

## GUIDING PRINCIPLES FOR ADDRESSING RX-TO-OTC SWITCH IN THE CONTEXT OF NOVEL CONDITIONS OF USE FOR NONPRESCRIPTION MEDICINES

R. WILLIAM SOLLER, THEODORE TONG, MARY ANNE KODA KIMBLE, RANDY JUHL, Y. W. FRANCIS LAM, LORIE RICE

### Members of The Self Care Collaborative:

**R. William Soller, PhD** - Health Sciences Professor of Clinical Pharmacy and Executive Director –  
Center for Self Care, UCSF School of Pharmacy, San Francisco CA

**Theodore Tong, PharmD** - Associate Dean, Professor, Exec. Dir. - Arizona Poison & Drug Information Center, University of Arizona

**Mary Anne Koda-Kimble, PharmD** - Dean, Clinical Professor of Pharmacy, UCSF School of Pharmacy, San Francisco CA

**Randy P. Juhl, Ph.D** - Vice Chancellor and Distinguished Service Professor of Pharmacy, University of Pittsburgh

**Y. W. Frances Lam, PharmD** - Professor of Pharmacology, Associate Professor of Medicine University of Texas

**Lorie G. Rice, MPH** - Associate Dean for External Affairs, UCSF School of Pharmacy, San Francisco CA

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Over the past 40 years, Rx to OTC switch has been an important process for offering greater access to important medications for responsible self care by consumers<sup>1,2,3,4</sup>. FDA's public hearing of March 22-23, 2012 represents an important step to gain input on a new paradigm of nonprescription availability<sup>5</sup>. The hearing offered a public exploration of ways to approve certain drugs that would otherwise require a prescription, for nonprescription use under drug-specific conditions of safe use.

The Self Care Collaborative is a group of academic-based health professionals with interests in Rx-to-Nonprescription switch and related conditions of use. Its contributors have variously served on the OTC Drugs Advisory Committee, consulted from an academic perspective to industry, and/or presented on numerous occasions to that committee. As a group, we generally encourage public hearings as a means to bring stakeholders together to share common and divergent viewpoints, the amalgamation of which can potentially spur drug development while ensuring public safety.

In its announcement of the public meeting, the agency has listed many of the key questions to address potential new nonprescription conditions of use, including those relating to limitations in the settings of nonprescription drug availability, information technologies, use of diagnostic devices, the types of studies needed to support decisions of approval, current patterns of use of medications, and other public health and economic issues. All are potentially extensive fields of inquiry, and as a result we have chosen to use our collective experience on Rx-to-OTC

switch to define over-arching principles that are needed to help guide discussions on novel approaches to self-selection, actual use and comprehension of labeling, as well as the design of studies in support of switch. The following table represents eight important guiding principles for Rx-to-OTC switch in today's environment.

**Table 1.**

Eight Guiding Principles for Rx-to-Nonprescription Switch
<ol style="list-style-type: none"> <li>1. <b>Self-care should be recognized as a pillar of health care</b>, and therefore defined as a national U.S. priority.</li> <li>2. <b>Equity in self-care</b> is a fundamental principle that applies to overcoming barriers to self care, such as language, literacy and technology and should be applied to all switches.</li> <li>3. <b>Flexibility in the approaches used to support consumer self-selection</b> is important and may encompass a learned intermediary with accountability (e.g., pharmacist) or other IT solutions to product self-selection.</li> <li>4. <b>New study designs</b> are needed to support novel conditions of nonprescription use.</li> <li>5. <b>The process of self care under novel conditions of use</b> must be driven by a principle of simplicity in design.</li> <li>6. <b>Evidence-based feedback</b> in the form of postmarketing surveillance on novel conditions of nonprescription use should be shared in public advisory committee meetings.</li> <li>7. <b>Economic data</b> should not be included in FDA advisory committee decisions on Rx and OTC drug approvals, per current policy.</li> <li>8. <b>Predictability</b> is essential, as achieved through (a) a very clear underlying national strategy (Principle #1); (b) defined expectations as to the dataset necessary to support novel switches; and (c) refinement as needed through industry guidance on the necessary evidence base for novel conditions of nonprescription use.</li> </ol>

