

# PHARMACOPEIAL FORUM

**35**

**NUMBER 2**

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## **Featured in This Issue**

USP has identified the following content areas in the March-April 2009 issue of *Pharmacopeial Forum* as noteworthy for the pharmaceutical industry worldwide.

- **Interim Revision Announcements Pertaining to *USP 31–NF 26* (official March 1, 2009)**
  - Galantamine Tablets
- **USP Redesigns *Pharmacopeial Forum***
- **USP Implements Guideline on Use of Accelerated Revision Processes**
- **USP Issues Call for Candidates for 2010-2015 Council of Experts, Its Expert Committees, and Its Advisory Panels**

A detailed listing of the Table of Contents of the March-April issue of *Pharmacopeial Forum* follows.



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This updated directory reflects assignment changes based on 2005–2010 Expert Committees. The general USP telephone number, (301) 881-0666, may still be used for general inquiries or when a particular Expert Committee is not identified. The fax number is (301) 816-8373.

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**USP REDESIGNS PHARMACOPEIAL FORUM.** USP has begun implementing a redesigned *Pharmacopeial Forum (PF)* as part of an initiative that will result in a completely online, freely available *PF* beginning in January 2011. Starting with this issue of *PF*, specific changes will include:

1. *Interim Revision Announcements (IRAs)* and *Errata* will join *Revision Bulletins* on [www.usp.org](http://www.usp.org) in a “New Official Text” section, as well as being printed in *PF*.
2. *In-Process Revision* monographs will appear in the new redesigned monograph format.
3. A new *Proposed IRA* section is now added to distinguish proposed IRAs from regular in-process revisions.
4. The “*Preview*” section has been removed.

The following sections will **not** be removed from the *PF* at this time, as originally reported in 35(1), and will remain in their original locations:

- The Priority New Monograph Items List (Drug Substances, Drug Products, and Excipients)
- The Reference Standards Abeyance List

General information about the USP *Pharmacopeial Forum* redesign initiative can be found at the *PF* Redesign FAQ page on [www.usp.org](http://www.usp.org). Contact Susan de Mars, J.D., USP Chief Legal Officer ([sdm@usp.org](mailto:sdm@usp.org)) with any questions about the *PF* redesign. If you have any questions about *PF* subscriptions, please contact USP Customer Service [[custsvc@usp.org](mailto:custsvc@usp.org) or 301-881-0666, 1-800-227-8772 (U.S. and Canada), or 00-800-4875-5555 (Europe)].

**USP IMPLEMENTS GUIDELINE ON THE USE OF ACCELERATED PROCESSES FOR REVISIONS TO THE USP–NF.** Sections 9.02 and 9.03 of the Rules and Procedures of the 2005–2010 Council of Experts specify various processes (Accelerated Revision Processes) that can be used to make revisions to the *USP–NF* official more quickly than through USP’s Standard Revision Process. USP, in collaboration with the Compendial Process Improvement Project Team, has posted the Guideline on the Use of Accelerated Processes for Revision to *USP–NF*, with an official date of January 1, 2009. The Guideline is available at [www.usp.org](http://www.usp.org).

USP’s Standard Revision Process calls for publication of a proposed revision in the *Pharmacopeial Forum (PF)* for a 90-day notice and comment period and, after the revision is approved by the relevant USP Expert Committee, publication in the next *USP–NF* or Supplement, as applicable. Accelerated Revision Processes, which include *Interim Revision Announcements*, *Revision Bulletins*, and *Errata* do not always require notice and comment and allow for a revision to become official prior to the next *USP–NF* or Supplement.

USP has issued this Guideline to delineate the circumstances under which these Accelerated Revision Processes are utilized. The Guideline includes a Decision Tree that specifies the criteria that are applied by USP in considering whether an Accelerated Revision Process is appropriate rather than USP’s Standard Revision Process. This Guideline also addresses the use of delayed official dates for revisions made through the Standard Revision Process, where such revisions have broad industry impact and require additional time to implement.

Contact Susan de Mars, J.D., USP Chief Legal Officer ([sdm@usp.org](mailto:sdm@usp.org)), with any questions.

**USP ISSUES CALL FOR CANDIDATES FOR 2010–2015 COUNCIL OF EXPERTS, ITS EXPERT COMMITTEES, AND ITS ADVISORY PANELS.** In accordance with the Bylaws of the USP Convention, USP is issuing a *Call for Candidates* for the 2010–2015 Council of Experts. The 2010–2015 Council of Experts includes 20 Expert Committees in the areas of Nomenclature, Small Molecules, Biologics and Biotechnology, Excipients, General Chapters, Reference Standards, Compounding, Food Ingredients, and Dietary Supplements. In the 2010–2015 cycle, USP is expanding the number of Expert Panels (formerly Advisory Panels) that report to Expert Committees. These new Expert Committees and Expert Panels align with the new USP Strategic Plan, which focuses on expanding and enhancing USP’s core compendial and standards-setting activities.

