People • Science • Regulation

PDA Letter

Regional Edition: Asia

Volume 1 • Issue 2
July 2020
www.pda.org/pdaletter

# Pandemic Marks 1st PDA Asia Pacific's Anniversary

Having just passed the milestone of our first-year initiation as the PDA Asia Pacific leadership, we find ourselves in a totally unpredictable situation. Thankfully, we belong to a network of association industry professionals who followed the situation in China starting in January. This enabled us to adapt to the situation quickly.

Marcel Ewals, PDA Asia Pacific Office

Aside from the operational precautionary measures by operating our team in Singapore under the business continuity plan protocol early on, we had yet to see the impact in the region and the duration of it. Without giving away my age, I recall the days of SARS and applied what I learned from that time. Still, as we now all know, not much could have prepared us for this.

Following the launch of PDA Asia Pacific last year, we reached out to PDA's chapters in Japan, Korea, Taiwan and Singapore. We listened and we learned, adding three new events in these markets. We recognized that PDA members in several countries had a wonderful process in place, providing a good quantity of education for members. PDA's Japan Chapter already has a strong framework. We also learned regulatory agencies and other organizations in the region PDA was well known but its presence not felt. With this in mind, we drafted an ambitious plan to be represented at events, industry meetings and digital offerings. Of course, digital resources have become more critical as of late and we hope that you have encountered more PDA activities whilst browsing the internet feedback is always welcome.

Tony Chan, PDA Asia Pacific Office

Under COVID-19, our objectives for the year have not changed, but the means of delivery has certainly changed. We will continue our growth in Southeast Asia, in particular, in Indonesia, Thailand and Vietnam. Furthermore, we intend to support those chapters that need our assistance.

We will be partnering with events such as CPHI and Interphex for both in-person and virtual events.

PDA Asia Pacific will also engage in the following educational online programs:

- **PDA Training Courses —** Around 2-3 hours at a cost of $200 USD.
- **PDA Partnered Training Courses —** Around 2-3 hours at a cost up to $200USD.
- **PDA Knowledge Sharing Webinars —** Around 1 hour and free to attend

We are currently still pursuing two conferences, one on pharmaceutical manufacturing and quality, and the other on aseptic processing of biopharmaceuticals. Both will be in a hybrid virtual/in-person form. Continue to check the PDA website for details as the situation changes.

Finally, we want to reach out to all the readers who want to engage with us. There are also opportunities to volunteer. In particular, we are looking for volunteers interested in writing content for the PDA Letter. Local language content is welcome!

Share your ideas, suggestions and interests via our email asia-pacific@pda.org.

PDA
Parenteral Drug Association

community.pda.org

# Join the Conversation on **PDA CONNECT℠**


**The interactive, online community exclusively *for you!***

**With PDA CONNECT℠ you can:**

- Network and collaborate with fellow PDA members around the world
- Participate in discussions about niche topics in your Interest Groups
- Gain access to members-only digital resources
- Connect and engage with your local chapter

CONNECTING PEOPLE SCIENCE AND REGULATION®

**Not a PDA Member?**

*Join today to gain full access to PDA CONNECT℠ and more!*

July 2020

# PDA Letter

*The PDA Letter is published 6 times per year in print, exclusively for PDA members.*

*Articles published in the PDA Letter do not represent the official positions of PDA, Inc., but are the opinions of the authors submitting the articles.*

*Subscriptions are not available.*







## 1 Pandemic Marks First Anniversary of PDA Asia Pacific Office

*People*

**8** **Chapter Update** | Singapore Chapter Elects New Board via Electronic Voting

*Manufacturing Science*

## 9 New Vial Tech Shows Promise for Pharma Productivity

*Voices of PDA*

**5** The Year When Corona Came

**14** **Voices of the Board** | PDA Continues Global Expansion

**PDA GLOBAL HEADQUARTERS**
4350 East West Hwy., Suite 600
Bethesda, MD 20814 USA
Tel: +1 (301) 656-5900
Fax: +1 (301) 986-0296
*info@pda.org*
*www.pda.org*

