate the value of OTC medicines to the U.S. healthcare system.¹⁷ The study determined value for seven of the largest OTC treatment categories based on the cost of alternatives, including non-treatment, if OTC medicines were not available. It looked at behavior based on both actual experience with prescription-to-nonprescription switch case studies and a nationally representative survey of 3,200 Americans.

Among the study’s key findings:

- OTC medicines save the entire U.S. health care system – employer sponsored health plans; government programs; self-insured and the uninsured -- \$102 billion annually.
- For every dollar spent on OTC medicines, the health care system saves six to seven dollars.

¹³ Lipsky, et al., “An economic analysis for treating viral upper respiratory tract infection in the United States,” paper presentation to the World Self-Medication Industry Asia/Pacific regional conference, October 2004 (and Northwestern University press release, October 26, 2004).

¹⁴ Avalere Health, prepared for Consumer Healthcare Products Association, “Managing access to pseudoephedrine: potential impacts of a prescription-only policy versus real-time stop sale technology,” December 2011.

¹⁵ Mansfield and Callahan, Nielsen Company, prepared for Consumer Healthcare Products Association, “Benefits of over-the-counter heartburn medication to consumers and the healthcare system,” December 2008.

¹⁶ Harris, et al., “Effects on the cost and utilization of proton pump inhibitors from adding over-the-counter omeprazole to drug benefit coverage in a state employee health plan,” *Journal of Managed Care Pharmacy* 10: (2004).

¹⁷ Booz & Co. and Consumer Healthcare Products Association, “The Value of OTC Medicines to the United States,” January 2012.

- The availability of OTC medicines provides relief for 240 million people in the U.S., 60 million of whom would not seek treatment if OTCs weren't available. This speaks directly to increased utilization of treatment due to OTC access.
- Without access to OTCs, consumers would resort to more expensive medical care options for minor ailments; driving up costs throughout the health care system and, in some cases, receiving no treatment at all.
- The study also found that OTC medicines offer an *additional* \$23 billion in potential productivity benefits by keeping the American workforce at work and not at home or in doctor's offices.

This study captures the current systemic benefits in seven major OTC treatment categories. By using tools and technologies in addition to the OTC Drug Facts label to allow more innovative switches, the future holds even greater promise for positive public health benefits.

7. What types of studies could be conducted to evaluate the effects of conditions of safe use on the safety and efficacy of particular drugs and on behavior and health outcomes?

Regarding safety and efficacy, a sponsor should not be required to *re*-establish drug efficacy or safety in the nonprescription setting in the presence or absence of conditions of safe use. Drug efficacy is normally well-established before prescription drug approval. Drug safety is established before prescription drug approval, and before moving to nonprescription status, after thorough evaluation of post-marketing drug safety data. As a sponsor considers the switch of a prescription drug to nonprescription status, it is important to evaluate the product labeling and its impact on appropriate selection and safe use of the product. While we would not expect conditions of safe use to be the norm, if the data show that the label alone is insufficient to achieve appropriate selection and safe use of the product, conditions for safe use should be considered.

There are many types of research methodologies that are well suited to evaluate the effects of conditions of safe use on behavior and health outcomes. These research methodologies come primarily from the social and behavioral sciences fields, rather than from traditional clinical drug development research. The research is complex and requires the measurement of multiple behavioral endpoints. Prescription medicines as candidates for nonprescription status are typically evaluated in label comprehension, self-selection and actual use testing. Across the regulated industry, there are decades of experience with these research methodologies, and they continue to be refined. It is clearly possible to measure consumer behavior and the results that a technology or other intervention would have in a consumer setting. One example is the actual use study by Melin, et al, showing that the Mevacor Over-the-Counter Self-Management System could effectively guide consumers in the management of their cholesterol levels.¹⁸

¹⁸ Melin, et al., "A consumer use study of over-the-counter lovastatin (CUSTOM)," *American Journal of Cardiology* 94: 1243-1248 (2004).

8. *What types of studies could be conducted to evaluate the safety and efficacy of any technologies that might be relied upon as conditions of safe use?*

Technologies relied upon as conditions of safe use, such as those described in our response to Questions 2 and 3, should not require research as to their safety or efficacy. Rather, a sponsor should demonstrate that the drug product labeled for nonprescription use, plus the conditions for safe use, together, meet the success criteria agreed upon by the sponsor with FDA for appropriate self-selection and safe use of the nonprescription medicine. There are many types of research methodologies that are well suited to evaluate the effect of the technology as a condition of safe use, on consumer behavior. These are listed in our response to Question 7.

