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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 Spring 2020 edition of the ASTM Committee E55 Newsletter. The planned face-to-face meetings scheduled for Prague, Czech Republic, had to be cancelled due to the coronavirus pandemic. Nevertheless, we held a series of successful virtual meetings during the period April 27 through 30, 2020. This issue of the Newsletter contains updates and details on new activities of the committee since last Fall.

In addition to the usual distribution the Fall 2019 Newsletter was sent to thirty-nine industry leaders to inform them of E55 activities and potential benefits of committee membership to their organizations. We have the intention to connect with some of them to create a Forum where their needs for Standardization can be discussed.

The group also held a kick-off meeting in February of this year at ASTM headquarters in Conshohocken, Pennsylvania, regarding standards for Combination Products. The meeting focused on defining those products and what standards might be useful.

This issue also includes updates for the second E55 membership survey under the able leadership of Lou Traglia. See his report regarding the results and how it will help to inform future E55 standards and activities.

The second meeting of the E55 Academic Leadership Forum took place virtually on April 27, 2020. Guests of the meeting included ASTM Director, Pat Picariello, who presented on ASTM's AM (Additive Manufacturing sector) Footprint; Clive Badman, UK Medicines Manufacturing Innovation Centre (MMIC) on ways to industrialize new manufacturing technologies and bridge clinical and early-launch supply gaps; Bob Steininger covered cell and gene therapy needs for standards; Caterina Minelli regarding UK National Physical Laboratory's standards-related activities; Alastair Florence on an overview of activities related to the Continuous Manufacturing and Advanced Crystallization hub (CMAC) and key manufacturing and skills needs; and Carl Lawton regarding continuous manufacturing, cell and gene therapy and integrated continuous bioreactor and chromatographic processes. A full report on the Academic Leadership Forum and the activities of the various E55 Subcommittees can be found in this issue of the Newsletter.

Also, please mark your calendar for the next E55 face-to-face meetings currently scheduled for October 6-8, 2020, at the J&J facilities in Raritan, New Jersey. The meeting is in the planning stages and will likely include a workshop on microbial and sterility assurance.

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

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 chairmen.

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

Chair: Benoît Igne, Vertex Pharmaceuticals

The E55.01 subcommittee activities in 2020 will be focused on advancing the revision of several standards due for review and reapproved.

As part of these major revisions, the subcommittee would like to start by thanking James Rydzak for leading the revision of **E2898-14** *Standard Guide for Risk-Based Validation of Analytical Methods for PAT Applications*. The standard went to ballot earlier this year and is currently pending publication as a 2020 standard. **E2891-13** *Standard Guide for Multivariate Data Analysis in Pharmaceutical Development and Manufacturing Applications* is now being balloted after addressing comments gathered in late 2019. Next up for the subcommittee is the revision of **E2968-14** *Standard Guide for Application of Continuous Processing in the Pharmaceutical Industry* (WK57018) which will be going out for ballot in the coming months. And after much consideration and discussion during the April meetings, the subcommittee has decided that **E2474-14** *Practice for Pharmaceutical Process Design Utilizing Process Analytical Technology* is being balloted for withdrawal. A major part of this decision is that the current version no longer reflects modern process design methodologies endorsed by ICH and regulatory agencies. E55.01 is also working on additional updates to **E2629-19** *Standard Guide for Verification of Process Analytical Technology (PAT) Enabled Control Systems* based on comments from the previous revision cycle.

E55.03 General Pharmaceutical Standards

Chair: Paul Gil, Amicus Therapeutics, Inc.