The ability to add Expert Panels according to the needs of USP introduces flexibility and scalability into USP’s activities. USP plans to continue to attract global base experts, and therefore encourages any qualified individual to apply. Importantly, this approach also enables USP to closely align USP’s documentary and reference standards activities for a more efficient standards-setting process.

Specific Expert Committees and Expert Panels for which USP is seeking candidates are listed on the 2010–2015 Council of Experts area of the USP website ([www.usp.org](http://www.usp.org)). The deadline for applications for the Council of Experts is **December 31, 2009**. The deadline for applications for Expert Committee members is **May 15, 2010**. Recruitment for Advisory Panels members will be continuous.

For further information, contact Angela G. Long, Vice President, Volunteer and Organizational Affairs ([agl@usp.org](mailto:agl@usp.org) or [nominate@usp.org](mailto:nominate@usp.org)).

**USP ANNOUNCES REVISIONS TO GALANTAMINE TABLETS.** The Biopharmaceutics Expert Committee (BPC EC) has revised the Galantamine Tablets monograph that was proposed in *Pharmacopeial Forum* volume 34(6). The revisions expand the impurities list, add *Dissolution Test 2*, and revise the Q value. The revised monograph was proposed in *Pharmacopeial Forum* volume 34(6) with an intended official date of April 1, 2009. The official text is presented in this *Pharmacopeial Forum* as an *Interim Revision Announcement*.

Contact Margareth R. C. Marques, M. Sc., Ph.D. with any questions (301-816-8106 or mrm@usp.org).

**PHARMACOPEIAL FORUM PUBLIC REVIEW AND COMMENT PERIOD DEADLINES.** The USP welcomes and encourages interested parties to submit comments and data regarding potential, proposed, or adopted (official) standards. In accordance with the Rules and Procedures of the 2005–2010 Council of Experts, USP has implemented a 90-day comment period by providing a deadline for each issue of *PF* unless otherwise stated in the individual briefing. The listing of comment period deadlines and the targeted official publications appears below.

Pharmacopeial Forum	Comment Deadline	Targeted Official Publication	Release Date	Official Date
PF 34(6)	February 15, 2009	USP 33–NF 28	November 2009	May 1, 2010
PF 35(1)	April 15, 2009			
PF 35(2)	June 15, 2009	USP 33–NF 28 1st Supplement	February 2010	August 1, 2010
PF 35(3)	August 15, 2009			
PF 35(4)	October 15, 2009	USP 33–NF 28 2nd Supplement	June 2010	December 1, 2010
PF 35(5)	December 15, 2009			
PF 35(6)	February 15, 2010	USP 34–NF 29	November 2010	May 1, 2011
PF 36(1)	March 31, 2010			

All official revisions are published in the annual edition or *Supplements to USP–NF* (twice yearly). Between these publications, official revisions are published in *PF* in the *Interim Revision Announcement* section and incorporated in the upcoming *Supplement* or book. They may also be published as *Revision Bulletins* on [www.usp.org](http://www.usp.org) in the “New Official Text” section. The official publication in which an *IRA* is incorporated will depend upon publica-

tion deadlines. See table below. The electronic version of *USP–NF* is updated as each *Supplement* becomes available and, therefore, contains all official text up to and including the contents of the latest *Supplement*. The table below outlines the publications and their release and official dates, and the book or supplement which supersedes them.

**Publication Schedules**

Publication	Release Date	Official Date	Superseded by
USP 32–NF 27	November 1, 2008	May 1, 2009	1st Supplement to USP 32–NF 27
IRA [PF 35(1)]	January 1, 2009	February 1, 2009	2nd Supplement to USP 32–NF 27
1st Supplement to USP 32–NF 27	February 1, 2009	August 1, 2009	2nd Supplement to USP 32–NF 27
IRA [PF 35(2)]	March 1, 2009	April 1, 2009	2nd Supplement to USP 32–NF 27
IRA [PF 35(3)]	May 1, 2009	June 1, 2009	USP 33–NF 28
2nd Supplement to USP 32–NF 27	June 1, 2009	December 1, 2009	USP 33–NF 28
IRA [PF 35(4)]	July 1, 2009	August 1, 2009	1st Supplement to USP 33–NF 28
IRA [PF 35(5)]	September 1, 2009	October 1, 2009	1st Supplement to USP 33–NF 28
IRA [PF 35(6)]	November 1, 2009	December 1, 2009	2nd Supplement to USP 33–NF 28
USP 33–NF 28	November 1, 2009	May 1, 2010	1st Supplement to USP 33–NF 28

## INSTRUCTIONS TO AUTHORS

Contributions in the form of original research reports, evaluations of new and existing compendial methods, and other commentaries and articles relevant to drug standards or to *USP–NF* revision will be considered for publication in *Pharmacopeial Forum* under the section *Stimuli to the Revision Process*. Manuscripts are received with the explicit understanding that they have not been published previously in any language or medium and that they are not simultaneously under consideration by any other publication.