B. Pharmacy, Consumer, and Health Care Provider Issues

1. *Would this new paradigm increase consumer access to necessary medical care?*

As noted in Question 6 under part A, studies have shown the value of increased access to consumers themselves and to the healthcare system, and in many instances have shown greater utilization of treatment.

At the same time, this does not mean patient choice to use nonprescription medicines precludes consultation with doctors, pharmacists, or other healthcare professionals. For example, Americans treating heartburn symptoms with nonprescription medicines averaged 1.31 doctor visits per year, contrasted with those treating heartburn or GERD symptoms averaging 1.86 doctor visits per year.¹⁹

2. *Are data available about the number of consumers who require drug therapy for conditions or diseases but who currently do not take such medication because of the burdens associated with obtaining a prescription?*

While CHPA is not aware of specific data about the number of consumers who require drug therapy for conditions or diseases but who currently do not take medication because of the burdens associated with obtaining a prescription, research shows treatment gaps exist within our current system. Based on data from the 2005-2006 Centers for Disease Control's National Health and Nutrition Examination Survey, only 54.4% of adults aged 20 years and over who were told they had high cholesterol self-reported use of cholesterol-lowering medications.²⁰ The percentage of use of such medications increased by age with 14.7% of individuals aged 20-39 years reporting use, 47.9% of individuals aged 40-59 years reporting use, and 74.3% of individuals aged 60+ years reporting use.²¹ Additionally, a 2009 Kaiser Health Tracking poll found that 53% of Americans had cut back on medical care in the previous year due to cost

¹⁹ Mansfield and Callahan, *supra*.

²⁰ Ford, et al., "Trends in hypercholesterolemia, treatment and control among United States adults," *International Journal of Cardiology* 140: 226-235 (2010).

²¹ *Id.*

concerns. For 35% of Americans this included relying on home remedies and OTCs rather than visiting a doctor.²²

Further, recent data illustrates that per capita use of medicines in general is declining largely from reduced use of chronic medicines.²³ In conjunction, there was a 4.7% decline in doctor visits between 2010 and 2011 and during this same time period, emergency room visits increased 7.4%.²⁴ It is speculated that such increase may be due to high levels of uninsured patients associated with the continued high unemployment rates.²⁵ This data is indicative of a treatment gap in our healthcare system.

Seeking treatment can be particularly challenging in rural areas, given 25% of the U.S. population lives in rural areas, but only 10% of physicians practice in rural areas.²⁶

3. Would a lack of oversight from a practitioner, including involvement in diagnosing the condition or monitoring for drug interactions or other drug effects, be a concern? If so, how address?

Lack of oversight from a practitioner would not be a concern under this paradigm of nonprescription drugs with conditions of safe use, as such approvals would only occur where the Agency has been provided with testing and research that demonstrate that the “conditions of safe use” satisfy the requirements for OTC marketing. As mentioned earlier, this does not preclude the involvement of healthcare professionals.

There is nearly a 40 year history of prescription-to-nonprescription switches that includes many switches breaking what were thought to be the standard paradigm for OTC medicines. Many of these switches utilize new methods to assess consumer behavior, including label comprehension studies, self-selection studies, and actual use trials. Sponsors are continually developing new methods to answer the key questions about whether a medicine is appropriate for OTC use and developing tools for consumers to utilize in their healthcare decision making. For example, recent switches for frequently recurring heartburn used self-selection studies and actual use trials to show consumers could appropriately read and follow the label. Additionally, the switches for nicotine replacement therapy and orlistat for weight loss involved tools beyond the drug facts label such as helplines and online, personalized information to support optimal outcomes. As technologies continue to advance, additional tools enabling consumers to make appropriate healthcare decisions without oversight from a practitioner will be developed. Through a conditions of safe use mechanism, FDA will have the ability to evaluate these tools and appropriately approve a wider range of products for OTC use.

²² Henry J. Kaiser Family Foundation, “Health Care Costs: A Primer- Key Information on Health Care Costs and their Impact,” March 2009.

²³ IMS Institute for Healthcare Informatics, “The Use of Medicines in the United States: Review of 2011,” April 2012.

²⁴ Id.

²⁵ Id.

²⁶ National Rural Recruitment and Retention Network for Healthcare Professionals issue paper, 2006, accessed at <http://www.hrsa.gov/ruralhealth/media/102108ruralhealthslides.pdf>, May 4, 2012.

Further, the existing system regulating OTCs, with mandatory adverse event reporting, ensures safe use and monitoring of the marketplace once new OTC medicines are in the hands of consumers. While manufacturers of OTCs have adverse event reporting obligations, reporting by medical professionals in the point of care setting is voluntary. Other existing systems also provide means to monitoring potential negative outcomes, including those which capture emergency department visits (via NEISS-CADES at CDC) or poison center calls (via the National Poison Data System).