**PDA EUROPE — AM BORSIGTURM 60**
Am Borsigturm 60
13507 Berlin, Germany
Tel: 49 30 4365508-0
Fax: +49 30 4365508-66
*info-europe@pda.org*

**PDA TRAINING & RESEARCH INSTITUTE**
4350 East West Hwy., Suite 150
Bethesda, MD 20814 USA
Tel: +1 (301) 656-5900
Fax: +1 (240) 482-1659
*info-tri@pda.org*


PDA
Parenteral Drug Association

# PDA Chapters

## Your Local PDA Connection

### Are you curious about the issues unique to your region?

Another layer of PDA leadership resides at the grassroots level in the Chapter organizations. Regional PDA Chapters provide local services to the membership, including translations of PDA publications, networking social events, student scholarship and annual regulatory and technical conferences. Each Chapter is managed by volunteer leaders.

**Learn more about your local Chapter at *pda.org/Chapters***

CONNECTING PEOPLE SCIENCE AND REGULATION®

# The Year When Corona Came

Ivy Louis

Subrata Chakraborty

Living has certainly changed due to the novel coronavirus pandemic, all within three months. Even in the face of this virus, collaborations in healthcare have gained traction.

For India's pharmaceutical industry, there have been positive changes in the horizon. The Indian pharmaceutical industry is the world's third largest medicines producer by volume, occupying about 20% share of generic medicines supplied globally. India is the source of 60,000 generic brands across 60 therapeutic categories and more than 500 different APIs. With these figures in mind, the industry realized this is not the time to relax and that they must join the healthcare professionals in the fight against this dreaded enemy.

Several new SOPs were born overnight to handle this pandemic situation. Regulatory authorities within the country issued new orders. With its new rules of the game, the industry unlearnt many lessons and picked up newer ones at lightning speed in order to thrive and survive. Figure 1 illustrates a potential control strategies for ensuring employee safety while also ensuring continuity of supply.

For one, all non-shop floor and support staff were to work from home. This was a new term for the pharma industry, which never realized its potential until now. Today, with a vast portion of the workforce operating remotely, many employees find the experience positive.

Virtual meetings have opened an enormous opportunity for the industry. In addition to reducing travel time and expenses, it has uncovered a whole world of training and


**Figure 1** A Typical Control Strategy to Ensure Employee Safety and Supply Continuity in Pharmaceutical Plants

knowledge sharing in a platform that is more accessible to the entire industry. With lockdowns in place, it is a great opportunity for improving one's knowledge and skills with best in-class resources now available on online platforms.With new social distancing norms, the industry is identifying innovative ways to become more productive with fewer human resources in the shop floor. Facility audits, an integral part of pharma operations, are now being conducted between manufacturers and regulators remotely. And adoption of Industry 4.0 technologies will build more resilience in systems and processes.

Amidst all the adversity, COVID-19 has revived a flame of humane values. Heroes have risen from unknown quarters and the pharmaceutical industry is no stranger. Teams are becoming more purpose-inspired and responsibility-centered. Employees at all levels are delivering more to compensate for colleagues who are stuck at the adjoining states due to cross-border lockdowns. The comradeship that extends beyond worktimes has taken on newer meaning.

The society in which pharmaceutical professional life has started to be cognizant of the contribution made towards the well-being of the world. The respect and adulation that people are experiencing are new, not just for individuals, but also for the communities.

## About the Authors

**Ivy Louis** volunteers with the PDA India Chapter. She is a pharmacist a Director of VIENNI Training & Consulting LLP. Her experience encompasses over 30 years of teaching, handling pharmaceutical manufacturing and quality systems in various capacities and being in the service providing domain for sterile products.

**Subrata Chakraborty** works as Senior Director, Technical Services with Cipla. He has over 23 years of experience in handling pharmaceutical manufacturing and quality systems in various capacities.

