Excipient Focus Group
3Q 2012 Newsletter

Newsletter of AAPS Excipient Focus Group

A Message from Excipient Focus Group Chair and Chair-Elect
Dear EFG Members,

As we are approaching the 2012 AAPS national meeting, we take pride in what has been accomplished through great contribution of EFG members in 2012 activities. The monthly meetings were a very useful forum for members to find synergies in supporting activates. It is our privilege to be part of the steering committee and as we strive to improve our group’s efficiency, please do not hesitate to contact us with your suggestions and thoughts on ways to excel.

EFG—Current Activities and 2012 Primary Goals
We welcomed this year, Firouz Asgarzadeh, as chair elect. The current chair, Ajit Narang, will be leading the group during 2012, until AAPS annual meeting in Chicago at which point Firouz will be taking over his responsibilities and the 2013 chair-elect will be selected through member voting.

Below are a summary of EFG goals in 2012:
- Member outreach through
  - Periodic newsletters
  - Website discussion forums
- AAPS programming influence/participation
  - Webinar/other distance learning programs
  - Influence NBC & AM programming
- Monitor and participate in excipient-related publications
  - Operational:
    - Monthly teleconference with steering committee
    - Participation in monthly teleconference and support affiliated section activities [FDD (primary section), PPB and RS (secondary sections)]

See you at: 2012 AAPS Annual Meeting:

2012 AAPS Annual Meeting and Exposition
October 14-18, 2012
McCormick Place, Chicago

Excipients Focus Group Face-to-Face Membership Meeting @ AAPS: Mon Oct 15th @ 12:15 – 1:15 pm

Agenda includes:
- Introduction of EFG Leadership
- 2012 Objectives and Achievements
- 2013 Objectives
- Opportunities for greater involvement in the focus group and networking with fellow AAPS members with similar interests.

Mission Statement
To promote understanding of excipients and their use in pharmaceutical formulations. This includes understanding of excipient quality, functionality, drug-excipient interactions and regulatory considerations.

The Excipients Focus Group can be reached at: http://www.aaps.org/inside/focus_groups/Excip/index.asp

EFG is affiliated with FDD, PPB and RS Sections.

Website Suggestions/comments: Wei_Min@Lilly.com

Chair-Elect 2013
EFG is accepting nominations for chair-elect 2013. Please contact Ajit (ajit.narang@bms.com) or Firouz (firouz.asgarzadeh@evonik.com) for details.
Excipients Focus of Themed Journal

This issue provides latest advances in research and use of pharmaceutical excipients. Articles cover a broad range of topics in the utilization of novel materials and the functionality and testing of excipients.

2013 Programming Jamboree meeting!
Jamboree is the meeting of AAPS leadership to identify focus areas for programming for the annual meeting the following year.

The meeting was held on August 16 and 17 in Alexandria, VA. All sections and focus groups were present, including the excipient focus group. EFG was represented by Firouz. EFG presented several ideas for 2013 themes, which covered QbD aspects, excipient functionality, impurities in excipients, use of excipients as actives, process for introduction of new excipients and related topics. These ideas were presented to and discussed with the AAPS programming committee and the AAPS leadership that attended the meeting.

EFG leadership encourages all members to submit programming proposals for the 2013 annual meeting through the EFG programming sub-committee. Please contact Ajit (ajit.narang@bms.com) or Firouz (firouz.asgarzadeh@evonik.com) for details.

EFG Webinar
EFG proposed two webinars on the theme of “Mechanisms of Excipient Effect on Oral Drug Bioavailability” for 2013 calendar year. These webinars will address the unexpected influence of excipients on oral drug bioavailability. The first webinar will focus on inter-individual variability in drug absorption due to differences in the influence of excipients on biologic processes (1). Pharmacogenetic responses to drugs formulated with polymeric excipients is an emerging area of research (2-6) that has recently also been evaluated in the clinic (7, 8). This webinar will address how the impact of excipients on the genetic response of target cells can influence cellular responses to therapeutic agents, and their clinical potential for improving therapeutic outcomes. The second webinar will discuss binding interactions of drugs with excipients that can affect formulation and analytical method development and may reduce drug bioavailability (9). Using published case studies (10-15), the presenter will discuss identification of threshold where the drug-excipient binding interactions may become relevant for analytical method development and oral drug bioavailability. Methods of characterization and risk-assessment of impact of binding on drug bioavailability will be discussed. In addition, potential implications of such interactions on selection of excipients, changes in composition during development, and the tolerable range of excipient variability will be addressed.

A thorough mechanistic understanding of these excipient effects is not only expected in the current quality-by-design drug product development regulatory paradigm, but can also significantly impact clinical drug development. Regulatory and clinical implications of these effects will be discussed in both presentations.

Bibliography:
EFG leadership welcomes members to submit additional webinar proposal to the EFG programming sub-committee. Please contact Ajit (ajit.narang@bms.com) or Firouz (firouz.asgarzadeh@evonik.com) for details.

Invited Article on Current Topics in Excipients

Starting with the 3Q2012 newsletter, the EFG would like to introduce invited articles on topics of current interest in excipients for publication in the EFG newsletters. This issue brings forth a paper on elemental impurities in excipients by Dave Schonecker. Members are encouraged to submit their proposals for articles for the EFG newsletter. Please contact Ajit (ajit.narang@bms.com) or Firouz (firouz.asgarzadeh@evonik.com) for details.