4. How might the new paradigm be expected to affect consumers financially or otherwise affect access to and delivery of health care generally?

Nonprescription medicines already play a very important role in the U.S. healthcare system. The study by Booz & Co. discussed in Question 6 of part A found that for every dollar spent on OTC medicines, the healthcare system saves \$6-\$7 dollars.²⁷ Without access to OTCs, consumers might turn to more expensive medical care options. It is estimated that without OTC medicines, additional Emergency Department visits would cost the U.S. healthcare system \$4 billion annually with a large percentage of the increased costs driven by patients on Medicaid and the uninsured.²⁸ Further, if consumers did not have access to OTCs, 56,000 medical practitioners would be needed to meet the demand for increased office visits by consumers seeking treatment.²⁹

As also discussed in Question 6 of part A, the prescription-to-nonprescription switch of nicotine replacement therapies provides a specific example of how switching an product to OTC can directly impact the health of Americans and the burden on the healthcare system: When nicotine replacement therapies used to quit smoking went OTC, there was a 150% to 200% increase in their use in the first year after the switch. That easier access enabled tens of thousands of smokers to use these products to help quit smoking.³⁰

Expanding access to OTC medicines through conditions of safe use would further increase savings to the healthcare system and allow medical practitioners to focus care on patients with the greatest needs.

5. Would expanding what could be considered nonprescription drugs under the new paradigm, and thus creating greater consumer access to needed drug products, reduce burden on ERs and individual health care providers, or otherwise increase the availability of these resources for other consumers? Are there other ways in which the new paradigm might reduce the burden on the health care system?

As discussed in the previous question as well as Question 6 of part A, the Booz & Co. study conducted for CHPA suggests that yes, there would be a marginally reduced burden on emergency departments and individual healthcare providers through expanded access.

²⁷ Booz & Co., supra.

²⁸ Id.

²⁹ Id.

³⁰ See Shiffman, supra, and Keeler, supra.

Further support for this premise is seen in the case of vaginal antifungals, where Lipsky found a 15% decline in the number of vaginitis visits from 1990 to 1994 could be attributed to the switch of OTC antifungals.³¹ A similar study found doctor visits for vaginitis fell by .66 per 100 females in the first year after the switch of such medicines.³²

9. What experiences have practitioners, pharmacists, and insurers had with state-authorized arrangements under which access to prescription drugs has been expanded that might be relevant to and inform our consideration of this paradigm (e.g., a collaborative practice agreement between a pharmacist and a practitioner that allows the pharmacist to dispense a prescription drug to a consumer who meets certain criteria under a standing or open prescription, when that consumer did not obtain a prescription directly from a practitioner, or that allows a pharmacist to refill a prescription after an initial prescription from a practitioner pursuant to a similar agreement)?

While CHPA represents the manufacturers of nonprescription medicines, we note that expanded access to prescription medicines is already occurring in many different ways. Currently, at least 43 states allow pharmacists to initiate, modify, and/or discontinue drug therapy pursuant to a collaborative practice agreement or protocol.³³ These agreements or protocols vary by state but include programs for blood pressure management³⁴, depression³⁵, emergency contraception³⁶, and diabetes care³⁷ and have shown success in enhancing access to medications and increasing medication adherence. Further, in Florida, by law, pharmacists are explicitly permitted to dispense certain drugs from a specified formulary using their professional judgment.³⁸

Additionally, all 50 states now allow pharmacists to administer immunizations when specified requirements are met.³⁹ Providing access to vaccines through pharmacies has enhanced consumers' abilities to obtain vaccinations through an increase in vaccination sites and extended hours of operation.⁴⁰

³¹ Lipsky, et al., "Impact of vaginal antifungal products on utilization of health care services: evidence from physician visits," *Journal of the American Board of Family Practice* 13: 178 (2000).

³² Gurwitz, et al., "The effect of an Rx-to-OTC switch on medication prescribing patterns and utilization of physician services: the case of vaginal antifungal products," *Health Services Research* 20: 672 (1995).

³³ National Association of Boards of Pharmacy, 2012 Survey of Pharmacy Law (2011).

³⁴ St Peter, et al., "Role of collaborative care models including pharmacists in improving blood pressure management in chronic kidney disease patients," *Curr Opin Nephrol Hypertens* 20: 498-503 (2011).

³⁵ Finley et al., "Impact of a collaborative pharmacy practice model on the treatment of depression in primary care," *American Journal of Health-System Pharmacy* 59: 1518-1526 (2002).

