Asia-Pacific
Economic Cooperation

Advancing Free Trade
for Asia-Pacific Prosperity

Capacity Building in Biotherapeutics and Cell/Gene Therapies in Latin America

APEC Life Sciences Innovation Forum

April 2023

Asia-Pacific
Economic Cooperation

Capacity Building in Biotherapeutics and Cell/Gene Therapies in Latin America

April 2022- December 2022

APEC Life Sciences Innovation Forum

April 2023

APEC Project: LSIF 01 2020

Produced by

Jared Auclair
Northeastern University College of Science
Associate Teaching Professor
Department of Chemistry and Chemical Biology
360 Huntington Ave.
Boston, MA 02115
United States

For
Asia-Pacific Economic Cooperation Secretariat
35 Heng Mui Keng Terrace
Singapore 119616
Tel: (65) 68919 600
Fax: (65) 68919 690
Email: info@apec.org
Website: www.apec.org

APEC#223-HT-04.2

1. Background

In 2011, the Asia Pacific Economic Cooperation (APEC) leaders recognized the importance of regulatory convergence within the APEC region to ensure that safe and effective medicinal/health products reach the region's population[1]. To this end, the leaders agreed on a plan under a strategic framework to achieve convergence on regulatory approval procedures for medical products by 2020 through the APEC Regulatory Harmonization Steering Committee (RHSC). The implementation of this plan included identifying gaps in the region's knowledge and regulatory systems, identifying regulatory best practices, and increasing regulatory capacity through the establishment of sustained regional Centers of Excellence (CoE). Between 2011 and 2021 hundreds of the region's regulators were trained, and 20 CoEs[2] were established in Asian and North American regions of APEC. The absence of CoEs in the Latin American region was noted by the RHSC. To assess the success of its efforts, the RHSC measured progress towards convergences with previously identified Key Performance Indicators (KPI), the results of which were published in a paper by Chong et al.[3]

In the paper, the authors noted that from 2008 to 2020 (after the establishment of CoE's and enhanced training), there was a 14.3% increase in the number of APEC member economy regulatory authorities sharing Good Manufacturing Practices (GMP) Certificates and a 28% increase in the number of regulatory authorities accepting multisite licenses in that same period. The authors also noted that APEC plays a key role in promoting and facilitating regulatory convergence, including reliance on the work of other regulatory authorities. They recommended that domestic regulatory authorities take advantage of APEC's network of CoE's to help build capacity and prepare to implement reliance pathways.

At its Chile meeting in 2019, the RHSC updated its vision for the next decade in the document entitled: Regulatory Harmonization Steering Committee Vision 2030 and Strategic Framework—Regulatory Convergence for Medical Products by 2030[4], also known as the 2030 RHSC vision. The 2030 RHSC vision considers the previous efforts of the RHSC and aims to build on, and expand, its efforts by among other things, strengthening and scaling APEC CoEs through state-of-the-art tools including virtual and ad hoc targeted training. The RHSC also explored the possibility of establishing a CoE in the Latin American region.

To aid in this effort of implementing the 2030 RHSC vision, the APEC RHSC commissioned Northeastern University to develop a yearlong combined biotherapeutics and cell and gene therapy training program that could be used as a template for expanded trainings considering new educational tools and techniques. Noting the increasing number of biotherapeutics and cell and gene therapies that are being developed and/or are in the pipeline of many companies, the RHSC deemed it necessary to ensure that APEC region regulators are properly trained on regulatory issues and challenges that may prevent approval of these products in a timely fashion. Accordingly, the first such training was directed to the Latin American region to fill existing scientific and regulatory knowledge gaps.

---

[1] https://www.apec.org/meeting-papers/annual-ministerial-meetings/2011/2011_amm

[2] https://www.apec.org/RHSC/Contact-Us/Centers-of-Excellence

[3] Chong et. Al, Measuring Progress of Regulatory Convergence and Cooperation Among Asia–Pacific Economic Cooperation (APEC) Member Economies in the Context of the COVID-19 Pandemic. Therapeutic Innovation in Regulatory Science 2021; 55(4): 786-798

[4] https://www.apec.org/docs/default-source/satellite/RHSC/General-RHSC-Documents/APEC-RHSCVision-2030-and-Strategic-Framework-2021-Jan.pdf

Moreover, in line with the 2030 vision which seeks to promote regulatory reliance and increased communication amongst the region's regulatory authorities, the RHSC deemed it necessary to include in the Northeastern led training, successful examples of regulatory reliance in its workshop. Referencing Chong et al. which recommended reliance as a tool to address the inefficiencies of the APEC region's regulatory systems for nascent technologies e.g., cell and gene therapies, the RHSC indicated that increased training in reliance and basic training in this technology area would be necessary as the APEC region's regulators face an increasing number of cell and gene therapy submissions.

Accordingly, the APEC RHSC agreed to address this void by moving ahead with a combined year-long training in this space addressing knowledge and regulatory gaps in the region. It was decided that the combined training would consist of online interactive modules to ensure that attending regulators are up to date on common terminology, an on-line 8-hour webinar, and in-person intensive training in a Latin American APEC economy.

2. Objectives of the project

As indicated above, the main charter of the APEC RHSC is to develop and implement strategies that bring the APEC region's regulatory systems in convergence. The main beneficiary of regulatory convergence is the patient. Streamlined regulatory systems reduce regulatory burdens on any one regulatory authority and therefore enable the timely approval of safe and effective medicines. The APEC RHSC determined the most effective means of achieving convergence to be through consistent and sustained training of regulators and increased regulatory capacity through the establishment of CoEs in regulatory sciences.

