Single-Use News L-e-t-t-e-r-s

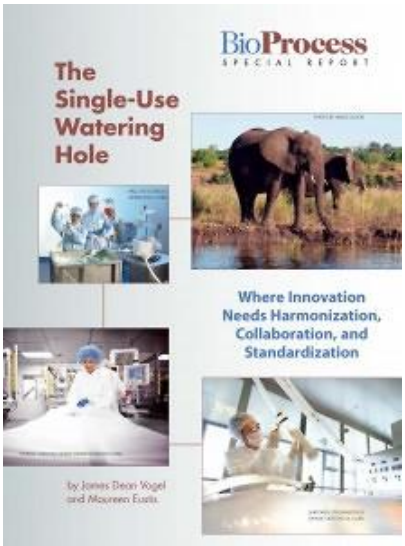
March 2015

This periodic newsletter serves as a central resource for information and updates on the exploding role of Single-Use Technologies in the World of Bioprocess Science and includes regular contributions from the following important "lettered" sources (in alphabetical order):

ASME-BPE (American Society of Mechanical Engineers-BioProcessing Equipment), **ASTM INTERNATIONAL**, **BPOG** (BioPhorum Operations Group), **BPSA** (Bio-Process Systems Alliance), **ELSIE** (The Extractables and Leachables Safety Information Exchange), **PDA** (Parenteral Drug Association), **PQRI** (Product Quality Research Institute), and **USP** (U.S. Pharmacopeial Convention)

[See Page 3 for a brief description of each.]

In January, BPSA and BPOG held a joint webinar presentation for more than 50 BPOG members on the BPSA publication "Recommendations for Testing, Evaluation, and Control of Particulates in Single-Use Process Equipment". The presentation was very well received. Days later, a similar presentation was made in San Diego, CA at the PepTalk event. On February 24th, BPSA hosted yet another session on this topic for BPSA members. Additional webinars will be scheduled in the next few months for the public. https://www.youtube.com/watch?v=FQPDRkdTBrE&feature=youtu.be. This is another example of the success of much current collaboration between the lettered groups represented in this newsletter. Many other efforts are underway as noted in this edition.



General SUT activities that do not fall into the categories to follow are also being addressed. You can read more about these efforts in the January 2015 Special Report (right) published by BioProcess International Magazine entitled: *The Single-Use Watering Hole: Where Innovation Needs Harmonization, Collaboration and Standardization*. Please read it at: *http://www.bioprocessintl.com/manufacturing/single-use/special-report-single-use-watering-hole/*

SUT ALIGNMENT UPDATES

LEACHABLES & EXTRACTABLES

The **ELSIE** Safety Information database now includes safety reports for 359 potential leachable and extractable compounds that could be associated with single-use systems and other pharmaceutical components. In addition to continuing to expand the Safety Database, **ELSIE** initiated a project to collect and compile additive, degradant, and extraction study information on materials used in packaging, devices, and manufacturing processes. Anyone interested in an **ELSIE** membership or collaboration is invited to contact Kelly Carty at Kelly.Carty@dbr.com or call 202-230-5619 for more information. **BPSA** and **BPOG** spent a great deal of time together last year working on a mutually acceptable standardized Extractables Protocol. **BPOG**'s recent article in ISPE Pharma Engineering entitled *Standardized Extractable Testing Protocol for Single-Use Systems in Biomanufacturing* prompted **BPSA** to form an Extractables Response Team. This team answered with its own article in this month's Bioprocess International Single-Use Supplement. The purpose of that article is to reiterate **BPSA**'s stance on the value of developing an industry-wide consensus on Extractables testing of SU systems, obstacles, and suggested next steps toward agreement and, also, to provide differentiation between "stimuli" and true industry consensus standards. At the **ASME-BPE** meeting in Puerto Rico this past January, the Extractables and Leachables Task Group members met with **BPSA** members to discuss alignment of the definitions of Leachables and Extractables. A consensus on definitions seems to be within reach and the group ultimately agreed with the position held by **BPOG**'s since 2013 that the supply base is responsible for supplying Extractables data and the drug manufacturers are responsible for conducting Leachables testing. Final review of the definitions is currently taking place. If a consensus can be reached soon, they will appear in the **ASME-BPE** 2016 Standard. This is a strong step toward synchronicity and a positive indicator of the potential for successful future collaborations on the development of industry standards. **USP** has several projects ongoing on the general topic of safety qualification of plastic pharmaceutical systems. **USP** Chapters <1663> *Assessment of Extractables Associated with Pharmaceutical Packaging/Delivery Systems* and <1664> *Assessment of Drug Product Leachables Associated with Pharmaceutical Packaging/Delivery Systems* were published in the First Supplement to **USP** 38 – NF33 and will be