³⁶ Hayes, et al., "Reducing unintended pregnancy by increasing access to emergency contraceptive pills," *Maternal and Child Health Journal* 4: 203-208 (2000).

³⁷ Fera, et al., "The Diabetes Ten City Challenge: Interim clinical and humanistic outcomes of a multistate community pharmacy diabetes care program," *Journal of the American Pharmacists Association* 481: 181-190 (2008).

³⁸ FLA. ADMIN. CODE ANN. r. 64B8-36.003 (2012).

³⁹ National Association of Boards of Pharmacy, *supra*.

⁴⁰ See Canon, et al., "Vaccinations administered during off-clinic hours at a national community pharmacy: implications for increasing patient access and convenience (2012), accessed at <https://cdc.confex.com/cdc/nic2012/webprogram/Paper30288.html>, May 4, 2012.

Meanwhile, as to nonprescription medicines, pharmacists today play an important role in counseling consumers around how to select and use the medicine right for them. There may be unique instances where enhancing the pharmacist role could be part of a condition for safe use. As with other available tools, this should be a data-driven exception and considered on a case-by-case basis by the switch sponsor to include in an application.

C. Other Related Issues

1. How would insurance coverage of pharmaceuticals be affected by approving nonprescription products with conditions of safe use for widely prescribed prescription drugs under this paradigm?

In general, nonprescription medicines are not covered by insurance. Apart from Medicare, however, there is no reason why states in their employee benefit programs or in state Medicaid programs, or private insurers in their programs could not or would not cover nonprescription medicines under certain conditions. For example, a number of states cover certain nonprescription medicines in Medicaid.⁴¹

Insurers have included limited coverage for certain nonprescription medicines in step-therapy programs in areas such as GERD, dermatitis, or allergy.⁴²

Ultimately, as is the case today, coverage would vary among plans and geography, and market-based solutions would play a significant role.

2. How would out-of-pocket costs for the insured be affected by making prescription drugs available as nonprescription products with conditions of safe use?

While out-of-pocket costs would vary widely based on an individual's insurance coverage, overall for the healthcare system, for seven of the largest OTC treatment categories, on average, every dollar spent on OTC medicines saves \$1.60 on prescription spending.⁴³

Further, case studies support a common trend for product pricing to fall after a switch to nonprescription status. For instance, prices for allergy medicines switched in the past decade fell approximately 26% following a switch.⁴⁴

⁴¹ See, for example, Massachusetts, New York, and Wisconsin separate nonprescription co-pay levels at <http://www.medicaid.gov/Medicaid-CHIP-Program-Information/By-Topics/Benefits/Prescription-Drugs/Downloads/4QStatePrescriptionDrugRes.pdf>, accessed April 25, 2012.

⁴² See, for example, BlueCross BlueShield of Illinois step therapy description at http://www.bcbsil.com/provider/pharmacy/step_therapy.html, accessed April 25, 2012; and Tufts Health Plan automated prior authorization at <http://www.tuftshealthplan.com/pdf/StepTherapyMedications.pdf>, accessed May 5, 2012.

⁴³ Booz & Co., supra.

⁴⁴ Avalere Health, supra.

4. What proprietary, technological, economic, or competitive barriers might impede widespread implementation of this paradigm? To the extent such impediments exist, are there suggestions for mitigating or avoiding the impediments specific to this paradigm?

Given the early nature of FDA's thinking on nonprescription availability under conditions of safe use, we cannot provide a full assessment at this time as to which barriers will be most critical.

We would note, however, that self-service access to nonprescription medicines is a critical element in taking full advantage of their value. The shift of pseudoephedrine-containing nonprescription medicine to behind-the-counter status for reasons apart from the safety or effectiveness of the medicines themselves led to significant reduction in their utilization.⁴⁵

Adding multiple barriers to access would increase the risk of not gaining the intended benefit of nonprescription medicines with conditions of safe use.

A corollary is seen in the lack of consumer utilization of a number of prescription-to-nonprescription medicines in the UK where they were accompanied by lengthy pharmacy protocol questionnaires, in at least one instance exceeding 20 questions.

Another area requiring further consideration by industry and other stakeholders concerns the protection of intellectual property investments that would be needed to support technology-enabled conditions of safe use, including data exclusivity, patent protection, and/or copyright and trademark protection. In the same vein, the current standard for exclusivity requires the sponsor to conduct clinical investigations (other than bioavailability studies) that are essential to the approval of the new drug application.⁴⁶ As currently interpreted by the agency, a rigorous large-scale validation study on a condition of safe use tool or technology would not qualify as an essential clinical unless the actual drug product was a part of the study. This becomes an impediment to implementation when a sponsor cannot justify the investment in such a study in the absence of exclusivity. We therefore recommend that the agency work with industry and other stakeholders to consider how to identify new mechanisms of exclusivity or a reinterpretation of what qualifies as an investigation essential to the approval of a switch application.

