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

September 2014

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 2 for a brief description of each.]

*[Below is an excerpt from an upcoming **January 2015** **BioProcess International** **Special Report** on the pressing need for collaboration to facilitate standardization of single-use components. This newsletter was created, in part, to begin to address this need.]*

The Single-Use Watering Hole

Where Innovation Needs Harmonization, Collaboration, and Standardization

Within the last few years, the Single-Use Technology (SUT) arena of the Biopharmaceutical industry has exploded. Leading organizations have predictably and understandably stampeded to the "watering hole" of single-use to drink up the ground-breaking advantages these components have over traditional multi-use parts and technologies in order to deliver safer drugs with less risk. Single-Use is growing so fast in size and importance that the organizations which could help manage the chaos can't keep up. Contributing to this may be things such as company needs, regulatory needs, market pressures, and even cost. The best way to eliminate the problem is for all parties involved to become a part of the solution. Federal agencies, such as the United States Food and Drug Administration (FDA), recognize the need for SUT standardization and have begun the process of addressing this issue. But the government is a slow-moving beast. In the meantime, the industry itself would benefit enormously by making a collaborative effort to solve the problem before it becomes even more unmanageable.

As SUT has become less of a novelty and more of a coveted necessity in the quest for industry survival, organizations such as ASME-BPE, ASTM, BPOG, BPSA, ELSIE, ISPE, PDA, PQRI, and USP have all arrived at the watering hole. In the time since the SUT watering hole has been accommodating these groups, some positive signs of progress have slowly surfaced. However, along the way it has become clear to this assortment of lettered organizations that the need for full harmonization and standardization is mostly unmet and, thus, they have each jockeyed to manage their own efforts. At times this has been chaotic. Who decides when novel becomes standard? Most people are calling for standardization of SUT, and some have tried, but it simply hasn't happened yet. Why not? **[read more in January]** □

October SU Town Hall in Boston!

The next town hall meeting is scheduled for **October 23, 2014 at the BioProcess International Conference and Exposition** in Boston. The "lettered" organizations have agreed to have a face-to-face summit in Boston prior to the Town Hall to discuss specific opportunities for better collaboration amongst the groups. Some of the goals include:

- Spreading the effort to more of a global base. The groups openly acknowledge that it has focused more on a North American centric; and
- Creating a list of topics including who is working on what, to help the SUT community be better informed of the "what" and the "who" if they wish to get involved and participate. □

This newsletter is facilitated by The BioProcess Institute www.bioprocessinstitute.com

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ORGANIZATION UPDATES

ASME-BPE

Reported by Mike Zumbrum and Jay Ankers

Publication of the 2014 Edition of the ASME-BPE Standard is expected within several weeks. Specific Single-Use Technology items in this upcoming edition include: Non-Mandatory Appendix K for Extractables and Leachables and Non-Mandatory Appendix N. Non-Mandatory Appendix N's purpose is to serve as a guide to manufacturers and end users of bioprocess equipment for developing and manufacturing systems and products which meet particle acceptance criteria such as standardized hygienic union dimensions, steam through connections and product/process contact as it relates to system boundaries and facility design. ASME-BPE is continuing discussions with ASTM regarding testing protocol for particulates in single-use systems. Also in the 2014 Standard, ASME aligned its definitions of "product" and "process" contact surfaces to line up with ISPE's Baseline Guide. Upcoming ASME-BPE meetings include Seattle, WA in October of this year, and San Juan, Puerto Rico in January of 2015.

ASTM

Reported by Bob Steininger

ASTM held one of their two annual meetings in Boston, MA this past May. This well attended meeting included a workshop focusing on the production and supply chain issues related to single-use systems as well as other raw materials. Nearly 100 individuals took part in this meeting. They represented end users, suppliers, and consultants alike. Importantly, the session included a talk on extractables by the FDA. A set of four standards have already been, or soon will be, submitted for review. They specifically are WK43741 *New Practice for Testing Integrity of Single-use Systems*, WK43742 *New Practice for Characterizing Particulates Burden from Single-use Systems*, WK43975 *New Practice for Determining and Characterizing Extractables from Materials used in Single-use Applications*, and WK46541 *New Guide for Specification, Design and Verification of Single Use Pharmaceutical and Biopharmaceutical Manufacturing Systems and Equipment*. The latter is based on the very successful standard for traditional Equipment – E2500-07. A first draft of WK46541 has been posted for discussion and ASTM aims to finalize the scope and team members at the upcoming face-to-face meeting in Conshohocken, PA.

