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Committee E55
Manufacture of Pharmaceutical and Biopharmaceutical Products

NEWSLETTER

Introduction

E55 Newsletter

E55 on Manufacture of Pharmaceutical and Biopharmaceutical Products

Chair: Ferdinando Aspesi, Bridge Associates International
Vice-chair: Russell Madsen, The Williamsburg Group, LLC

Welcome to the Fall 2020 edition of the ASTM Committee E55 Newsletter. Although our planned face-to-face meetings and the Workshop scheduled at J&J ahead of our Fall meeting this year had to be cancelled due to the coronavirus pandemic, we held a series of successful Webex committee and subcommittee meetings for Spring 2020 in April and just concluded our annual Fall meetings this October. This issue of the Newsletter contains updates and details activities of the committee since last Spring.

Virtual meetings were held with Sara Gobbi, ASTM's Director of European Affairs and Louis Fredricks, European Affairs Advisor, and Graham Cook to discuss strategies to increase E55's presence and influence in Europe and with European regulators. We will work out an initial European Strategy where we are targeting some countries' industry organizations and academia. We have initiated contacts with stakeholders in Ireland, Switzerland and Italy.

We will report the outcomes of these contacts in the 2021 Spring Newsletter.

The third meeting of the E55 Academia Forum took place on October 5, 2020, by Webex.

Because Carl Lawton and Alastair Florence, of U. Mass. Lowell and U. Strathclyde, respectively, had previously presented their ideas on work areas and innovation, the current session focused on which technology platforms and projects might be the most promising for evaluating what ASTM E55 standards may be needed. Martin Warman, Caterina Minelli and Alastair Florence provided an overview of Technology Readiness Levels (TRL's) and their applications to research, development and deployment phases at CMAC, MMIC and NPL. Discussions centered on the following topics:

- How to raise awareness in ASTM of on-going activities (E55.94)
- How to feedback awareness of the ASTM process into fundamental research (E55.94)
- Define opportunities for raising awareness of ASTM activities into university level training (graduate, postgraduate, doctoral, CPD) (E55.94)
- How to survey landscape to define and prioritize needs for standards, as well as identify experts for ASTM working group/integrate with ASTM Roadmap (E55.95).
- Including how to survey standard bodies to identify synergies and harmonize standards.
- How to define "maturity" of a technology, e.g., when to recognize when a technology is sufficiently mature to be standardized. By adoption? By TRL? By regulator's steer?

The ASTM E55 Academia Forum will meet in April and October 2021 to continue dialogue.

More information on the Academic Forum and the activities of the various E55 Subcommittees can be found in the body of this publication.

An Industry Forum is planned to get input on how E55 may better serve that segment of the membership. The first virtual meeting is scheduled for December 11, 2020. Details will be provided in future issues of this Newsletter.

The next meeting of E55 is planned for April or May 2021. The meeting may be face-to-face at ASTM in Conshohocken, Pa., or it may be virtual depending on the COVID-19 situation. Watch for an announcement on the ASTM E55 website.

As always, everyone is invited to contact the E55 ASTM Staff Manager, Travis Murdock, with any questions of other feedback on the Newsletter.

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Subcommittee Reports

Path to Success

Under the direction of the Executive Subcommittee and through the input of our members, E55 continues to make significant progress towards revising and expanding its catalog of international standards. This section covers subcommittee reports highlighting the accomplishments and ongoing efforts in standards development. All members and interested industry stakeholders are encouraged to contribute to any of these efforts by reaching out to the subcommittee chairs.

E55.01 Process Understanding and PAT System Management, Implementation and Practice

Chair: Benoît Igne, Vertex Pharmaceuticals

Throughout the year 2020, the E55.01 subcommittee activities have been primarily focused on the revision of multiple existing standards while exploring potential standard opportunities in the biopharmaceutical space.

As part of these major revisions, **E2898-20** *Standard Guide for Risk-Based Validation of Analytical Methods for PAT Applications* and **E2891-20** *Standard Guide for Multivariate Data Analysis in Pharmaceutical Development and Manufacturing Applications* were re-approved. **E2968-14** *Standard Guide for Application of Continuous Processing in the Pharmaceutical Industry* is undergoing ballot. Such a revision/renew process will continue in 2021 on standards such as **E2476-16** *Standard Guide for Risk Assessment and Risk Control as it Impacts the Design, Development, and Operation of PAT Processes for Pharmaceutical Manufacture*.

In term of future standards, our subcommittee actively participated in the E55 survey distributed earlier in the year and translated the responses to multiple active working areas. Among them, a standard on the use of PAT for biologic processes was proposed. A group of SMEs representative of 20+ pharmaceutical and biopharmaceutical companies plan to start a brainstorming session in November 2020 to define the scope of such a standard. Finally, advanced process control and machine learning /artificial intelligence will be the subject of active working groups in 2021.