The continued openness of the agency in encouraging discussion of these issues, as the agency demonstrated by holding the March 22-23 public meeting on nonprescription availability with conditions of safe use, may help mitigate or avoid impediments.

A final suggestion to mitigate or avoid impediments to a paradigm allowing nonprescription availability with conditions of safe use is to consider incremental, rather than sweeping, changes to existing regulation or law. As the agency demonstrated with the prescription-to-nonprescription switches of nicotine replacement therapies, orlistat for weight loss, and

⁴⁵ Johnson, IRI, presentation to the Consumer Healthcare Products Association Regulatory and Scientific Conference, May 10, 2007.

⁴⁶ See 21 USC 355(j) (Federal Food, Drug, and Cosmetic Act sec. 505(j)).

levonorgestrel for emergency contraception, tools, approaches, and technologies beyond the traditional Drug Facts label can be used to support a switch to nonprescription status.

In contrast, suggestions of prescription and nonprescription dual status for the same drug (ingredient strength, dosage form, and indication), changes to the definition of a nonprescription drug, or imposition of conditions of safe use in the absence of supporting data would be a significant impediment to widespread implementation. Impediments such as these would undermine how switch sponsors plan switch approval programs and raise novel challenges to the U.S. market-driven system.

5. Would overall health care costs decrease if this paradigm were instituted?

As discussed in Question 6 of part A, and in other questions throughout this submission, CHPA believes and evidence from the availability of nonprescription medicines today strongly suggests that yes, increasing the availability of nonprescription medicines, including nonprescription medicines with conditions of safe use, would have an impact in addressing healthcare cost pressures. We caution, however, that our optimism is based on a paradigm involving application of technologies on a case-by-case basis, supported by data, as a means to achieve novel, future switches in exceptional cases where reliance on the Drug Facts label alone might be insufficient to assure proper consumer selection and use.

Conclusion

The nearly 40 year history of prescription-to-nonprescription switches providing value to consumers directly and to the healthcare system suggests there is continued promise for prescription-to-nonprescription switches in the future, including under conditions of safe use.

There is also a long history of switches breaking what were thought to be the standard paradigm for OTC medicines. Many of these breakthrough switches utilized new methods to assess consumer behavior, including label comprehension studies, self-selection studies, and actual use trials. In the cases of nicotine replacement therapy and orlistat for weight loss or control, the approval of these switches went well beyond the Drug Facts label to include a wealth of tools – such as helplines; or on-line, personalized information – to support optimal outcomes, including behavior modification. These were evolutionary changes, achieved over decades, that benefitted consumers and our healthcare system.

As we look to the future, we know that today's consumers know more, have access to greater information, and can do more than ever before, thanks in large part to the ubiquitous nature of technology. Our collective challenge is to acknowledge these developments and to keep up with consumer capabilities and demands.

As we think about the promise of using more tools and technologies to support innovative switches, we look forward to a continuing engagement with the agency. In doing so, there are

three core principles under existing law and under the existing regulatory approach that have served our healthcare system well:

1. Self-selection – the ability for a consumer to pick up a product and read and understand its label – is the cornerstone of OTC medicines. Even with the addition of tools beyond the package label, such as nonprescription medicines under conditions of safe use, a consumer-centered approach remains of highest importance.
2. Tools or conditions of safe use are means to address benefits and risks unique to each switch and should be applied as an exception and on a case-by-case basis. As history has shown, not all switched products would require special conditions for use, and there will be switches that continue to rely on the Drug Facts label. Further, application of conditions of safe use on a case-by-case basis will assure that the design and application of tools are data-driven. A place of sale restriction such as a behind-the-counter requirement in the absence of data designed to answer a key question for a particular switch does not meet the data-driven test.
3. The existing approach of a clear distinction between prescription and nonprescription drugs – the Durham-Humphrey drug definition – has and should continue to serve our society well. Consumers understand the clear distinction between prescription and OTC products. If a medicine can be safely and effectively used as an OTC, then it should be sold as an OTC. Finally, pharmacist dispensing of prescription medicines, including refills, speaks to the practice of medicine and pharmacy. We view drugs under such a scenario as prescription.

We thank the agency for providing the opportunity to submit these comments and for calling the March 22-23 public meeting, and look forward to continuing to identify ways to enhance the value that nonprescription medicines provide to American consumers and our healthcare system.

Submitted,

/signed/

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