PDA Parenteral Drug Association

www.pda.org/pdaletter http://journal.pda.org

# Where do **leading experts** turn to communicate with the PDA community?

RICHARD FRIEDMAN
JANET WOODCOCK
STEPHAN ROENNINGER
ANDERS VINTHER
JAMES AGALLOCO
JAMES AKERS
JAMES COOPER
DENNIS JENKE
IRVING PFLUG
MARK JORNITZ
MICHAEL MILLER
KURT BRORSON

## The *PDA Letter* and *PDA JPST*



Interested in Peer Reviewing?
The *PDA JPST* is looking for peer reviewers!

CONNECTING PEOPLE SCIENCE AND REGULATION®

***For more information on PDA publishing please visit:***

***www.pda.org/pdaletter***
***http://journal.pda.org***

# Singapore Chapter Elects New Board via Electronic Voting

The PDA Singapore Chapter recently announced the results of the election for the chapter board.

**Singapore Chapter Board 2020–2022**
**President: Bruce Loxley,** GSK
**President-Elect: Emily Cheah,** Charles River Laboratories
**Secretary: Andyanto Sutandar,** HGP Asia/NNIT Singapore
**Treasurer: Christina Chen,** CAI

**Members-at-Large:**
**Richard Chai,** STERIS Corporation
**Li Wei Chan,** GSK
**Shi Ming Chau,** Johnson & Johnson
**Katie Parks,** Amgen
**Priyabrata Pattnaik,** Merck
**Rama Tummala,** GSK

Due to the COVID-19 situation, the election was carried out by electronic voting, the first for the chapter. The Annual General Meeting, where the outgoing board shared the previous year's events and financials along with the election results, was done by Skype—another first for the Chapter.

The 2020–2022 board brings a wealth and breadth of experience. Half of the Board Members were active Board Members and volunteers in 2018–2020 term. Chapter President Loxley is responsible for audit risk assessment preparation, audit planning and execution and reporting at GSK. President-Elect Cheah is currently the Managing Director of Charles River Laboratories Singapore (Microbial Solutions). Secretary Sutandar is a manager in the NNIT Group Life Sciences Divisions of HGP Asia Pte Ltd, Singapore, and leads HGP's Manufacturing Science and Technology service unit. Secretary Chen is Director of Operations at CAI (Southeast Asia). She has 18 years of commissioning and qualification and cGMP experience in the operation and validation of various types of equipment, manufacturing facilities, cleaning processes and process validation with various clients across Asia.

Please note that, at this time, chapter events originally planned for May will likely continue as virtual events. Where possible, the chapter is seeking an opportunity to collaborate with other chapters in the region for their coming virtual events. Check the chapter website https://www.pda.org/chapters/asia-pacific/singapore for the status of other upcoming events.

# New Vial Tech Shows Promise for Pharma Productivity

**Dawn Watson and Jeff Cremi, Merck & Co., Inc.**

Advances in pharmaceutical glass packaging offer advantages for both patients and manufacturers, but the potential of new innovations will not be reached without rigorous testing and line trials to confirm their benefits.

Valor® Glass, one example of such new technology, was introduced in 2017 as a tubular glass packaging solution with Type I hydrolytic performance that would substantially reduce particle contamination and prevent cracks. The idea was that its use would significantly increase throughput for pharmaceutical manufacturers ***(1–3).*** Considering that the U.S. FDA has called for improvement in glass manufacturing ***(4),*** Merck & Co. conducted a series of line trials to ensure the compatibility of Valor Glass vials with existing and new lines. The goal was to demonstrate that this innovative product could be introduced as a "drop in" solution and, potentially, deliver a higher quality glass solution. So, the company compared the performance of Valor Glass vials against the conventional borosilicate (Type I) vials currently used on their manufacturing lines.