**First, self-care through responsible evidence-based use of nonprescription medicines and diagnostics should be recognized as a pillar of health care, and therefore defined as a national priority.** We advocate development of a national strategic focus to the reclassification of prescription medicines to nonprescription status, including over-the-counter (i.e., general sale across all distribution channels) as well as restricted channels of distribution (e.g., pharmacy only). This should emanate from the U.S. Health and Human Services Secretary and be driven through the Food and Drug Administration to ensure that self care – e.g., as manifested in novel product development to support an expanded role of self care – is recognized as an essential pillar of health care and thus as a national priority. The U.K. National Health Service has been a government-based leader in developing a self care national strategy to expand access to safe and effective medicines<sup>6,7,8</sup>.

**Second, equity in self-care is a fundamental principle that applies to overcoming barriers to self care, such as language, literacy and technology.** As such self-care equity should be an underlying principle of the novel conditions of use that are under consideration by FDA. A core question for more complex switches is: How do cultural perspectives, socio-economic, and health literacy issues affect patient/consumer safety considerations that are fundamental to defining specific novel conditions of use? This question should be a component of more complex switch proposals.

**Third, while recognizing the nonprescription OTC label is important for consumer self-selection of drug dose and dose regimen, a learned intermediary with accountability may be a preferred choice for nonprescription drug and device availability.** For example, a learned intermediary such as a pharmacist may be a preferred choice when, among possible other examples:

- The algorithm for product selection is too complex;
- Benefit/risk decisions are not narrowly defined, requiring judgment at times of selection and/or monitoring;
- Referral to a primary care physician is an important step in the selection algorithm and in monitoring;
- Interpretation of diagnostic findings from a nonprescription device (e.g., borderline results) requires professional judgment;
- Understanding the label information is essential to safe use.

The situation has changed since FDA and the Government Accounting Office last assessed pharmacy only classification of medicines<sup>9</sup>. Today, pharmacists are recognized as important partners of a patient's health care team for providing medication therapy management (MTM) services. Pharmacists are recognized as providers of medication therapy management for persons with chronic diseases, and the medication literature supports the clinical and humanistic benefits of pharmacist care MTM services<sup>10,11</sup>.

Thus, FDA should draw on the experience of the pharmacy-only classification in the United Kingdom as it relates to the scope and nature of professional support given to community pharmacists when medicines are reclassified (e.g., standardized materials for consumer counseling, training staff personnel, and protocols for diagnosis, self selection and referral). Such standardization (e.g., through use of diagnostic and selection protocols, quick reference guides, patient education sheets, staff training manuals) is important to ensure consistency in counseling across community pharmacy practitioners and across pharmacies. For example, the Royal Pharmaceutical Society has provided practice protocols, quick reference guides, staff training manuals and other materials for generic version of "P" (pharmacy) medicines. See references 12 and 13 as examples<sup>12,13</sup>. A list of selected examples of U.K. Pharmacy ("P") medicines can be found in Table 2<sup>14</sup>.