E55.03 General Pharmaceutical Standards

Chair: Paul Gil, MeiraGTx

Subcommittee E55.03 has made significant progress with multiple standards projects over of the course of the past months. The bulk of which comes from the hard work and leadership of Andrew Walsh and his Cleaning Validation task group. The latest standard from the team includes **E3263-20** *Standard Practice Guide for the Qualification of Visual Inspection of Pharmaceutical Manufacturing Equipment and Medical Devices for Residues* (developed under **WK67425**) which was recently approved by the committee and is now available on the ASTM website. The task group is now working on another new standard **WK64938** *Standard Practice for the Calculation of Cleaning Validation Limits* along with revisions to **E3106-18e1** *Standard Guide for Science-Based and Risk Based Cleaning Process Development and Validation* to incorporate references from these new standards.

Other work around the subcommittee includes the revisions to the Committee's most popular standard, **E2500-13**, *Standard Guide for Specification, Design, and Verification of Pharmaceutical and Biopharmaceutical Manufacturing Systems and Equipment* (**WK66032**), which recently passed ballot. Congratulations to Lou Traglia, technical contact for the standard, and your task group team.

A revision to **F838-15ae1** *Standard Test Method for Determining Bacterial Retention of Membrane Filters Utilized for Liquid Filtration* (**WK70828**) was also recently approved by the committee and is currently in the final stages of publication. Thanks to Russ Madsen, technical contact for the standard, for all the hard work you and your task group put into this revision.

Another new project was launched within E55.03 earlier this year in the area of Combination Products. Under the leadership of Manfred Maeder of Novartis, a task group was established and held several virtual meetings throughout 2020. As a result, the group has registered **WK72293** *Standard Guide for Definition of Combination Products (Drug, Device, Biologic Combinations).* The task group continues to gain interest and will likely lead into additional standards following its completion. The task group expects to send their first draft out for ballot in Q1 2020.

Finally, in response to COVID-19 pandemic, the subcommittee recently registered **WK73465** *Accelerated CMC development, manufacture and supply of therapies and vaccines for use in pandemics such as COVID-19*. Under the leadership of E55's previous committee chair, Graham Cook, Pfizer, a task group was assembled to seek to rapid develop of a new draft standard to provide CMC-GMDP approaches for accelerated development that might be helpful to developers, regulators and other stakeholders involved with new medicines for COVID-19. Leveraging the ASTM process for rapid balloting of new standards, and with the approval of the E55.03 Subcommittee, the task group was able to proceed with a concurrent Main and Subcommittee ballot of the first draft on the E55 20-05 ballot. Although many positive comments were received, there were several Negative votes suggesting that the scope of the standard covered regulatory issues that agencies would need to evaluate, and that an ASTM standard could be mis-interpreted. The task group has considered these Negative comments and found them 'persuasive' and will therefore stop further development of **WK73465**. The task group is currently exploring alternative means of publication for some of the detailed content described. Nevertheless, we want to thank Graham, and everyone involved, for their support and quick feedback during the drafting and balloting process.

E55.04 General Biopharmaceutical Standards

Chair: Bob Steininger, Surface Oncology

The E55.04 subcommittee continues to focus on standards for single-use systems. These systems are being used to make many protein drugs, and now are being adapted to produce new gene and cell therapy products. Recently, a new work item has been proposed and registered for the development of **WK74440,** *Standard Test Methods for Physical Integrity Testing of Single-Use Systems*.

Current work of the subcommittee includes ongoing balloting of **WK65429**, *New Practice for the Process to Remove Retrovirus by a Small Virus Retentive Filter*. This standard was balloted earlier this year and received negative comments which were found persuasive. The task group plans to send an updated version out for ballot soon. Once approved, the ability to follow three viral removal\inactivation standards to insure >15 log reduction of a potential retrovirus load within a protein production process will be available. In addition, **WK64991**, *Standard Practice for Stability of Early Phase Protein Products* was approved by subcommittee ballot. The task group has incorporated minor edits that will be included once it is sent back out for main committee vote. These standards focusing on viral reduction and stability should aid in the efficient movement of early phase drugs into the clinic safely.

Lastly, work remains ongoing for **WK65428**, *Standard Guide for the Application of Continuous Processing in the Biopharmaceutical Industry*. The most recent draft has received a number of comments which are being addressed. Additional separate standards have been proposed to expand the information related to both a continuous upstream cell culture process and a continuous downstream purification process.

E55.05 Lyophilization

Chair: Arnab Ganguly, Amgen

Subcommittee E55.05 is continuing its efforts to approve its first work item, **WK63507,** *New Standard Practice for Product Temperature and Equipment Pressure Instrumentation in Pharmaceutical Freeze Drying*. The group has incorporated comments captured during the previous ballot and subsequent reviews of the draft, including useful inputs from E55 members with NIST and the FDA. An updated version of the draft is anticipated for concurrent ballot in Q1 2021.