To start the trials, a cross-functional team was established to provide the necessary expertise and experience to enable an objective assessment of the new technology. Strong sponsorship of the team ensured the availability of appropriate resources, funding and line time. This team developed a standard assessment approach that would be applied across multiple sites and products, so data gathered across various lines could be easily compared. Trials were designed to assess machinability performance, particulate generation, interventions, glass breakage and performance using visual inspection on filling and packaging lines.

The team, which included experts in glass manufacturing and handling, product ➤


## Speed-to-Market is Critical.

With over 100 vaccines and therapies in development, a constrained supply chain could affect COVID-19 response. Primary packaging that improves fill/finish efficiency and enables higher speeds could be critical for drug manufacturers during this global pandemic.

Valor technology reduces breaks, cracks and glass particulate generation that put production volumes and supply chains at risk. In addition, Valor Glass enables smooth operations and has demonstrated a 20-50% throughput improvement at various filling line speeds. This ability to increase capacity of existing and new lines may play an important role in meeting global demand for COVID-19 vaccines and therapies.

A webinar on how Valor Glass can meet your primary packaging needs is available.
Contact Lisa Guan (guanz@corning.com) for more information.
www.corning.com/valor

impact/stability, manufacturing process, quality risk management and regulatory affairs, evaluated the performance of the vials. They set success criteria and maintained an objective viewpoint throughout the various line trials. Early engagement with regulatory agencies facilitated understanding of expectations and requirements needed for implementation ***(5).***

## Study Protocol Overview and Summary Results

For initial assessment, multiple engineering trials were run on a single line, demonstrating that the Valor Glass vials performed better when compared to historic conventional glass data. The new vials enabled a higher effective line speed (more vials filled and passing final inspection per unit of time), required fewer glass-related interventions and generated lower particulate contamination. These line trials tested 50,000 to more than 1,000,000 Valor vials These line trials ranged from 50,000 to more than1,000,000 Valor vials. The result of the largest line trial is summarized in **Table 1.**

The results of the line trial confirmed the improved performance of Valor Glass vials compared to the conventional borosilicate vials currently in use.

Additional trials were conducted on different filling lines, including relatively new filling lines. The trials varied from hours to a single day of run time, with volumes ranging from 5,000 to 150,000 vials. Machinability was successful on each of these lines.

## Efficiency on the Line

Valor Glass vials have a coating applied only to the outside of the vial, so there is no increased risk with respect to extractables and leachables. The external coating reduces the coefficient of friction of the vials, allowing them to process with less resistance on a filling line than conventional borosilicate vials. Consequently, the improved flow required adjustments to certain filling lines—lines where vials are moved "en masse" with accumulation points or that move glass via backpressure—to accommodate the smoother transfer of vials and the new flow pattern **(Figure 1)**.

**Table 1** Results of an Engineering Line Trial Comparing Valor Glass to Conventional Glass

| Machinability Outcome | | | |
|---|---|---|---|
| | Conventional Glass | Valor® Glass | Performance of Valor Glass Vials compared to Conventional Vials |
| Effective Line Speed | 326 +/- 26 vpm | 440 vpm | 25% improvement |
| Interventions | 247 | 95 | 61% reduction |
| Particulates (at In-feed) | 50 | 4 | 92% reduction in nonviable particles at in-feed locations |
| Lubrication Events | 5 | 0 | 100% |