Awards and Honors

The Ralph Shangraw Memorial Award

The Ralph Shangraw Memorial Award is awarded to any person who has provided an outstanding research in the study of excipients or excipient-related technology. The award recognizes research achievements broadly in the field of pharmaceutical excipients including but not limited to research that contributes to an understanding of the basic science underlying excipients functionally; excipient safety, including the development of test methods and standards; the development of new excipients or novel use of existing in new applications; and the development of rational compendial/regulatory standards for excipients. The award recipients will receive $10,000.

IPEC Foundation Graduate Student Awards

The IPEC Foundation is sponsoring five annual awards to acknowledge excellence in research conducted at graduate level pertaining to the field of excipients. The awards focus on recent significant contributions to formulation science and technology with excipients brought about by highly innovative research. All interested candidates engaged in their final year of graduate studies leading to Ph.D. degree (or to be awarded in the year of submission) are encouraged to apply. The awardees will receive a cash award of $1,000 and a commemorative plaque. If selected, the applicant must attend the 2011 AAPS Annual Meeting &

Current EFG Leadership

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<tr>
<th>Role</th>
<th>Name</th>
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<tr>
<td>Chair</td>
<td>Ajit Narang</td>
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<td>Chair-elect</td>
<td>Firouz Asgarzadeh</td>
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<td>Past Chair</td>
<td>Thomas Farrell</td>
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<td>Secretary</td>
<td>Ken Liljegren</td>
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<td>Webinars</td>
<td>Susan Lum &amp; Chris Moreton</td>
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<td>Webmaster</td>
<td>Min Wei</td>
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<td>RS Section</td>
<td>David Schoneker</td>
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<td>Other Steering Committee members</td>
<td>Sameer Late, Jennifer L’Hote-Gaston, Allison Radwick, Otilia Koo, Yongmei Wu, Sai Boddu, Ming Zhou, Anthony Palmieri</td>
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Coalition for the Rational Implementation of the Elemental Impurities Requirements
By: Dave Schoneker (DSchoneker@colorcon.com)

The ICH Q3D Expert Working Group (EWG) met in June 2012 in Japan to continue their discussions about the development of the Q3D Metal Impurities guideline. IPEC Americas, CHPA and SOCMA hosted a Q3D metal Impurities Workshop in April to assess the impact that these requirements will have on industry and to develop ideas on what will be needed to implement these requirements in a rational way and what type of timeline will be needed by industry to gain an appropriate understanding of the actual metal impurity levels in excipients and APIs and to properly prepare for official implementation.

After the workshop the group of trade associations submitted a report with the outcomes from the workshop to the ICH Q3D EWG for their consideration in Japan. A copy was also sent to USP for their review along with requests that USP implement their General Chapters using the same implementation timeline that the ICH Q3D EWG will work out once they finalize the Q3D guideline. USP also attended the workshop and heard the discussions. The presentations, outcomes from the workshop and the recommendations that were provided to the ICH Q3D Expert Working Group and USP can be found at:
http://ipecamericas.org/content/ich-q3d-workshop-breakout-sessions-report-and-feedback

Unfortunately, the USP has decided that they want to unilaterally officially implement their Elemental Impurity General Chapters in May 2014 even though the ICH Q3D EWG decided not to move the guideline on Metal Impurities to Step 2 in June 2012 due to much controversy that occurred in the discussions in Japan!!! The Q3D guideline and the final limits, once finalized, will need to be met by pharmaceutical companies on their finished dosage forms. The Q3D guideline will probably not move to Step 2 which will finalize the limits until at least November 2012 at this stage. Industry does not have enough time to prepare for a May 2014 implementation date for the USP Elemental Impurity requirements given the amount of unknown unknowns that currently exist about actual metal impurity levels in excipients and APIs and the impact of unplanned excursions that typically may come up, especially with mined excipients.

It appears that the USP didn't believe any of the discussions at the Q3D workshop about why USP should wait and implement the Elemental Impurity requirements in sync with how ICH Q3D is implemented. This message was loud and clear during the workshop and USP was involved in many of the discussions. However, a few weeks after the workshop USP announced their intentions to make the General Chapters on Elemental Impurities official in May, 2014 regardless. Many in industry feel that this is a major mistake and will lead to significant problems for drug manufacturers, API and excipient manufacturers.

IPEC Americas is currently forming a Coalition for Rational Implementation of the Elemental Impurity General Chapters. This group will be made up of individuals from most of the major trade associations who feel that the USP’s May 2014 deadline is not feasible for implementation of these chapters due to the lack of data that currently exists on many of the metal impurity levels which might exist in commonly used materials. The group feels that the USP should align their implementation efforts on Elemental Impurities with those of the ICH Q3D EWG. The coalition’s first priority will be to work with USP and FDA to try to get the May 2014 implementation date changed so that USP implementation can be aligned with that of ICH Q3D. There appears to be no real justified reason for USP to move unilaterally on Elemental Impurities. Secondly, the coalition will help makers and users of excipients and APIs begin to develop the needed data that should be in place PRIOR to implementation of both ICH Q3D AND the USP’s Elemental Impurity requirements.

New Excipients Book
EFG members are working towards a multi-authored Excipients-focused book that would highlight the latest developments and address unmet needs in the current literature. Interested?
Contact ajit.narang@bms.com

New EFG Discussion Board
Several EFG Members have started actively participating in the new EFG discussion board at the following website: https://www.aaps.org/Excipients/

Please feel free to post questions or comments.