effective August 1, 2015. These chapters, originally approved for packaging but now considered applicable to other plastic systems as well, are intended to serve as guides for how to conduct E/L studies. **USP** Chapters <661> *Plastic Packaging Systems and Their Materials of Construction*, <661.1> *Plastic Materials of Construction* and <661.2> *Plastic Packaging Systems for Pharmaceutical Use* have been revised consistent with solicited reviews and are proceeding to the publication and implementation phases. Additional **USP** Expert Panels are working to review and revise **USP** <381> *Elastomeric Closures for Injections and to generate* <661.3>, tentatively titled *Plastic Components and Systems Used to Manufacture Pharmaceutical Drug Products* (which includes SUS). Lastly, **USP** has seated an Expert Panel for the purpose of reviewing and revising, as appropriate, **USP** Chapters <87> *Biological Reactivity Tests, In Vitro* and <88> *Biological Reactivity Tests, In Vivo*. **ASTM** has been focusing on Extractables pertaining to process equipment. Ballot analysis has revealed a rich set of input through nearly 500 comments from end-users, suppliers and general users. These comments can be viewed on the WK43975 Workspace at www.astm.org. These comments were also shared with **BPOG** and **BPSA**. **ASTM** plans to schedule open calls through their website to elicit more comments in the following 4 areas: Editorial, Terminology, Analytical, and Solvents and Test Times. Following those calls, **ASTM** plans to assemble smaller groups of SMEs to discuss all comments and create a document for balloting. **ASTM** is reviewing the topic of Leachables and qualification and leaks from within single-use equipment as well as a long term quality agreement centered on single-use.

SUPPLY CHAIN

As mentioned earlier, **BPOG** made a cGMP Expectations presentation to **BPSA** and a presentation at BioProcess International on the topic of supply chains in SUT. They continue to conduct webinars and write papers on this topic as well. **ASTM** held a follow-up meeting last October to the very well-attended May 2014 workshop focusing on production and supply chain issues related to raw materials--predominantly single-use systems. Suppliers and end-users alike took part in that workshop.

PARTICULATES

In addition to the cover story, other particulate-related activities are as follows: **ASTM** has drafted a particulate chapter. Updates will be provided in the next newsletter. Along with Change Control and Hygienic Clamp Unions, **ASME BPE** intends to address the topic of Particulates at its May meeting in Philadelphia, PA, for possible inclusion in the 2016 Standard.

CHANGE MANAGEMENT

BPOG has accepted an invitation by **BPSA** to collaborate on a Change Notification project. According to the most recent **BPSA** Bulletin, *"The objectives of the project are: to establish understanding between suppliers and end users of each other's concerns and needs; establish for suppliers a consistent end user definition of what is a change; establish the data points required; and create for suppliers an End-User Template of changes and data that would apply to 95% of supplier/end user agreements/contracts."* A January teleconference, hosted by **BPOG**, included input from **BPSA** and **BPOG** members in the key component areas of bags, tubing, filters, filter housings, aseptic connectors, resin, media and fill finish, and a systems integrator. A transcript of this teleconference – *The Summary and Next Steps from Joint BPSA/BPOG Change Notification Project Teleconference: January 28, 2015* - can be accessed by **BPSA** members at www.bpsalliance.org. Weekly teleconferences will continue and a face-to-face meeting between **BPSA** and **BPOG** will take place in New Jersey in April of this year.