All manuscripts are subject to review by USP headquarters staff, Committee members, or qualified outside referees, and if accepted for publication they will be subject to editing by USP staff. Accepted manuscripts become the property of the USP Convention (USPC) and may not be subsequently published elsewhere without written permission from the USPC. Authors are also responsible for obtaining permission for reprinting any illustrations that have been published elsewhere.

**Abstract**—Include an abstract of not more than 250 words stating the purpose and the results or conclusions of the article.

**Style and Usage**—*Stimuli* articles generally follow the current *Chicago Manual of Style* except in scientific usage (numbers, abbreviations, etc.). For the latter, authors should use the current *AMA Manual of Style* or the current *ACS Style Guide*. Authors may usefully consult a current copy of *Pharmacopeial Forum*.

**References**—Consult the current *AMA Manual of Style*, which is generally consistent with the National Library of Medicine's *Recommended Formats for Bibliographic Citation*. A current copy of *Pharmacopeial Forum* will offer examples of reference formats.

**Copyright**—Copyright transfer documents will be sent to authors after manuscripts have been accepted for publication.

**Contact Person**—USP will designate a Scientific Liaison in the Documentary Standards Division as the corresponding author. This ensures that USP receives all comments generated by the *Stimuli* article. Authors should contact the Scientific Liaison if they would like to receive copies of comments generated by their *Stimuli* articles.

**Submission Instructions**—Manuscripts must be submitted both as an electronic file and as a printed copy of the electronic file. Submit the text in Microsoft® Word or another current word-processing application. The preferred format for graphics submitted electronically is tagged image file format (TIFF). Photocopies are not acceptable. Manuscripts submitted for publication should be addressed to:

*Pharmacopeial Forum*  
Executive Secretariat, USP  
12601 Twinbrook Pkwy.  
Rockville, MD 20852

## A Discussion of Net Water Gain for Water Vapor Transmission Rate Determinations

S. Yoon, Eli Lilly and Company, D. Sparks, Eli Lilly and Company, S. Selke, Michigan State University<sup>a</sup>

**ABSTRACT** This *Stimuli* article discusses the USP General Chapter *Containers—Permeation* (671) method to determine net water gain. This article introduces a proposal to change the procedure based on an analysis of the steady-state conditions of the plastic walls of containers. The analysis discussed in this paper shows that the plastic walls of *controls* have a higher water concentration than do the plastic walls of *test containers* and that the current Water Vapor Transmission Rate calculation in USP (671) is not theoretically correct. Although this proposal does not have an important impact on test results, this method change advances the scientific basis by providing more accurate test results.

### INTRODUCTION

USP General Chapter *Containers—Permeation* (671) (1) provides a method to determine the net water gain of anhydrous calcium chloride or other desiccant in a plastic bottle container–closure system. The net water gain is used to calculate water vapor transmission rate (WVTR) of the sealed container–closure system. The current method employs test container–closure systems filled with desiccant (*test containers*) and container–closure systems filled with glass beads (*controls*). The net water gain is determined by subtracting the weight gain of *controls* from the weight gain of *test containers*. This is then used as the weight gain of desiccant only. This method is based on two assumptions: 1) the glass beads do not absorb water, and 2) the *test container* walls and *control* walls absorb the same amount of water.

However, the net water gain calculated in this manner is not theoretically correct because the water content of the plastic walls of the *controls* is not the same as the water content of the plastic walls of *test containers*. Theoretically, the plastic walls of *controls* achieve a higher water concentration than do the plastic walls of *test containers* at the steady-state conditions of the test. Therefore, the subtraction of a higher water concentration in *controls* from the lower concentration in *test containers* results in a net water gain that is lower than the actual net water gain. Further, this would result in a WVTR that is lower than the actual WVTR.

Plastic (e.g., polyethylene and polypropylene) container walls reach a steady state of water concentration. The steady-state condition is a gradient that depends on the storage conditions and the conditions of the headspace in the container. This gradient is maintained as constant during testing if the conditions of storage and

the container headspace are constant. This *Stimuli* article proposes an alternative approach for determining net water gain and calculating WVTR of plastic container–closure systems (bottles and blisters).

### DISCUSSION

#### 1. Water Vapor Transmission into Plastic Container Walls

**Theory**—Water vapor from a high vapor pressure environment permeates plastic container walls of a sealed container that has a low water vapor pressure internal environment. This is described by Equation (1), Fick's Second Law of Diffusion:

$$\frac{\partial C}{\partial t} = D \frac{\partial^2 C}{\partial x^2} \quad (1)$$

where  $C$  is the concentration of water in the plastic container wall,  $t$  is time,  $D$  is the diffusion coefficient, and  $x$  is the spatial coordinate in the direction of transfer (2,3). >

*Figure 1* describes Fick's Second Law of Diffusion graphically and shows a graphical representation of water concentration across the plastic container wall as a function of time ( $t$ ). The total change in water concentration across the plastic container wall with time is directly proportional to the change in concentration gradient with the permeant penetration depth. At a steady-state rate of water transmission, the concentration gradient remains constant across the plastic wall.

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