In addition to this work, the subcommittee is also focused on a parallel effort to establish best practice guidance on equipment performance validation, scale-up, and validation strategy applied to lyophilization. Following the completion of **WK63507**, the group will turn its attention to this new effort, register the necessary work items, and invite interested members.

E55.06 Microbial/Sterility Assurance for Pharmaceutical and Biopharmaceutical Products

Chair: Scott Drummond, Johnson & Johnson

Subcommittee E55.06 remains focused on addressing an unmet industry need to develop new standard practice and

guidance documents in support of the microbiological quality and sterility assurance of pharmaceutical products. E55.06 welcomes its newest officer, Dr. Martin Muellner as sub chair for E55.06. Dr. Muellner comes from Boehringer Ingelheim in Germany and helps to strengthens the international scope of ASTM. Membership of E55.06 currently is 42 members. During the October 2020 meeting, the subcommittee approved the final draft of **WK69826**, *Standard Practice for Standard Template for Environmental Monitoring Trend Analysis* for its first subcommittee ballot. The subcommittee is also working on the development of **WK69660**, *Standard Guide for Microbiological Quality and Contamination Prevention Strategy*.

In additional to this work, another new work item was approved during the October meeting. A task group and collaboration area have been launched for **WK74412,** *Standard Guide for Critical Airflow Visualization.* The task group will have its first meeting in November and look to establish a regular meeting cycle. The subcommittee also approved the start of work to develop a standard on Selection and Management of Aseptic Gowning with work toward the creation of this standard coming soon.

During the E55 October, E55.06 invited guest speaker Dr. Julian Rosenberg at the Center for Biopharmaceutical Education and Training, at Albany College of Pharmacy and Health Sciences to present on his efforts at Albany College. Dr. Rosenberg spoke about the centers new Professional Science Master's program in biomanufacturing and bioprocessing. More information can be found at https://www.cbetalbany.com.

For any questions or to participate in standards development please reach out to either Scott Drummond, Johnson and Johnson organization or Martin Muellner at Boehringer Ingelheim.

E55.95 Roadmap for Standards Development

Chair: Louis Traglia, Commissioning Agents Inc.

The roadmap subcommittee has three main objectives at the moment, with a strong focus on two primary goals. First goal is to have a committee and system that allows the executive subcommittee and the general membership to see what we are doing, as well as where we want to go within E55. The second goal is to have a mechanism whereby E55 can convey to both ourselves and our industry peers the full extent of how E55 can help with guidance and solutions.

Part of any roadmap is to not only see where you have been, but help you determine where you want to go. In support of this, the group has been working on a series of surveys, all of which are designed to help the executive subcommittee understand where standards are needed. To this end, a new survey has been designed and will be distributed soon to both the membership and industry thought leaders. Within the survey, the first set of questions addresses "*What areas do you think additional standards would help your company*?". This is broken down into 10 segments, from Aseptic operations to Lyophilization to Cleaning. The intent is to determine generally where additional guidance can help the industry. The second part of the survey then poses specific standards within an area, and a relative sense of urgency for each. A simple rating system indicating an urgent need, a future need, or not a priority will be used to rate each proposed topic. The goal is to determine a handful of standards that the industry and membership feels are needed now. We have had suggestions for over 60 topics from our last survey, and realize it is not feasible to develop that many within a few years, so we want to focus on what specific standards would be of most benefit. Of course, we will also be soliciting names of volunteers to make this whole thing work.

Two other projects will round out the next year. We are working on a format where we can provide to the industry a way of sorting and searching all of the standards currently under the providence of E55. The intent is to produce something that will provide searches with either keywords or pre-defined search categories such as PAT, Laboratory, SUT, or C&Q. Ideally this will provide the user with a better understanding of all of the ways in which E55 can provide guidance.

The final project is to develop a graphical method to display the work of the committee in such a way as to allow macro analysis of what we are doing, where we are going, and where are the gaps. This long-term project is intended to convey the volume and breadth of standards already produced and allow for assessment of where we need to go as a team. As a committee of volunteers, anyone interested

in contributing to this work is encouraged to join the subcommittee.

Committee Outreach

Reaching the Global Community

E55 Leaders Respond to EMA Survey

In September of 2020, members of the ASTM E55 Executive Subcommittee, with support from the ASTM D.C. and EU offices, prepared and submitted a response to the EMA European Medicines Regulatory Network survey on "*Public consultation on European Medicines Agencies Network Strategy to 2025"*. The strategy is intended to align with the broader Pharmaceutical Strategy for Europe being developed by the European Commission.

The response from ASTM E55 provided details of the Committee and the Standards under its jurisdiction and suggested that the European regulatory agencies could leverage ASTM International activities to support relevant goals in the strategy document.