BPOG

Reported by Tony White

BPOG's SUT Leadership Team is now up and running and the team's views on the gap in expectation between suppliers and end users were presented at the BPSA International Single-Use Summit this past July in Washington, D.C. It is felt that this 'gap' in understanding is one of the things impeding progress and adoption in commercial operations. In an effort to narrow this gap, BPOG is collaborating with BPSA to host a number of public webinar's over the coming year.

BPSA

Reported by Jerry Martin & Kevin Ott

At their International Single-Use Summit in Washington, D.C. this past July, BPSA issued two important documents:

Recommendations for Testing, Evaluation, and Control of Particulates in Single-Use Process Equipment was developed by Subject Matter Experts from both the supplier and end user sides of the bioprocess industry—in order to meet a need. This informative document not only helps readers to characterize and quantify types and levels of particles in single-use systems and components, but also recommends procedures for minimizing these types and levels. In addition, the document offers a look ahead to the future and what the industry should expect by way of improvements in particle control to protect the health and safety of pharmaceutical patients. [This document can be purchased at www.bpsalliance.org.]

Consensus Quality Agreement Template for Single-Use Biopharmaceutical Manufacturing Products is intended to give an example of a common structure and to facilitate a dialog between Suppliers and End Users for Quality Agreements. Such dialog will reveal the specific needs of the end user and the many attributes of the quality system and operating mechanisms of the supplier, which in turn will provide the content for the final Quality Agreement between the two parties. [Free download available at www.bpsalliance.org]

A third document, a revision of *Component Quality Test Reference Matrices*, is currently being updated to include the addition of new sections as well as current topics such as filters, tubing, connectors, and bags.

ELSIE

ELSIE continues to populate the Safety Information Database with safety information on extractables and leachables compounds. Additionally, ELSIE has prepared three papers on evaluation of results from a controlled extraction study Pilot Program. These papers are expected to be available soon.

PDA

Reported by Richard Levy

At this time, PDA Technical Report No. 66 – Application of Single-Use-Systems in Pharmaceutical Manufacturing Technical Report is ready for publication. Publication should take place in the Fall of 2014. The PDA Scientific Advisory Boards, PDA members and staff are in the process of discussing next steps in supporting the implementation of SUS.

On May 14, 2014 at their headquarters in Bethesda MD, PDA hosted Single-Use Systems Cross-Organizational Workshop. Twenty industry representatives and ten FDA staff attended the meeting. Representatives from ASME, ASTM, BPOG, BPSA, ELSIE, PDA, PQRI and USP attended and made formal presentations. The objective of this workshop was twofold: (1) to promote a harmonized approach to supporting SUS activities within the industry and in so doing to minimize duplication of efforts and (2) to communicate ongoing SUS initiatives among the group. The morning sessions focused on describing the SUS Organization landscape and ongoing activities with presentations from the various organizations followed by discussion. During the afternoon working sessions participants identified a full spectrum of technology support needs and then these technology topics were used to develop the voting tables used during the meeting. Through this voting, attendees voted for prioritized Single Use Technology topics where the development of industry best practices would be valuable. There was a consensus that the meeting was valuable, and that it would be beneficial to hold this meeting again, possibly in 2015. PDA is committed to hosting the meeting again.

PQRI

PQRI members, including chemists and toxicologists, are currently concluding research in order to eventually propose methodology for the use of disposable systems in the absence of defined and specific regulatory guidance. The product of this research will include a recommendations document planned for publication in 2015.

USP

USP has recently published USP <790> *Visible Particulates in Injections* which requires inspection for the existence of visible particulate in all injectable products. <790> includes details on requirements for proper visual inspections, including the use of both black and white backgrounds to ensure that all visible particles can be located with the naked eye (without magnification). Used in combination with manufacturing inspections, this practice will help to verify that a product is "essentially free" of visible particulates.

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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 19 member companies with over 500 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.

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