On the topic of certificates, an **ASME BPE** task group was formed to align PM 2.2.1.1-1 with current classifications in an effort to harmonize terminology amongst the **ASME BPE** Standard, **BPSA**'s Component Quality Matrices and **BPOG**'s Extractables and Leachables paper. The component categories agreed upon by **ASME BPE** recently are the following: polymeric seals, hoses, tubing, filters, chromatography columns, connectors, polymeric containers, other process contact polymeric components, other process contact nonmetallic components, and single-use assemblies.

In May, **ASME BPE** will meet in Philadelphia, PA. Change Control is a topic which will be discussed as it pertains to the **ASME BPE**-2016 Standard.

SYSTEM INTEGRITY

The scope of ASTM's *Work Item WK43741 New Practice for Testing Integrity of Single-Use Systems at Vendors Manufacturing Facilities*, which seeks to develop a standardized approach for SUT vendors to use throughout the lifecycle of the SUT component, is available for viewing on their website. It is intended to help the supplier measure an SUT system's integrity based on risk assessment and can be applied to all categories of SUT components. The full document is in review by Subcommittee E55.04. Please visit their website for more information www.astm.org. At **USP**, an expert committee has been formed to review Chapter <1207> *Sterile Product Packaging – Integrity Evaluation.*

CONNECTORS

ASME-BPE's Polymeric Hygienic Unions Task Group, which is similar to their Metal Fitting Task Group, was recently formed and is holding regular teleconferences.

SUT DESIGN VERIFICATION

ASTM is in the ongoing process of reviewing a number of its standards and comments. A draft document in the spirit of **ASTM** E2500 and QBD is being developed. It will consider extractables, quality, leaks and particulate. Also, **ASTM** Work Item "Guide for Specification, Design and Verification of Single Use Pharmaceutical and Biopharmaceutical Manufacturing Systems and Equipment" has been submitted for ballot and will be discussed at the upcoming committee meeting in Lisbon, April 28-30, along with multiple other SUT topics. More details are available at https://myastm.astm.org/MEETINGS/filtrexx40.cgi?index.frm. **ASTM** has reported that the response so far has been very positive and they are looking forward to feedback from the industry, suppliers and regulators alike. □

A Summary of Current SUT

	ASME BPE	ASTM E55	BPOG	BPSA	ELSIE	PDA	PQRI	USP
Leachables and Extractables	●	●	●	●	●			●
SUT Supply Chain		●	●	●				
Particulates in SUT	●	●						●
Change Mgmt/Control	●		●	●				
SUT System Integrity	●							
Connectors	●	●						●
SUT Design Verification		●						

A brief description of the major organizations involved in Single-Use Technologies can be found below. Please visit their websites for a broader description of their industry involvement, a list of their upcoming meetings and events, and volunteer membership information.

ASME-BPE (American Society of Mechanical Engineers - BioProcessing Equipment Standard) www.asme.org
The ASME-BPE Standard is intended for design, materials, construction, inspection, and testing of vessels, piping and related accessories such as pumps, valves, and fittings for use in the biopharmaceutical industry. This standard (www.asme.org/products/codes-standards/bpe-2012-bioprocessing-equipment) also provides requirements for Single-Use Systems and components.

ASTM International www.astm.org
ASTM International develops international voluntary consensus standards similar to the ASME BPE. Twelve thousand ASTM standards are used around the world to improve product quality, enhance safety, facilitate market access and trade, and build consumer confidence. ASTM International includes more than 30,000 of the world's top technical experts and business professionals, representing 150 countries. Working in an open and transparent process and using ASTM's advanced electronic infrastructure, ASTM members deliver the test methods, specifications, guides, and practices which support industries and governments worldwide.

