

IPEC-Americas News

April, 2008

Perrigo Company Becomes IPEC-Americas Member

During April, the Perrigo Company, a global healthcare product supplier whose headquarters is in Allegan, Michigan USA became the 57th IPEC-Americas member. In addition to developing, manufacturing and distributing active pharmaceutical ingredients (APIs), Perrigo also manufactures and markets prescription and over-the-counter (OTC) pharmaceuticals, and both nutritional and consumer personal care products. In fact, the Company is the world's largest manufacturer of OTC products for the private label store brand market. It presently has manufacturing facilities in the United States, Mexico, Israel and the United Kingdom.

Ms. Kari Dylhoff (Associate Director, Material Quality Assurance Operations) and Michael Bradley (Director of Quality, Perrigo South Carolina) have been named as the company's principal day-to day contact persons for IPEC-Americas matters; along with Paul Weninger (Vice President, Global Quality and Compliance) and Louis Yu (Senior Vice President, Global Quality and Compliance).

It is expected that Perrigo representatives will be active participants on IPEC-Americas committees as this has been the company's history in other industry associations of which it is a member. For example, John T. Hendrickson, Executive Vice President of Perrigo Global Operations and Supply Chain, was recently elected to a second term as Chairman of the Consumer Healthcare Products Association (CHPA).

Project Team Comments to Proposed Revision of USP General Notices

On April 15, important comments to the proposed revision of USP General Notices that appeared in the January-February Pharmacopeial Forum were

submitted by its internal General Notices Project Team. The Project Team is composed of designates from seven industry associations and FDA and currently is chaired by IPEC-Americas representative, Neil Schwarzwaldner of Eli Lilly & Company.

Seven major comments were included in the submission which Team members believe have special importance. These are summarized below.

1. USP Legal Status – The Project Team recommends that text emphasizing the importance of USP/NF standards under U.S. law and those of other countries that follow USP and NF should be included in the General Notices in Section 2, Official Status and explained as follows:

“USP-NF is recognized in the laws and regulations of many countries throughout the world. In the United States, the Federal Food, Drug, and Cosmetic Act (FD&C Act) defines the term ‘official compendium’ to include the USP and NF or any supplement to them. FDA may enforce compliance with official standards in USP-NF under adulteration and misbranding provisions of the FD&C Act. These provisions extend broad authority to FDA to prevent entry to or remove designated products from the United States market based on standards in the USP-NF. Recognition of USP and NF in different countries varies; applicable laws and regulations should be consulted.”

2. General Notice Reference to Need for GMP – Here the Team objected to removal of reference to the need for preparing official substances “...according to recognized principles of good manufacturing practice...” that appears in current General Notices and recommends that the text be strengthened and included in Section 2.2; as follows:

“Official articles are prepared according to recognized principles of good manufacturing practice. Official substances are prepared from ingredients complying with specifications designated to ensure that the resultant substances meet the requirements of the compendial monographs.

Conformance with the official USP-NF tests and acceptance criteria is, by itself, insufficient for an article to be considered of USP-NF quality. It is also necessary that the article be produced in a manner consistent with the principles of good manufacturing practices applicable to the drug substance, excipient, or product, and that appropriate control of supply chains be maintained. Consult relevant requirements of the governing regulatory agency.”

3. Section 3.1 Conformance to Standards/Applicability of Standard

The Project Team agreed that although articles must be able to meet compendial requirements, it pointed out that "...routine testing is not the only means of demonstrating compliance, nor even necessarily the best means." The Team also noted that proposed text in the draft did not meet the principle in the current General Notices which states that data derived from manufacturing process validation studies and from in-process controls could provide "...greater assurance that a batch meets a particular monograph requirement..." This should be retained, the Team recommends, because it addresses the principle of "will pass if tested".

4. 5.2 Ingredients and Added Substances – In its comments the Team noted several concerns about the organization and wording in the draft section and recommended that the term "excipient" should be used instead of "added substances" when referring to materials added to drug products. The following text was proposed:

"Added Substances in Official Articles

Additives in Official Substances

Official substances may contain additives (e.g., antioxidants, emulsifiers, flow enhancers) only where specifically permitted in the individual monograph. Where such addition is permitted, the label must indicate the name(s) and amount(s) of any additive(s).

Excipients in Official Products

Suitable additives or excipients such as antimicrobial agents, bases, carriers, coatings, colors, flavors, preservatives, stabilizers, and vehicles may be included in the formulation of an official product to enhance its stability, usefulness, or elegance, or to facilitate its preparation, unless otherwise specified in the individual monograph.

Additives or excipients which impair the bioavailability, therapeutic efficacy, or safety of the official product are prohibited."

Should the USP not accept these changes, the Team added, it recommended that revisions be delayed to Phase 2 of the process and Text in the current General Notices be retained.