Subcommittee E55.03 has made significant progress with multiple standards projects over of the course of the past few months. The bulk of which comes from the hard work and leadership of Andrew Walsh and his Cleaning Validation task group. The group recently completed work on new standard **E3219-20** *Standard Guide for Derivation of Health-Based Exposure Limits (HBELs)*, which is now available. The team is now focusing on two other new work items; **WK64938** *Standard Practice for the Calculation of Cleaning Validation Limits* and **WK67425** *Standard Practice for the Qualification of Visual Inspection of Pharmaceutical Manufacturing Equipment and Medical Devices for Residues*. WK67425 was recently sent for out for its first ballot to the subcommittee. The group as also enlisted the help of members from ASTM Technical Committee F04 on Medical and Surgical Materials and Devices. The task group also announced plans to update **E3106-18e1** *Standard Guide for Science-Based and Risk-Based Cleaning Process Development and Validation* to incorporate references from these new standards.

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 its first meeting at the ASTM Headquarters in February 2020. As a result, the group has registered **WK72293** *Standard Guide for Definition of Combination Products (Drug, Device, Biologic Combinations)*. See the *Committee Outreach* section for more info about the kick-off meeting.

Other work around the subcommittee includes the ongoing revisions to E55's most popular standard, **E2500-13**, *Standard Guide for Specification, Design, and Verification of Pharmaceutical and Biopharmaceutical Manufacturing Systems and Equipment* (**WK66032**), which will be balloted later in 2020. The subcommittee recently reviews and reapproved **E2503-13(2020)** *Standard Practice for Qualification of Basket and Paddle Dissolution Apparatus.* A revision to **F838-15ae1** *Standard Test Method for Determining Bacterial Retention of Membrane Filters Utilized for Liquid Filtration* are also underway and anticipated for ballot in June.

E55.04 General Biopharmaceutical Standards

Chair: Bob Steininger, Surface Oncology

Recent work of the E55.04 subcommittee has focused around the area of single-use systems (SUS), resulting in a series of new standards. Since the previous issue of the Newsletter, E55.04 has completed and published **E3230-20** *Standard Practice for Extraction of Particulate Matter from the Surfaces of Single-Use Components and Assemblies Designed for Use in Biopharmaceutical Manufacturing,* **E3244-20** *Standard Practice for Integrity Assurance and Testing of Single-Use Systems,* and **E3251-20** *Standard Test Method for Microbial Ingress Testing on Single-Use Systems*.

With the completion of these standards, the group is now focused on three other proposed new standards. First is **WK65429** *Standard Practice for the Process to Remove Retrovirus by a Small Virus Retentive Filter* is currently out for concurrent ballot. Once approved, the Committee will

have three standards that collectively would provide 15 log removal of retrovirus if incorporated into a production process and followed for an early phase GMP process. Next is **WK64991** *Standard Practice for Stability of Early Phase Protein Products* deals with stability for proteins made for early phase clinical trials held at less than or equal to -65°C. Having been previously at subcommittee, the draft is currently being updated for concurrent ballot. Finally, work on **WK65428** *Standard Guide for the Application of Continuous Processing in the Biopharmaceutical Industry* is wrapping up and the group anticipates this going out for subcommittee ballot later in 2020.

E55.05 Lyophilization

Chair: Arnab Ganguly, IMA Life

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. An updated version of the draft is anticipated for concurrent ballot later in 2020.

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. Since its creation last year, the subcommittee has grown in size with total of 36 members. The subcommittee is actively developing **WK69826**, *Practice for Standard Template for Environmental Monitoring Trend Analysis*. This practice is intended to provide a template that can be used to standardize the reporting of microbiological environmental monitoring data from surfaces and air and provide recommendations on what information should be trended to establish evidence of control over clean areas and systems. In addition, the subcommittee recently initiated work to start **WK69660**, *Standard Guide for Microbiological Quality and Prevention Strategy* and is intended to provide guidance for firms when establishing a control strategy.

E55.95 Roadmap for Standards Development

Chair: Louis Traglia, Commissioning Agents Inc.