BPOG (BioPhorum Operations Group) www.biophorum.com
BPOG consists of experts from biopharma drug substance operations who meet and work together at fact-to-face meetings in the U.S. and Europe on a regular basis. They have 32 member companies with over 1,400 participating representatives. BPOG has established best practices on a wide range of quality, engineering and organizational topics central to the challenge of mastering a biotech drug substance operations. BPOG is made of up exclusively of end users.

BPSA (Bio-Process Systems Alliance) www.bpsalliance.org
The BPSA is an industry-led corporate member trade association dedicated to encouraging and accelerating the adoption of Single-Use manufacturing technologies used in the production of biopharmaceuticals and vaccines. BPSA facilitates education, sharing of best practices, development of consensus guides and business-to-business networking opportunities among its member company employees.

ELSIE (The Extractables and Leachables Safety Information Exchange) www.elsiedata.org
ELSIE was formed in 2007 with the core objective of establishing a comprehensive database which provides a jointly-developed and credible source of safety information on extractables and leachables as well as extraction profiles and standardized study protocols for a range of materials commonly used in pharmaceutical, biological and device applications and processes (e.g. container closure systems, devices, manufacturing/processing, etc.).

PDA (Parenteral Drug Association) www.pda.org
PDA is the worldwide leading provider of science, technology and regulatory information and education for the pharmaceutical and biopharmaceutical industries. Founded in 1946 as a nonprofit organization, PDA now has over 9,500 members worldwide. Using their expertise, these members are committed to developing scientifically sound technical information for practical uses in order to advance science and its regulations.

PQRI (Product Quality Research Institute) www.pqri.org
The Product Quality Research Institute (PQRI) is a non-profit consortium of organizations working together to generate and share timely, relevant, and impactful information that advances drug product quality and development. PQRI provides a unique forum to focus critical thinking, conduct research, exchange information, and propose methodology or guidance to pharmaceutical companies, regulators, and standard setting organizations.

USP (U.S. Pharmacopeial Convention) www.usp.org
The USP is a scientific nonprofit organization that sets standards for the quality, purity, strength, and identity of medicines, food ingredients, and supplements. USP's drug standards are enforceable in the United States by the Food and Drug Administration (FDA). These standards are also used in more than 140 other countries.

UPCOMING 2015 MEETINGS & EVENTS

PDA's Annual Meeting – LAS VEGAS, NV
March 16-18, 2015

IBC Life Science's BDP Week – HUNTINGTON BEACH, CA
March 30 – April 2, 2015
Town Hall Forum: Standardization of Single-Use Systems: What is the Next Step for the Industry? **www.ibclifesciences.com/BDPWeek/overview**

INTERPHEX – NEW YORK, NY
April 21-23, 2015 **www.interphex.com/**

ASTM INTERNATIONAL – LISBON, PORTUGAL
April 28-30, 2015
E55 Manufacture of Pharmaceutical Products
www.astm.org/MEETINGS/filtrexx40.cgi?+-P+MAINCOMM+E55+-P+EVENT_ID+2819+-ETING_ID+96999+otherinfomain.frm

USP – EXTRACTABLES & LEACHABLES COURSE
April 9-10. 2015
www.usp.org/meetings-courses/courses/extractables-and-leachables

ASME-BPE – PHILADELPHIA, PA
May 18-21, 2015

PDA – BETHESDA, MD
June 24-25, 2015
2015 PDA Single Use Systems Workshop

Harmonizing Best Practice Recommendations and Standardization Guides and Connecting Manufacturers, Suppliers and Global Health Authorities **www.pda.org/global-event-calendar/event-detail/2015-pda-single-use-system-workshop**

BPSA International Single-Use Summit – WASHINGTON, D.C.
July 13-15, 2015 **www.bpsalliance.org/bpsa-summit/**

ASME-BPE – PHOENIX, AZ
September 2015

BIOPROCESS INTERNATIONAL – BOSTON, MA
October 26-29, 2015

ECI Single-Use Technologies Conference – WASHINGTON, DC
www.engconf.org/15aj
October 2015

ISPE – PHILADELPHIA, PA
November 8-11, 2015
Annual Meeting
www.ispe.org/annualmeeting

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