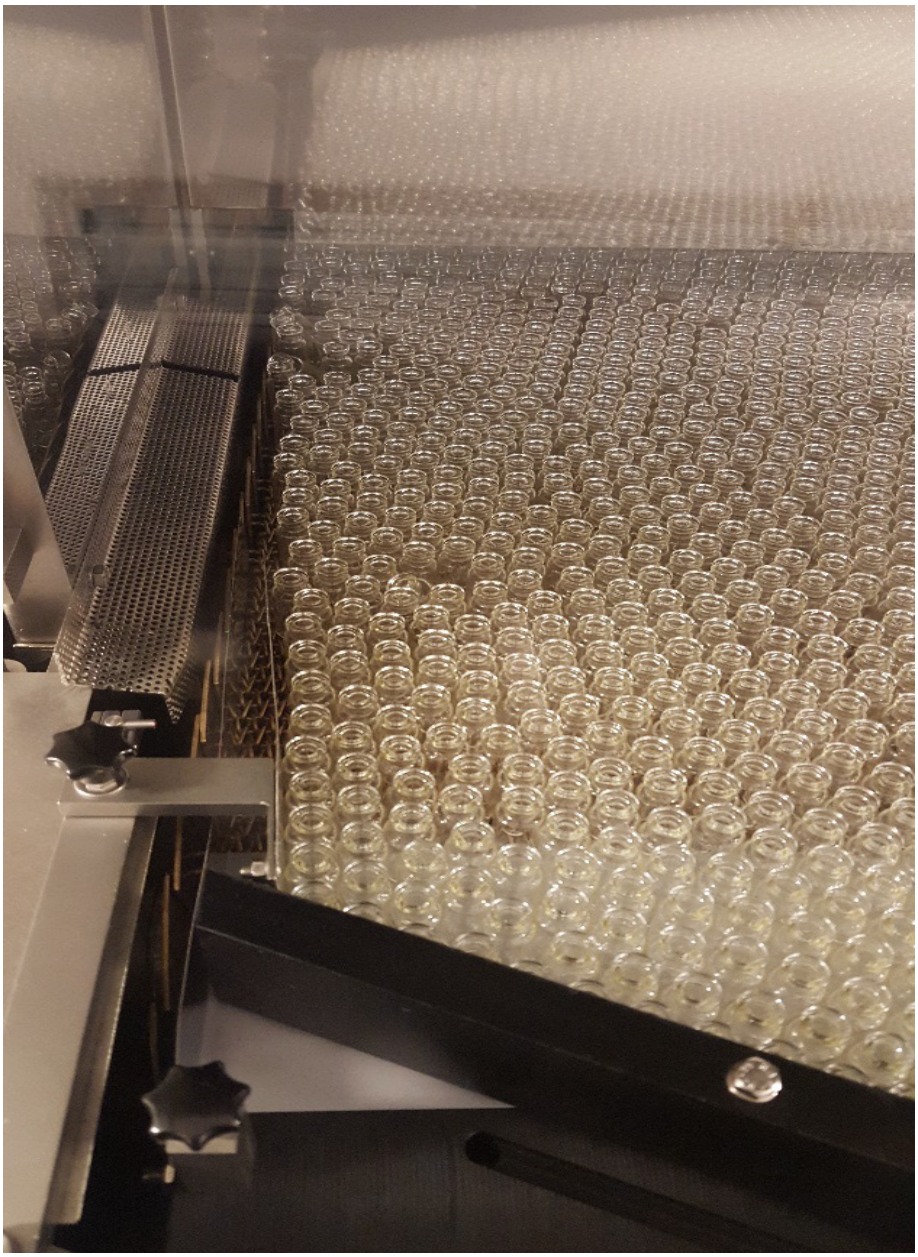

**Figure 1** "En Masse" Movement of Glass on One of the First Trial Lines

As shown in the observation of Lubrication Events in **Table 1,** the external coating on the vials eliminated the need for the application of lubricant on the line, which is used during the filling process for conventional borosilicate glass vials to improve glass flow and reduce glass events.

## Crack Prevention

Valor Glass is inherently stronger and more damage-resistant than borosilicate vials. The product was designed with significantly greater mechanical strength and higher internal energy than conventional borosilicate glass vials, which also prevents the occurrence of cracks. While Valor Glass is inherently stronger, breakage is still possible. Unlike conventional vials that can incur difficult-to-detect cracks when severely damaged, Valor Glass is engineered to break rather than crack when severely damaged, and it breaks in a more controlled manner than conventional vials. That breakage signals a quality issue, such as improper line set-up, allowing operators to take corrective action immediately. Breakage events with Valor Glass vials, for example, can enable line operators to detect and correct such issues as:

- Misaligned transition that impacts the heel of the vial
- Improper capper set-up that causes the disk/rail to damage the neck of the vial
- Filling-needle strikes that occur at the top of the vial
- The Valor Glass has not damaged equipment or exhibited cracks in any of the line testing performed to date.