The E55 Exec will continue to monitor the outcome of this survey along with other EMA activities as the group continues to increase awareness within Europe.

Full Committee Meets Virtually in October

E55 was forced once again to hold its semi-annual meeting virtual this past October due to the ongoing COVID-19 pandemic. The meeting was originally planned to be held at the Johnson & Johnson Quality Assurance Laboratories in Raritan, NJ. However, the group was able to modify the schedule and held various meetings over the course of three days during the week of October 5, 2020 via Webex.

E55 officers and the J&J members involved in planning the event agreed to postpone the in-person meetings at the facility until October 2021 should safe travel resume by then.

Upcoming Events

Future Meetings

Next E55 Meeting: Q2 2021

E55 Committee leadership is currently working closely with ASTM staff to plan for the next semi-annual full committee meetings for 2nd quarter 2021. Based on the current status of the COVID-19 pandemic, it is very likely that the group will once again meet virtually.

Stay tuned for additional information regarding the 2021 meeting which will be distributed to all members in the coming months.

Membership Updates

Colleagues in Industry

E55 Recognizes Task Group Chairs

Thanks to the hard work and leadership of our members, several major E55 standards development and revision efforts were completed in 2020. In recognition of these achievements, the committee honored the following members for their role as task group chairs and technical contacts during the October 2020 meeting:

- **Gregory Bremer**, technical contact for new standard *E3231 Standard Guide for Cell Culture Growth Assessment of Single-Use Material*
- **Marc Hogreve**, technical contact for new standards *E3244 Standard Practice for Integrity Assurance and Testing of Single-Use Systems* and *E3251 Standard Test Method for Microbial Ingress Testing on Single-Use Systems*
- **James Rydzak**, technical contact for revised standard *E2898 Standard Guide for Risk-Based Validation of Analytical Methods for PAT Applications*
- **Andrew Walsh**, technical contact for new standard *E3219 Standard Guide for Derivation of Health-Based Exposure Limits (HBELs)*
- **Martin Warman**, technical contact for revised standard *E2629 Standard Guide for Verification of Process Analytical Technology (PAT) Enabled Control Systems*

- **Klaus Wormuth**, technical contact for new standard *E3230 Standard Practice for Extraction of Particulate Matter from the Surfaces of Single-Use Components and Assemblies Designed for Use in Biopharmaceutical Manufacturing*

Welcome New E55 Members

For those just joining the Committee – Welcome! Your participation in the technical committee allows you to directly impact the content of the standards. The following list of new members includes those who joined E55 since the previous issue of the E55 Newsletter.

New Member	Organization
Cousin, Stephane	GSK Vaccines
Trautman, Kimberly	
Sharma, Padam	Johnson & Johnson
Cameron, Nancy	Medtronic
Muellner, Dr. Martin	Boehringer Ingelheim Corporate Center GmbH
Moelgaard, Gert	Moelgaard Consulting
Huang, Ting Kuo	Genentech
Vazquez, David	Pfizer
Heinz, Denise	
Wells, Katrina	Advanced Regenerative Manufacturing Institute
Morbey, Kelly	ARMI BioFabUSA

The current E55 membership consists of over 200 subject matter experts from around the world. Countries represented include Belgium, Canada, Chile, China, Denmark, France, Germany, Ireland, Japan, Luxembourg, Malta, Mexico, Nepal, New Zealand, Peru, Singapore, Spain, Switzerland, UK, and USA.

Not a Member? Here's How to Get Involved

Any individual or organization from any country with interests in the pharmaceutical and biopharmaceutical industry are welcome to join Committee E55 and share your ideas. Existing ASTM International members can join E55 via their MyASTM account page. If you are not already an ASTM member, all you need to do is complete an application at www.astm.org/MEMBERSHIP/. Should you ever have any questions regarding the organization, the Committee, or standards in general, do not hesitate to contact our E55 Staff Manager, Travis Murdock, at tmurdock@astm.org.

Effective Participation Tips

Maximize Your Investment

Proactive Participation

After joining your committee(s), we encourage you to be proactive – build a foundation of knowledge and engage with the committee leadership. Here is some key information to get you started.

ASTM Member Specific Training

We offer live online training year-round, as well as face-to-face training at most technical committee meetings. The sessions provide information on navigating our website and the standards development process and include situational questions and solutions.

View member training topics and upcoming sessions at
www.astm.org/MEMBER_TRAINING

Voting

E55 members with official voting rights are encouraged to vote on all ballot items in order to maintain voting rights and help ballots meet the necessary response requirements. Voters not familiar with an item can vote abstain to help the item move forward in the approval process. If you have any questions about an item on ballot, you can always contact the technical contact of the item or the E55 Staff Manager.

Additional Information

Other Tools: ASTM Regulations
ASTM Form & Style Manual
How Standards Get Developed