5. Section 1, Title and Revision – In this section the Team recommended that information pertaining to errata (errors) in official text and subsequent

corrections be explained so that readers understand that the corrected text is effective “immediately”/when issued. The Team added:

“We believe the GNs is the appropriate place to note the existence of errata and its location in order to ensure awareness by all users of USP. The suggested text below is taken from the standard introduction used for Errata in IRAs, with added clarification that errata ‘are not revisions’ and that corrected text ‘is considered effective immediately.’

Errata are published as part of the Interim Revision Announcements in the Pharmacopeial Forum. Errata are not revisions to official text, but are considered to be items erroneously published that have not received the approval of the Council of Experts and that do not reflect the official requirements. Corrected text published as Errata is considered effective immediately.

In addition to the placement of this text at the end of section 1, Title and Revision, we propose that the standard text introducing Errata in the IRAs be revised to match. We also suggest that a cumulative list of all errata for a volume or supplement be posted at the USP web site to improve awareness, especially for users who do not subscribe to the PF.”

6. Preservation, Packaging, Storage and Labeling – The Project Team agreed with the current decision to delay restructuring of these requirements until Phase 2 to allow further evaluation by USP expert committees, FDA, and industry. However, the Team recommends that existing text in current USP and NF General Notices Section 9.1, Storage under Non-Specific Conditions be used in the interim which says:

“For articles recognized in the National Formulary, regardless of quantity, where no specific storage directions or limitations are provided in the individual monograph or stated in the article’s labeling, it is understood that conditions of storage and distribution include protection from moisture, freezing, excessive heat, and, where necessary, protection from light.

For excipients stable over a wide temperature range, the phrase ‘No Storage requirements specified’ in the Packaging and storage statement of the monograph would be appropriate” should be restored and moved to the Phase 2 process for consideration there as well.

7. Use of Year of Publication – According to its comment:

“The Project Team supports using the year to identify USP and NF books and supplements, e.g. USP-NF 2009, as suggested in the Explanatory Note. This approach would simplify references to main volumes and supplements (e.g., USP-NF 2009(1) for USP32-NF27 Supplement 1) and be more meaningful to users. The year designation would then correspond to the year of the effective dates of the main volumes and supplements. We also recommend that the effective date of the main volumes be printed on the front covers, as is now done on supplements, to clarify that the main volumes are effective May 1.”

**Temple Spring FDA Industry Conference
Includes Ingredient Safety Session**

A special break-out session on Safety of Pharmaceutical Ingredients has been added to the morning program of the May 6 Spring 2008 FDA/Industry Conference sponsored by the Temple University School of Pharmacy. Speaking will be Dr. Richard Friedman, Director of the Division of Manufacturing and Product Quality within CDER’s Office of Compliance at FDA and David R. Schoneker, IPEC-Americas Chairman.

During Dr. Friedman’s remarks it is anticipated that he will discuss FDA’s current efforts to deal with supply chain security issues and steps the agency is taking and plans to take to prevent future situations such as have occurred with heparin, contaminated toothpaste, pet food, and glycerin.

Mr. Schoneker plans to provide an update on current IPEC activities in connection with the excipient supplier qualification process, GMP and identity auditing throughout the entire distribution chain, and need for full traceability of material from manufacture until its receipt and acceptance by the ultimate user, e.g. verification of an excipient’s “pedigree.”

IPEC-Americas Members Who They Are

As noted elsewhere in this issue of IPEC-Americas News, the Council's membership now stands at 57. The total includes 35 full member companies which either manufacture excipients for use in pharmaceuticals or dietary supplements or are those which use excipients in their finished products; 1 affiliate, which is a division of a full member company; and 21 associates.

Associates are individuals, companies, and other bodies that supply specialized services of different kinds to full members and therefore are interested in IPEC-Americas programs and activities. At the present time associate members include:

- 8 companies that distribute excipients manufactured by other firms to companies that use them in finished product formulations;
- 6 small consulting firms;
- 2 publishers of pharmaceutical industry magazines;
- 2 companies that develop and produce ingredients, blends, etc. on a contract basis for others;
- 2 professors of pharmacy and pharmaceuticals; and
- 1 non-profit scientific research organization.

Next IPEA GMP Auditing Workshop To Be Held In Houston, Texas

A comprehensive three day excipient GMP Auditor Training Workshop offered by International Pharmaceutical Excipients Auditing (IPEA) will be held September 23-25, 2008 in Houston, Texas at the Marriott Houston Hobby Airport hotel. IPEA is IPEC-Americas GMP auditing subsidiary company that also conducts on-site training for company auditors and offers

its workshops on a global basis using the IPEC-PQG GMP Guide and related materials.