## Lyophilization with Valor Glass

The team also compared lyophilization between Valor Glass and current vials, following a multistage approach. The team established equivalence for critical dimensions between Valor Glass vials and conventional borosilicate vials. Laboratory-scale runs were conducted to assess respective freezing kinetics of both types of vials. Head-to-head comparisons were conducted using gravimetric analysis, and sublimation rate data were used to determine the relative heat transfer coefficients via mathematical modeling. The studies showed that Valor Glass had a slightly lower average heat transfer coefficient relative to conventional borosilicate glass. This finding was negligible, however, with no anticipated impact to the current primary drying times for the production lyophilization cycle.

Following these comparability tests, commercial runs were conducted to assess the freezing profile, product moisture content, chamber pressure and overall lyophilization cake appearance (**Figure 2**). The results of the commercial-scale testing are summarized in **Table 2.**

Both laboratory- and commercial-scale testing demonstrated there was no need for adjustment in lyophilization-cycle parameters. No Valor Glass vials broke or cracked through the lyophilization process. The lyophilization performance of Valor Glass was deemed equivalent to that of conventional borosilicate glass vials for this specific application.

## Thoughts on Control Strategy

As with most packaging changes, the engineering trials required minor equipment adjustments to enable smoother operations. The external coating of the Valor Glass vials imparts a significantly lower coefficient of friction than con-

**Figure 2** Overall Appearance of Lyophilization Cakes in the Commercial-Scale Run

**Table 2** Comparability Assessment of Valor Glass versus Conventional Borosilicate Vials for Lyophilization

| Lyophilization Comparability | Commercial-Scale Results |
|---|---|
| Freezing Profile and Chamber Pressure | Comparable |
| Moisture Mapping | Moisture results were within specification and comparable to historical performance |
| Lyophilization Cake Appearance | No change was observed |

ventional glass, which can impact vial handling. This should be considered for machinability. The coating is durable but can be affected by extended durations at depyrogenation temperatures. The time should be monitored during extended line stoppages within the depyrogenation tunnel, and control measures should be set up to reduce the overall temperature exposure during prolonged stoppages to prevent coating degradation. Coating degradation results in a slight increase in coefficient of friction, but no loss in functional performance over the typical duration for normal processing at depyrogenation temperatures.

Valor Glass has an engineered binary response to damage, meaning that the vial is intact, or it breaks under extreme insult. This property could potentially enable enhanced quality assurance. When damaged in the uncoated flange region (specifically, the radii), Valor Glass may chip comparably to borosilicate containers; however, flange damage will not result in cracks. Breakage events with Valor Glass serve as a clear signal that suboptimal conditions may be present. While no equipment was damaged in any of the trials, precision in set-up and sensitivity to dimensional variation must be factored into engineering trials. The increased strength of the Valor Glass vial may also require equipment adjustments to ensure appropriate over-torque settings are in place in case of an event.

Any potential dimensional differences of the test vials compared to the current conventional borosilicate vials in use must also be evaluated and assessed. This is important to confirm both machinability and lyophilization equivalence.

## Discussion

Valor Glass vials were specifically designed for use by pharmaceutical manufacturers. This new package solution is optimized to resist breakage and prevent cracks through ion exchange strengthening and a thermally stable exterior coating.

The external coating of Valor Glass imparts a low coefficient of friction, which should be considered for machinability. It also protects vials from damage or insults that can occur during processing, resulting in fewer particulates. The results of line trials for Valor Glass vials demonstrated more effective line speeds, fewer glass-related interventions required on the line and a significant reduction in particulate levels.