The E55.95 roadmap subcommittee has been working on three 3 main objectives. First is to document standards that have been developed, so as a group we can see where we have been and what has been done. Second, is to help convey where we are going; to this effort we developed a brochure and presentation that have been used by the E55 executive committee to help convey to the larger industry what E55 is doing. Finally, the roadmap subcommittee is working to help determine where we want to go and responding to the question *"what standards does the industry want and need?"*

To help answer that last question, we have conducted periodic surveys, with the most recent being generated and distributed earlier this year. The survey had two main areas of focus First of which is *are our current standards useful and are they being used within industry*. The results of this first series of questions was quite encouraging, with over 94% of the respondents agreeing that E55 standards meet valid industry needs. Also encouraging is the 70% positive response to two questions that point to ease of access and awareness of E55 standards. While 70% is a great rate, the 30% who can't easily find all E55 standards that would be useful when starting a new project, or who don't look to standards when faced with a problem, means we have opportunities to improve how we get the word out.

Using the data from the survey, the roadmap subcommittee will continue to work with the Executive subcommittee on programs designed to improve how we can educate the industry on the wide variety of materials we have available, and more importantly, how E55 standards can help provide solutions to problems.

The second area of focus was a series of questions that asked *are current standards adequate, and if not, what is*

needed. These two questions were repeated for a variety of area of interest for E55, including Single Use Systems, Continuous Manufacturing, Process Analytical Technology, Lyophilization, C&Q, Cell and Gene Therapy, Cleaning, computer Validation, Microbial and Sterility assurance and Combination Products. Quite a wide variety.

For each area, we asked specifically *"are additional standards needed to support…? And if yes, what is needed?"* The results were interesting because in every one of the ten areas, new standards were suggested. In some areas such as PAT and Continuous Manufacturing, a full 30% of the respondents said additional standards were needed, with numerous suggestions being made. For a few areas, we received strong feedback that no additional standards are desired. However, even in the areas where up to 88% of the respondents said no additional standards were needed, the 12% who said yes made positive suggestions for specific standards.

The results of the survey have been given to the Executive subcommittee, as well as each of the subcommittee officers. All of the suggested standards have been passed to the responsible subcommittees to assess for action. With the suggestions for new standards, 66% of the respondents also volunteered to help write future standards. This is probably the most encouraging metric from the survey, the number of people who are willing to step forward to help advance our industry.

In addition to the survey, the roadmap committee is constantly looking for other areas where standards can help improve our efficiency and compliance. In support of this basic function, twice a year an academic forum is held in conjunction with our semi-annual meetings. The purpose of this is assess where academia, as a precursor to industry innovation, is working and where they perceive standards could help integrate new technology, techniques or processes into our industry. Topics being looked at in this forum include of course gene and cell therapy, but also items such as "Additive Manufacturing" (3D printing for laymen) that is now being used to construct artificial organs and may be used for building advanced therapeutics.

The E55 Roadmap provides a crucial function. It can help document where we have been, help us plan how to get where we want to go, and can even be used to help find new destinations. E55.95 plans to continue working on all three of these aspects.

Committee Outreach

Reaching the Global Community

Combination Products Task Group Launched at ASTM Headquarters

After months of collaboration, the new E55.03 task group on Combination Products held its first official face-to-face meeting at the ASTM International main office in West Conshohocken, PA on February 25-26, 2020. Attendees at the event included existing and new members of the committee representing various companies as well as regulatory agencies such as the FDA Office of Combination Products and the European Medicines Agency.

The two-day event resulted in the registration of a new work item, **WK72293** *Standard Guide for Definition of Combination Products (Drug, Device, Biologic Combinations),* which aims to harmonize how combination products are defined around the world. The task group has

since continued to meet on a monthly basis. ASTM staff is current working on a feature article on this effort for the upcoming July/August issue of *Standardization News*.

E55 Academic Leadership Forum

The recently formed E55 Academic Leadership Forum held its second meeting on May 27, 2020. The Forum was first developed start a dialogue with Academia to identify new technologies and platforms under development or anticipated to emerge in the next five years that might benefit from consensus standards.