**Table 2.**

Selected "P" Conditions (n=26) in the United Kingdom The Self Care Collaboration, March 2012 (derived from MHRA website)	
1. Allergic rhinitis	Budesonide, Flunisolide, Fluticasone
2. Analgesic, general	Diclofenac (3 dTx duration)
3. Analgesic, topical (acute trauma/joints tendons)	Diclofenac sodium
4. Analgesic, topical (non serious arthritic conditions)	Felbinac
5. Analgesic, throat lozenge	Flurbiprofen
6. Analgesic, Migraine	Sumatriptan
7. Analgesia, Migraine adjunct for nausea/vomiting	Prochlorperazine
8. Antacid combo ingredient, local anesthetic	Oxetacaine
9. Athlete's foot	Griseofulvin
10. Conjunctivitis, acute bacterial	Chloramphenicol
11. Conjunctivitis, allergic	Lodoxamide trometamol
12. Contraception, emergency	Levonogestrel
13. Diarrhea: Adjunct for rehydration	Diphenoxylate
14. Enterobiasis (pinworm)	Medendazole
15. Herpes labialis	Penicyclovir
16. Indigestion (Excessive fullness w/or w/ heartburn)	Domperidone
17. Irritable Bowel Syndrome	Mebeverine
18. Lipid control (lipid lowering agent, moderate risk CVD)	Simvastatin
19. Menstrual Period, heavy bleeding	Tranexamic acid
20. Mouth ulcers	Triamcinolone
21. Onychomycoses (toenail fungus)	Amorolfine
22. Psoriasis/Eczema	Alclometasone
23. Eczema	Clobetasone
24. STD: Chlamydia trachomatis	Azithromycin
25. Travel sickness (nausea/vomiting)	Hyoscine
26. Urticaria, acute or chronic	Hydroxyzine

Fourth, Rx-to-nonprescription switch involving novel conditions of use should be evidence based. In this regard, new types of studies designs may be needed to support novel conditions of nonprescription use, such as:

- Diagnostic device comprehension studies (instruction manual)
- Redesign of the actual use study to accommodate a learned intermediary (e.g., pharmacist) or proposed IT solution to self selection and/or monitoring;
- Validation studies of consumer-required self-selection surveys which might be undertaken with community pharmacists, or through a community pharmacy technician with referral to a pharmacist as needed;
- Validation and FDA approval of technology, such as kiosks, smart pad or smart phone apps supporting pharmacist-mediated or consumer-driven self-selection;
- Usability of integrated foreign language components to self selection, monitoring etc.;
- Postmarketing surveillance of pharmacist-documented self-selection, or technology-based self-selection; among others.

**Fifth, novel approaches to defining novel conditions of use for specific medicines should also focus on the process of self care and be driven by a principle of simplicity in design.** The positive public health impact of an approval for a nonprescription drug with novel conditions of use may be hindered by lack of consumer and practitioner acceptance of complex risk mitigation strategies. The implication of this is that actual use studies might be designed with a greater emphasis on consumer/patient and practitioner satisfaction with the process of self care. Simplicity is also important to help ensure equity in self care. Close attention should be paid to simplicity in design regarding: labeling and practitioner-mediated self-selection; documentation; post-marketing surveillance.

**Sixth, new approaches to postmarketing surveillance may be needed to support novel conditions of nonprescription use.** Postmarketing surveillance methods may need to be tailored to proposed novel conditions of use in order to achieve appropriate evidence-based feedback to further improve the nonprescription availability, just as current Rx and OTC medicines are in a continuous cycle of revision, for example, regarding label warnings. Hence, an iterative model of continuous quality improvement should be considered in relation to accurate diagnosis, appropriate product selection, and success of self-monitoring, and adverse experience surveillance.

**Seventh, Rx and OTC drug approvals are not based on evaluations of economic data.** Nonprescription drug development should not be stifled by attempting to change this policy. In the end, it is up to the company to decide if their market projections provide a viable opportunity to pursue an Rx to nonprescription switch with novel conditions of use. However, FDA's inquiry into novel nonprescription conditions of use is more broadly cast to consider potential public health ramifications of changing channels of drug distribution for improved access, in the context of associated costs changes, to determine whether or not improved access through nonprescription status is sensitive to such changes. Thus, as important as this issue may be, it should nevertheless be pursued on a separate health policy track unrelated to specific drug approvals.

