

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

November 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), DECHEMA (Gesellschaft für Chemische Technik und Biotechnologie/Society for Chemical Engineering and Biotechnology), 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 4 for a brief description of each]

TWO YEARS AND COUNTING FOR SINGLE-USE NEWS LETTERS EFFORT!

Two years have passed since the launch of *Single-Use News Letters*, an effort the SU industry had been clamoring for ever since it became apparent that single-use technologies would revolutionize the production of biopharmaceuticals. The seeds of collaboration are starting take root, but we have a long way to go before the “farm” of consensus is successful enough to feed the industry. And we need more farmers.

Recently, the Single Use Technology Assessment Program (SUTAP) suggested to the ASTM semi-annual meeting a hierarchy/road map that describes all of the proposed ASTM standards in a better context relative to each other, rather than starting off with the most contentious one. In addition to this, the ASTM WK 46541 on Design Verification, etc. has benefited from the efforts of the PDA TR 66 team, and will go to full committee ballot very soon. The BPSA/BPOG User Requirement Specification Team will reference this work in their efforts. Inter-organizational progress like this is precisely why this newsletter effort originated.

Before this effort began, major lettered organizations operated independently of one another while marching toward similar goals. But during the past two years, many of these groups have pitched in together for the common good. The new “Group of 9”, for example, includes an equal number of representatives from ASTM, BPOG and BPSA.

However, given the complexity of some of the topics, it takes significant effort to achieve consensus necessary to development of a standard. ASTM has been working on development of an Extractables standard for over a year. One ballot indicated a significant difference between end users and suppliers involved in the ASTM process. Discussions can be dynamic, even



heated at time, but the end goal of improving the safety and effectiveness of the use of SUS technology is worth the effort.

Despite challenges like this, and perhaps because of them, we are in need of active, engaged individuals like you to help move things along. In addition to your specific talents and knowledge, you can bring a better understanding of how these lettered organization work and a help them find a path toward consensus. The fewer participants who take part in these volunteer industry organizations, the greater the likelihood that a few squeaky wheels will drown out the voices of others and pull the cart in a potentially unhelpful direction. When more people get involved, the final consensus will be more complete and valuable.

We aren't looking for unanimity. We are looking to arrive at something that most agree with for the benefit of all, most importantly the patients.

The BPSA/BPOG Change Notification success story began with an understanding by these two organizations of the benefits to putting their collective heads together to make change. It's a great start, but we still need more. It is not easy to find the right fit, but if we can make it work, it will help single-use technologies meet it potential to make better therapies. We need you in the room, or on the teleconference, to help define what it is and how to get there.

We look forward to continuing this effort and will keep up the dialog. This month, our lettered organizations will be presenting on our past, current, and future work at ISPE's annual meeting in Philadelphia, PA. Stay tuned for upcoming news in 2016. Check out Page 4 of this issue to find contact information for all of these lettered groups. If you like to plan ahead, please pencil in joining a lettered group as your **2016 New Year's Resolution!** □

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SINGLE-USE ALIGNMENT UPDATES

EXTRACTABLES

ASTM's E55 committee approved a technical approach to the next ballot at the recently concluded semi-annual meeting [*WK43975-New Standard for Determining and Characterizing Extractable from Materials Used in Single-Use Application*]. In addition, this group's Change Notification project is off to a promising start. They have had several face-to-face meetings and have already sent collective comments to ASME BPE on that organization's Change Notification ballot for their 2016 Standard. A new ballot is expected out this quarter (Q4). An update to the ASME-BPE 2016 Standard ballot has been approved. Appendix O has been updated to include five solvents. Similar to those under discussion at ASTM and it includes a flowchart in the Standard assisting the evaluation of bioprocess equipment/components, related to extractables and leachables characterization. USP-General Chapter <661> was revised and will appear in USP 39-NF 34 with an official date of May 1, 2016. These revisions included changes to the title of General Chapter <661>, as well as moving section into new General Chapters <661.1> and <661.2> [[click for more](#)]. USP <1661>, <1663> and <1664> are now official. BPOG and BPSA both have established active work groups and continue their participation with ASTM.

LEACHABLES

ASME BPE's 2016 Standard will clarify that leachables involve the final drug product and, as such, are the responsibility of the end user. BPOG has established an active work group for leachables. DECHEMA is looking forward to their upcoming *Life Science Engineering* publication regarding recommendations for leachables studies. This will involve a standardized cell culture test for the early identification of critical films. Work continues on ASTM's *WK48084-New Standard for Determining and Characterizing Leachables Released from Materials Used in Single-Use Systems under Bioprocess Operating Conditions*.

PARTICULATES

USP is working on updates to <787> *Subvisible Particulate Matter in Therapeutic Protein Injections*, <788> *Injections Subvisible*, and <790> *Visible Particulates in Injections*. USP <1790> *Visual Inspection of Injectable Products* is to be republished this November. Progress continues on the following ASTM particulate working group guides: *WK43742-Facilities Practice for Characterizing Particulate Burden from Single-Use Systems for End-User Impact Assessment*; *WK47356-New Practice for Characterizing Particulates Burden from Single-Use Systems at Vendor Factory*; and *WK30195-New Guide for Particle Analysis Applications in Pharmaceutical Processes Including Sub-Visible Particle Analysis*. ASME BPE's Part PM Particulate Task Group's update has been approved to clarify the 2016 Standard.

SYSTEM INTEGRITY

Progress continues for ASTM's two integrity working groups: *WK43741-Practice for Testing Integrity of Single-Use Systems*

at Various Manufacturing Facilities and *WK47355-New Practice for Controlling Integrity of Single-Use Systems during Biopharmaceutical Manufacturing Process at End-use Factory*. Input is always welcome. ASME-BPE's Part PM-System Integrity Task Group continues their efforts focusing primarily on leak testing and test methods. BPSA's Leak Integrity Task Group continues their work on System Integrity issues for Single-Use systems. There has been some discussion about PDA considering adapting *TR27-Pharmaceutical Package Integrity to SUS*.