In addition, the Valor Glass vials showed no evidence of cracks in any of the trials. Instead, they exhibited a binary behavior in coated regions of the vial. The vials were either intact or broken; but cracks did not form in response to damage events. During machinability of Valor Glass vials, finish chips were noted, but only during atypical handling or when needle strikes resulted from misalignment. Valor Glass crack prevention is an important finding considering the challenges associated with cracked containers. These results may indicate an opportunity to decouple break events from concerns related to loss of sterility or purity of batch and could, ultimately, lead to a reevaluation of current regulatory notification expectations related to broken containers.

## Conclusion

These trials demonstrated that Valor Glass has the potential to reduce particulate contamination, prevent cracks, and enhance throughput. Enabling the benefits of Valor Glass may require some optimization of manufacturing control strategies related to extended time in depyrogenation chambers and equipment setup, as discussed above. In addition, the unique attribute relating to crack prevention has the potential to reduce response activities related to broken containers.

## References


1. Schaut, R.A., et al., "A New Glass Option for Parenteral Packaging." *PDA JPST* 68 (2014): 527–534.
2. Timmons, C., et al. "Particulate Generation Mechanisms during Bulk Filling and Mitigation via New Glass Vial." *PDA JPST* 71 (2017): 379–392.
3. Schaut, R.A., et al. "Enhancing Patient Safety through the Use of a Pharmaceutical Glass Designed to Prevent Cracked Containers." *PDA JPST* 71 (2017): 511–528.
4. U.S. Food and Drug Administration. "Summary of Recent Findings Related to Glass Delamination." May 9, 2018. www.fda.gov/drugs/pharmaceutical-quality-resources/summary-recent-findings-related-glass-delamination.
5. "Merck and Pfizer Collaborate with Corning to Modernize Pharmaceutical Glass Packaging." Press release. July 20, 2017. www.corning.com/worldwide/en/about-us/news-events/news-releases/2017/07/merck-and-pfizer-collaborate-with-corning-to-modernize-pharmaceutical-glass-packaging.html.

Masahiro Akimoto

# PDA Continues Global Expansion

As a member of PDA's Board of Directors, I am honored to be part of the team that helped organize this inaugural issue.

In 2006, PDA opened its first office outside the United States in Berlin. Today, 14 years later, our activities in Europe have grown. Last year, PDA opened its second overseas office, PDA Asia Pacific, in Singapore.

PDA recognizes the need for high-quality technical resources in the Asia-Pacific region and through the Singapore office and regional chapters is looking to expand our conference offerings. Of course, there have been changes in light of the novel coronavirus epidemic. Chapters, in particular, the Singapore Chapter, have risen to the occasion by offering virtual events.

In the fall, there are two conferences scheduled, the *2020 PDA Asia Pacific Pharmaceutical Manufacturing and Quality,* Sept. 22–23, in Singapore and the *2020 PDA Asia Pacific Conference,* Oct. 12–13 in Incheon, South Korea. I recommend that you check the PDA website for updates in the event that there are changes due to the pandemic.

In addition, PDA is moving forward with translating our technical documents, including our Technical Reports, into local languages.

This is a lot of work and the novel coronavirus is impacting the pharma industry worldwide. PDA will need volunteers to assist in these efforts, from helping with translations to speaking at conferences. If you are interested in volunteering, you can help at the local level through your chapter (https://www.pda.org/pda-chapters) or by contacting PDA's Volunteer Coordinator (volunteer@pda.org).

This is a challenging time around the world and we can achieve great things by working together.

PDA
Parenteral Drug Association

trarchive.pda.org

# PDA's Technical Report Portal


View the complete library of current PDA Technical Reports, anywhere, anytime

CONNECTING PEOPLE SCIENCE AND REGULATION®

***trarchive.pda.org***

***For licensing options contact Janny Chua at chua@pda.org***