For the May meeting, several individuals participated in presenting on new areas for E55 to consider for standards development. ASTM technical committee operations director, Pat Picariello, presented on efforts underway at within the area of Additive Manufacturing and the ASTM committee F42 responsible for the work. Global representation in F42 includes participation from 27 countries, U.S. government initiatives like America Makes, academia and other standards organizations including ISO; F42 and ISO TC261 have an existing agreement for cooperation on joint standards development. The committee has subcommittees that cover industries such as; aviation, spaceflight, transportation, maritime, electronics, construction, petroleum, and medical/biological. E55 intends to monitor the evolution of the F42 medical/biological subcommittee.

Also presenting was Clive Badman with the UK Medicines Manufacturing Innovation Centre (MMIC), who covered the activities of the Center. The MMIC provides a pre-competitive, collaborative environment centered around industrial innovation to solve so called “Grand Challenges”. The group is working on: Continuous Direct Compression Digital Test-Bed; Automated Clinical Supply Packing; Product Performance Particle Engineering; and Cost Effective and Sustainable Oligonucleotide Manufacturing in the CMAC Future Manufacturing Research Hub.

In addition, Clive provided three areas where they have an interest to engage with ASTM and E55. Those areas include: Digital Workflow Design and Control (Functionality Design); Process Controls & Regulatory Controls (Artificial intelligence and Machine Learning); and Metrologies (Quality of Data).

E55 founding member and former committee officer, Martin Warman, Research Director, University of Strathclyde has volunteered to be the point of contact for the work of the MMIC.

E55.04 subcommittee chair, Bob Steininger, also provided an overview on the need for standards related to cell and gene therapy. Since the October 2019 E55 meeting at Georgia Tech, he pointed out the need to help industry to move forward with some commonality. Area of interest identified include standard to transport cells from one place to another and maintain viability of cells and analytical aspects to look at multiple expressed products simultaneously via mass spectrophotometry.

Additional meetings are needed to identify which areas are most important in order to identify CQA’s and PAT Sensors.

New to the committee, Caterina Minelli, Principal Research Scientist – Medicine Manufacturing- UK National Physical Laboratories (NPL) presented the activities covered at her institute. The work has been focused on: Technical Innovation in both Established and Disruptive Technologies like Continuous Manufacturing; Predictive Manufacturing Models and Accelerated Manufacturing of new drugs; Digitalization of Medicine Manufacturing; Manufacturing of Personalized Medicine.

Furthermore, NPL is working on various case studies that are of interest to E55 such as: Small Molecules topics (Metadata Standardization, Continuous Manufacturing, Real time tablet classification); Nanomedicine (Instrument Validation, Selection of QA Methods); Biomanufacturing (Live Cell Imaging Methods, In line PAT for viral vector manufacturing, Raman Based Methods, Gene delivery)

Dr. Minelli and her NPL colleagues have experience with ASTM committees and look to get more involved with E55 as it relates to their work.

Prof. Alastair Florence from the UK CMAC Technology Innovation Center University of Strathclyde covered the CMAC mission in Continuous Manufacturing and API advanced crystallization. The CMAC was formed to address key manufacturing oral dosage form processes and people skills required. Overlapping areas of interest presented include: Crystalline Pharmaceutical Particles; Enable Flexible Process Stream for Oral Dosage Form;

Digital, Made Smarter & MMIP Roadmap; Quality by Digital Design (QbDD); API Crystals to Bulk API; Systematic and Experimental Workflow; Data & Digital Tools; and Integrated Process Design.

The final presentation for the Forum was made by Prof. Carl Lawton of the University of Massachusetts, Lowell College of Engineering, Massachusetts Life Science Center, presented on the areas of focus of: Continuous Biomanufacturing (integrated continuous bioreactor and chromatographic process); Gene/Cell Therapy; Bispecific Antibodies; Vaccines (viral like particles). Other topics for potential standards also included continuous biomanufacturing addressing communication for near-IR sensor data.