The Houston workshop on excipient auditing is designed to benefit both makers and users of pharmaceutical excipients. Training will analyze the essential elements of excipient good manufacturing practice for materials intended for use in pharmaceuticals, dietary supplements, food, or as industrial chemicals and explains how applicable product standards differ.

The workshop also will focus on excipient GMP compliance and attendees will learn auditing techniques, report writing, observation, and classification techniques that relate to the manufacture of excipient ingredients. It contains exercises to hone observation skills through participation in a hands-on mock excipient GMP audit. Participants also gain a thorough understanding of risk-based excipient auditing and learn how to assess whether an excipient GMP quality system can achieve a satisfactory level of compliance. Finally, attendees learn how to differentiate the requirements for excipient manufacture from those of APIs.

The three-day auditing workshop will be facilitated by Dr. Arthur Falk, IPEA President and Chief Executive Officer and Dr. Irwin Silverstein, IPEA Vice President and Chief Operating Officer.

For more information and for registration details – please contact Valeria Stewart at ipeainc@aol.com telephone: 703-351-5266. The workshop fills quickly, so early registration is recommended. The next US workshop is scheduled for December 2 – 4, 2008 in St. Louis, Missouri.

Online Regulatory Conference Registration Now Available!

Online registration for IPEC-Americas 2008 Regulatory Affairs Conference, September 15-16, at the Embassy Suites Old Town in Alexandria, Virginia is now available! Cost for IPEC-Americas member company employees will be \$795; non-members \$895; \$150 for government/USP/academic faculty registrants; and \$50 for graduate students in pharmacy and related sciences. Hotel fees are extra, but an excellent rate has been obtained for conference attendees. Hotel reservations should be made early, as those who tried to

register late last year discovered. The Embassy Suites Old Town is a popular stay-over site for Alexandria visitors; it contains a fine restaurant, is adjacent to the city's historical district, and is directly across the street from a Washington Metro station that services Reagan National Airport and the District of Columbia. To make reservations call: 1-800-362-2779 or 703-684-5900. To receive the \$239 rate you need to mention IPEC-Americas.

A tentative conference program is printed elsewhere in this bulletin. Looking forward to seeing you – September 15 & 16!

2008
IPEC-Americas Regulatory Affairs Conference

Tentative Program

Monday, September 15

7:30 AM – 5:00 PM Registration

7:30 AM – 8:00 AM Continental Breakfast

8:00 AM – 12:00 PM Morning Session

- **Welcoming Remarks** **Janeen Skutnik, Pfizer**
- **Chairman's Report** **David Schoneker, Colorcon**
- **Panel Session: Supply Chain Integrity**
Moderator: Phyllis Walsh, Schering-Plough

Speakers:

Excipient Manufacturer – Dale Carter, Archer Daniels Midland

Excipient Distributor – Linda Herzog, Mutchler, Inc.

Pharmaceutical Manufacturer – Robert Wiens, Eli Lilly & Co.

(Invited)

FDA spokesperson – TBA

U.S. Customs representative – TBA

Panel discussion and audience questions to follow

12:15 PM – 1:30 PM Luncheon

1:30 PM – 5:00 PM Afternoon Session

- **Panel Session: Excipient Qualification Next Steps**
Moderator: Dr. Maria Jacobs, Pfizer
Planned Topics/Speakers:
Excipient Pedigree – Dr. Arthur Falk, IPEA
Quality Agreements – TBA
New Excipient Qualification Guidance – TBA
- **Panel Session: Excipient Information Protocol (EIP) Implementation**
Moderator: TBA
Planned Topics/Speakers:
Excipient Manufacturer’s Perspective – TBA
Distributor’s Perspective – TBA
User’s Perspective – TBA

5:30 PM – 6:30 PM Reception

6:30 PM – 8:30 PM Dinner

Speaker – Janet Woodcock, MD (invited)
Director, Center for Drug Evaluation and Development
Food and Drug Administration

Tuesday, September 16

7:30 AM – 5:00 PM Registration

7:30 AM – 8:00 AM Continental Breakfast

8:00 AM – 12:00 PM Morning Session

- **Panel Session: Excipient Quality by Design – Functionality and Performance**
Moderator: Janeen Skutnik, Pfizer
Planned Topics/Speakers: from the perspective of the EDQM, USP, an excipient manufacturer and a pharmaceutical manufacturer

- **Panel Session: Novel Excipients and their Approval Process**
Moderator: Christopher DeMerlis, Colorcon

Program under Development

12:30 PM – 1:45 PM Luncheon

2:00 PM – 5:00 PM Afternoon Session

- **Panel Session: New and Co-Processed Excipients**
Moderator: Janeen Skutnik, Pfizer
Planned Topics:
How co-processed excipients are defined
How co-processing takes place in excipient manufacturing
What the regulatory implications are
- **Discussion Topic: The Need for a Global Excipient Forum and Whom Should Participate**

Adjourn

Jay Goldring, Ph.D., Authors Article for *American Pharmaceutical Review*

The March/April 2008 issue of *American Pharmaceutical Review* includes an article by Jay Goldring, Ph.D., (Director of Toxicology, Wyeth Consumer Healthcare) on “Novel Excipients: The New Pharmaceutical Frontier?” In his article, Dr. Goldring explores the challenges facing drug manufacturers who are hesitant to utilize novel excipients or ingredients in drug formulations and how the IPEC independent safety review evaluation can assist them and FDA in granting approval for new formulations.