CONNECTORS

ASME-BPE is in the process of establishing a Tubing Welding Task Group. Their Polymeric Hygienic Unions Task Group continues their discussions on alignment with stainless steel fittings dimensions listed in the 2014 Standard and are in the process of evaluating fitting and clamp tolerances. BPOG has sent a note to ASME BPE regarding hose barbs, specifically addressing ways to improve their use and operation. They are awaiting a response.

DESIGN AND APPLICATION

Progress is ongoing for ASTM's working groups: *WK46541-New Guide for Specification, Design and Verification of Single Use Pharmaceutical and Biopharmaceutical Manufacturing Systems and Equipment* will go to full committee ballot very soon, and other work items are being initiated in support of it; *WK47357-New Practice for Application of Single-Use System in Pharmaceutical and Biopharmaceutical Manufacturing*; *WK12892-New Guide for Standard Guide for Process Sampling*; and *WK42165-New Practice for Sampling*. BPOG and BPSA are progressing on their collaboration of a Single-Use URS Work Group. DECHEMA currently has two working groups, 1) Microbial Bioreactors for Biopharmaceutical Production, and 2) Single-Use Bioreactors for Stem Cell Expansion and Differentiation. They have also established a recommendation for engineering characterization of single-use bioreactors and single-use mixers.

SUPPLY CHAIN

ASME BPE has approved a Change Control addition to their 2016 Standard. BPOG/BPSA's joint Change Notification Team published an article in *BioProcess International* magazine entitled [Management, Notification, and Documentation of Single-Use Systems Change Orders: Challenges and Opportunities](#). This article was recently presented at the Bioprocess International Exhibition and Conference in Boston, MA last month. ASTM working group *WK51651-Standard Guide for Raw Material eData Exchange Between Biopharmaceuticals and Suppliers* is in progress at this time.

BIOCOMPATIBILITY

USP is currently revising their Biological Reactivity Tests <87> and <88> (in vitro and in vivo, respectively). ASTM has two working group guides in progress: *WK48956-New Practice for Biocompatibility of Single-Use System at End-user Factory* and *WK48957-New Practice for Purity, Biocompatibility and Toxicity of Raw Materials Used in the Manufacturing of Single-Use Systems*. □

A SUMMARY OF CURRENT SUT ACTIVITIES/WORK GROUPS

	ASME BPE	ASTM	BPOG	BPSA	DECHEMA	ELSIE	PDA	PQRI	USP
Extractables	Part PM Extractables Task Group 2016 updates to and Appendix O Updated	WK43975 Pending ballot	Active Work Group	Active Work Group	Recommendations for risk analysis	Database continues	TR66	Recommendations including methods and example data	Task Group on <661.3>, <661.1> and <661.2> published in May <1661>, <1663>, and <1664> official
Leachables	2016 Standard updated	WK48084	Active Work Group		Life Science Engineering publication (Recommendations for Leachable studies)		TR66	Recommendations	
Particulate	Part PM Particulate Task Group 2016 Standard Updated	WK43742 WK47356 WK30195		Active Work Group			TR66		Task Groups for <787>, <788>, <790>, <1790> to be republished in Nov.
System Integrity	Part PM System Integrity Task Group Activity	WK43741 WK47355		Leak Test Integrity Task Group			TR66 TR27?		Task Group on <1207> Sterile Product Packaging Integrity Evaluation
Connectors	Part PM Polymeric Hygienic Unions Task Group, Tubing Welding Task Group		Letter sent to ASME BPE on hose barbs				TR66		
Supply Chain	Part PM Change Control Task Group	WK51651 Out for Ballot	Change Notification Team Bioprocess International publication				TR66		
Design Verification		WK46541 WK47357 WK12892 WK41265	Single-Use URS Work Group		Multiple Work Groups		TR66		
Biocompatibility		WK48956 WK48957			Life Science Engineering publication (Recommendations for Leachable studies)		TR66		Task Group Revising <87> and <88> for 2016

FOR FURTHER INFORMATION ON THE DOCUMENTS AND WORKSTREAMS IN THIS TABLE, PLEASE VISIT www.bioprocessinstitute.com/sus-newsletter

UPCOMING MEETINGS

ASME BPE Meeting – SAN JUAN, PR

January 11-14, 2016

<http://calendar.asme.org/home.cfm?EventTypeID=4>

PDA Annual Mtg. – SAN ANTONIO, TX

March 14-16, 2016

<https://www.pda.org/global-event-calendar/event-detail/2016-pda-annual-meeting>

ASTM Meeting – UNITED KINGDOM

April 2016

<http://www.astm.org/MEETINGS/>

USP – tbd

June 2016

BPSA Int'l SU Summit – WASHINGTON, D.C.

July 11-13, 2016

<http://www.bpsalliance.org/>

DECHEMA Conference

September 5-7, 2016

<http://www.dechema.de/en/KS2016.html>

ASME BPE – BOSTON, MA

September 2016

ASTM – WASHINGTON, D.C.

October 2016

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



DECHEMA (Gesellschaft für Chemische Technik und Biotechnologie/Society for Chemical Engineering and Biotechnology)

www.dechema.de/en/

DECHEMA is the expert network for chemical engineering and biotechnology in Germany. As a non-profit professional society we represent these fields in science, industry, politics and the general public. DECHEMA promotes scientific and technical exchange among experts from different disciplines, organisations and generations. We consolidate the know-how of over 5,800 individual and sustaining members.



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

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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