The areas covered by the various presentations will also serve as additional input for the E55 Standards Roadmap. The Forum is set to meet again in conjunction with the next E55 committee meetings at the J&J Quality Assurance Laboratories in Raritan, NJ on October 5, 2020.

April Prague Meeting Moved Online

In light of the current Coronavirus/COVID-19 pandemic, ASTM International made the decision to cancel all in person committee meetings through June 2020. This move included the E55 April meeting original set for Prague, Czech Republic. However, with the support of our officers and members, the Committee was able to shift all technical and administrative subcommittee meetings to virtual meetings. The different groups managed to hold several productive meetings throughout the week of April 27, 2020.

The Committee will continue to plan all future meetings as in-person events but will continue to monitor the outbreak and inform members should the situation impact travel again in the near future.

Upcoming Events
Future Meetings

Save the Date: Next E55 Meeting Oct 2020

E55 Committee leadership is currently organizing the next full meetings set for the week of October 5, 2020. Previously announced plans to meet in person at the Johnson & Johnson Quality Assurance Laboratories in Raritan, NJ are currently on hold due to the COVID-19 pandemic and will likely result in the group meeting again virtually. We hope to resume in person meetings in 2021 and will continue to monitor the situation.

Stay tuned for additional information regarding the October 2020 meeting which will be distributed to all members in the coming months.

Call for Future Meeting Locations

As a technical committee that meets outside of the traditional ASTM Committee Week schedule, E55 routinely relies on committee members and industry partners for support in identifying future meeting locations. If you are interested or aware of an organization that would like to host a future E55 committee meeting or special event, you are encouraged to contact Travis Murdock (ASTM Staff Manager, Technical Committee E55; tmurdock@astm.org) to discuss meeting logistics and requirements.

Membership Updates
Colleagues in Industry

E55.06 Announces Leadership Change

E55 recently announced a change of leadership for the E55.06 subcommittee. Dieter Bachman, Director of Aseptic Processing, J&J Microbiological Quality and Sterility Assurance, has had to step down for the role as subchair, turning the reigns over to his J&J colleague, Scott Drummond, Senior Scientist, Aseptic Processing. Dieter was the founding subchair of E55.06 and plans to remain involved to support E55 European activities.

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
Desai, Parth	Nostrum Laboratories Inc.
Kanegsberg, Barbara F	Bfk Solutions Llc
Mobley, Marcus	J. Strickland Co.
Hederra, Luz M	Instituto de Salud Pública de Chile
Sthapit, Basundhara	Sigmapharm Laboratories, LLC
Robinson-Zeigler, Becky	BioFabUSA
Minelli, Caterina	National Physical Laboratory
Vincent, David W	VTI Life Science
Garcia, Alexis	Advanced Regenerative Manufacturing Inst.
Tumambac, Gilbert	Pall Corporation
Rathi, Kailash	Ocular Therapeutix
Buff, Noah	
Michels, Christine M	Rebiotix
Neadle, Susan W	Johnson Johnson
Bano, Khaudeja	
McCoy, Timothy	Sanofi
Roesch, Jasmin	Oetiker Deutschland GmbH
Muniz, Luis R	Johnson Johnson
Parnel, Dyanne	Standard Practices LLC
Maeder, Manfred	Novartis
Halperin, Frederick	Depuy Synthes
Burns, Melissa	FDA
Nguyen, Thinh	FDA
Yoon, Diana	FDA
Wagner, Thierry	DU PONT de NEMOURS LUXEMBOURG
Gamblin, Christophe	Theraxel
Rufner, Jeff E	Zimmer Biomet Holdings, LLC
Diyora, Jayen	Alnylam Pharmaceuticals

The current E55 membership consists of over 190 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