The definition of “novel excipients” from the U.S. perspective is provided along with discussion of the regulatory “Catch 22” and how that acts as a barrier to innovation. Dr. Goldring explains how the IPEC Novel Excipient Evaluation Procedure can provide a short term fix until a new regulatory paradigm can be developed which includes independent safety evaluation of

excipients. This type of a system could offer a low risk solution to the current shortage of new drug formulations, he concludes.

For additional information or to view the article in its entirety, (subscription required) please access:

<http://www.americanpharmaceuticalreview.com/ViewArticle.aspx?SID=3xqzmv45nsfxco55oiszii55&ContentID=3381&ID=3381>

Dr. Goldring also serves as a member of IPEC-Americas Executive Committee as Vice Chair Industrial Relations, and is also Chair of IPEC-Americas Safety Committee.

Important Industry Meetings May & June 2008

May 5-7

Advanced Practices in Pharmaceutical Tablet and Capsule Technology
Hilton Garden Inn, Las Vegas, Nevada
Register: <http://epd.engr.wisc.edu/webJ726>

May 6

Spring 2008 FDA/Industry Conference
Philadelphia Marriott Downtown at the Convention Center
Register:
www.temple.edu/pharmacy_qara/pdf/2008CONF_ONLINE_REG_FORM4.pdf

May 8-9

CHPA Regulatory & Scientific Conference
The Fairmont, Washington, D.C.
Register: www.chpa-info.org

May 19-21

AAPS Workshop – Drug Discovery Strategies and Critical Issues for
Clinical Candidate Selection

South San Francisco Conference Center, South San Francisco, CA

Register: www.registration@aaps.org

May 20-21

10th Annual FDA and the Current Challenges of GMPs Conference

Sponsored by University of Rhode Island College of Pharmacy

Hyatt Regency New Brunswick, New Brunswick, NJ

Register: www.pharmaconference.com

May 20-21

6th Edition European Pharmacopoeia Training Session

Sponsored by EDQM and the New Jersey Pharmaceutical Quality Control
Association

Sheraton Woodbridge Place Hotel, Iselin, New Jersey

Register: <http://www.edqm.eu/site/PhEur-Training-Session-New-Jersey-USA-260.html>

June 2-3

Statistical Design of Experiments for Pharmaceutical Process R&D and
Manufacturing:

A Practical Approach

Hilton Garden Inn, Las Vegas, Nevada

Register: <http://epd.engr.wisc.edu/webJ997>

June 2-4

Pharmaceutical Water Systems Design and Validation

Marriott Raleigh Crabtree Valley Hotel, Raleigh, North Carolina

Register: www.pdatraining.org/raleigh

June 17-18

ExcipientFest Conference & Pharma Expo
Radison SAS Hotel, Little Island, Cork, Ireland
Register: www.excipientfest.com

June 22-25

2008 AAPS National Biotechnology Conference
Metro Toronto Convention Centre, Toronto, Ontario, Canada
Register: www.aapspharmaceutica.com/nationalbiotech

June22-26

44th DIA Annual Meeting
Boston Convention and Exhibition Center, Boston, Massachusetts
Register: www.diahome.org

**IPEC-Americas Committee Meetings
May 2008**

May 20

QbD Product Development Committee	8:15am – 12:00pm	F1
Quality Agreement	8:15am – 12:00pm	F2
Excipient Composition	1:00pm – 5:00pm	F1
Executive Committee (by invitation only)	5:15pm – 8:30pm	F1/F2

May 21

Good Manufacturing Practices	8:15am – 12:00pm	ABC
Excipient Qualification	1:00pm – 5:00pm	ABC
General Update Briefing (open to all members)	5:30pm – 7:30pm	ABC

May 22

Compendial Review/Harmonization Committee	8:15am – 12:00pm	ABC
Regulatory Affairs	1:00pm – 5:00pm	ABC

Please note – All IPEC-Americas meetings currently are scheduled to be held at the Buchanan Ingersoll law offices at 1700 K. Street N.W., Suite 300, Washington, D.C. Notice of attendance is needed in advance by rodgersjw@bipc.com