**Eighth, predictability is an essential objective for facilitating drug development efforts and stakeholder input.** For novel conditions of use, there should be: (a) a very clear underlying national strategy; (b) defined expectations as to the dataset necessary to support switch; (c) follow-up guidance to help industry sort through the drug and device development paths to new conditions of nonprescription use. The benefit of this is predictability, which not only aids companies in forecasting development costs and potential return on investment, but is also of interest to FDA advisory committee members and other stakeholders as a means to optimize feedback to FDA.

In conclusion, FDA has taken an important step in developing a comprehensive list of questions to develop the public dialogue on novel nonprescription conditions of use. Crafting the approaches to answering these questions through the eight principles recommended in these comments offers a strategic approach to opening new avenues of self care to the American public.

**Corresponding author: Dr. Bill Soller, UCSF School of Pharmacy. email: [sollerrw@pharmacy.ucsf.edu](mailto:sollerrw@pharmacy.ucsf.edu); [rwsoller@gmail.com](mailto:rwsoller@gmail.com); 415-632-6434 (cell)**

## REFERENCES

1. Soller RW. Evolution of self-care with over-the-counter medications. *Clinical Therapeutics*. 1998;20 (Supplement C).
2. Juhl R. Prescription to over-the-counter switch: a regulatory perspective *Clinical Therapeutics*, 1998;20:C111-C117.
3. Soller RW. Prescription-to-over-the-counter switch criteria. *Drug Information Journal*. 2002;36:309-17.
4. Soller RW, Chan PV, and Shaheen C. OTC Considerations for Expanding Access to Nonprescription Medicines: A Critical Synthesis of Questions from FDA to its Advisory Committees on Rx-to-Switch. *SelfCare* 2011;2(5):117-138. <http://www.selfcarejournal.com/index.php?issue=12>
5. Food and Drug Administration. Using Innovative Technologies and Other Conditions of Safe Use To Expand Which Drug Products Can Be Considered Nonprescription; Public Hearing. *Federal Register* 2012;77(39): 12059-12062.
6. U.K. Department of Health. Self care - A real choice: Self care support - A practical option. January 12, 2005. Available at: [http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH\\_4100717](http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_4100717)
7. U.K. National Health Service. What is Self Care? October 11, 2011. Available at: <http://www.nhs.uk/Planners/Yourhealth/Pages/Whatisselfcare.aspx>
8. Department of Health (2006a) Supporting People with Long Term Conditions to Self Care: A Guide to Developing Local Strategies and Good Practice. DH, London.
9. U.S. Government Accounting Office. Nonprescription Drugs: Value of a Pharmacist-Controlled Class Has Yet to Be Demonstrated. August 2005. Available at: [http://www.chpa-info.org/media/resources/r\\_4266.pdf](http://www.chpa-info.org/media/resources/r_4266.pdf)
10. Chisholm-Burns, M et al. US Pharmacists' Effect as Team Members on Patient Care Systematic Review and Meta-Analysis. *Med Care* 2010;48: 923-93.
11. Giberson S, Yoder S, Lee MP. Improving Patient and Health System Outcomes through Advanced Pharmacy Practice. A Report to the U.S. Surgeon General. Office of the Chief Pharmacist. U.S. Public Health Service. December 2011. Available at: <http://www.usphs.gov/corpslinks/pharmacy/documents/2011AdvancedPharmacyPracticeReporttotheUS SG.pdf>
12. Royal Pharmaceutical Society. Tamsulosin – 400 micrograms. Practice Guidance. <http://www.rpharms.com/practice--science-and-research-full-guidance/otc-tamsulosin-full-guidance.asp#overall>
13. Royal Pharmaceutical Society. OTC Tamsulosin. A Quick Reference Guide. 2010. <http://www.rpharms.com/support-pdfs/otc-tamsulosin-quick-reference-final.pdf>
14. Medical and Healthcare products Regulatory Agency (MHRA). Recent Reclassifications. POM to P. Available at: <http://www.mhra.gov.uk/Howweregulate/Medicines/Licensingofmedicines/Legalstatusandreclassification/Recentreclassifications/index.htm#11>