APEC's LSIF 01 2020 is a yearlong training program designed to address the scientific and regulatory gaps in APEC's Latin American economies with respect to biotherapeutics and cell and gene therapies through innovative training techniques.
The project is in line with the capacity building priorities of APEC and trained participants through workshop activities such that they can apply risk-based, science-based approaches in the drug review process including: (1) Describing biologics and advanced therapies, (2) Explaining key internationally recognized guidelines and standards that are used in the drug review and approval process, (3) Explaining science-based, risk-based approaches to dossier review, and (4) Describing a patient-focused approach to biologics and advanced therapies. The project also addresses nonclinical and clinical issues associated with biotherapeutics and cell and gene therapies.

The project aligns with APEC priorities and goals in improving the capacity in the Latin American region for the approval of biologics and advanced therapies thereby helping to reduce the regulatory burden and cost of drug approval in the region. Coming on the heels of the COVID19 pandemic, training programs pertaining to the approval of safe, effective, and high-quality drugs gain significant importance. The project's objective to properly train regulators in the drug approval process, particularly in biotherapeutics and cell and gene therapies, enables a greater probability that patients receive quality medicines even during times of emergency. The training achieves this through the emphasis of science-based, risk-based, approaches utilizing examples and case studies.

APEC LSIF 012020 also aligns with the overall goals of the RHSC to achieve regulatory convergence in the APEC region. The project focuses on the development of, and implementation of training in biotherapeutics and advanced therapies touching on areas where regulatory authorities can take advantage of reliance practices to ensure products are safely and timely available to patients. In addition, the project aims to establish a CoE

in the Latin American region capable of providing capacity building for regulators in biotherapeutics and advanced therapies. Finally, the project aims to serve as the foundation for training in other APEC regions thus broadly supporting the mission towards global regulatory convergence.

3. Basic Data

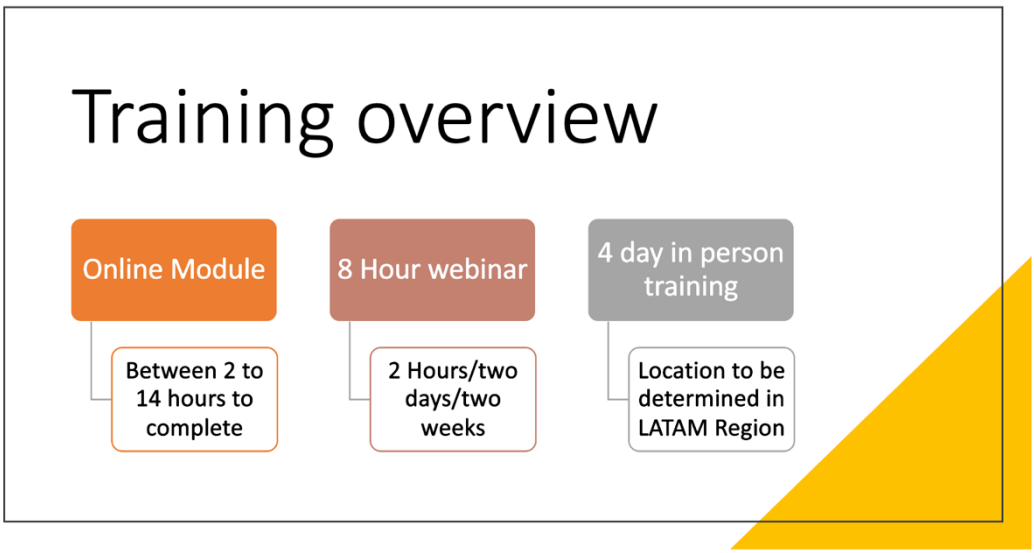
To identify the scientific and regulatory gaps in the Latin American APEC economies, Northeastern University drew from regulators as well as nonprofit institutions, other standard setting bodies, academia, and industry to form an APEC training advisory committee. Northeastern University's APEC training Advisory Committee consisted of 20 participants from the mentioned groups. Through regular advisory committee meetings, Northeastern university was able to identify areas where training was required.

REGULATORY AUTHORITIES	ACADEMIA	INDUSTRY	OTHER ORGANIZATIONS
USFDA	Northeastern University	Biogen	Alliance for Regenerative Medicine
Singapore HSA	University of Chile	Pfizer	U.S. Pharmacopeia
Former COFEPRIS		Roche	Bill and Melinda Gates Foundation
		Amgen	

Advisory Committee Composition

Once the gaps were identified, the advisory committee began the development of the yearlong training program which consisted of basic online modules in both biotherapeutics and cell and gene therapy; an 8-hour webinar over a two-week period parsed into two hours per two days; and a three-day intensive in-person training in one of APEC's Latin American economies.

Figure 1



Online Modules: The biotherapeutics online module had previously been developed and required minor updates, but the cell and gene therapy online module had to be developed de novo. To accomplish this, Northeastern University secured a learning design specialist and a content expert. Over the course of several months, the content expert and learning design specialists worked with input from the Advisory committee to update the biotherapeutics module and develop the cell and gene therapy online module. The online interactive training modules incorporated written materials, videos, and slide presentations to train regulators. Figure 2 below provides a detailed outline of the materials covered in the basic online cell and gene therapy modules.

Figure 2

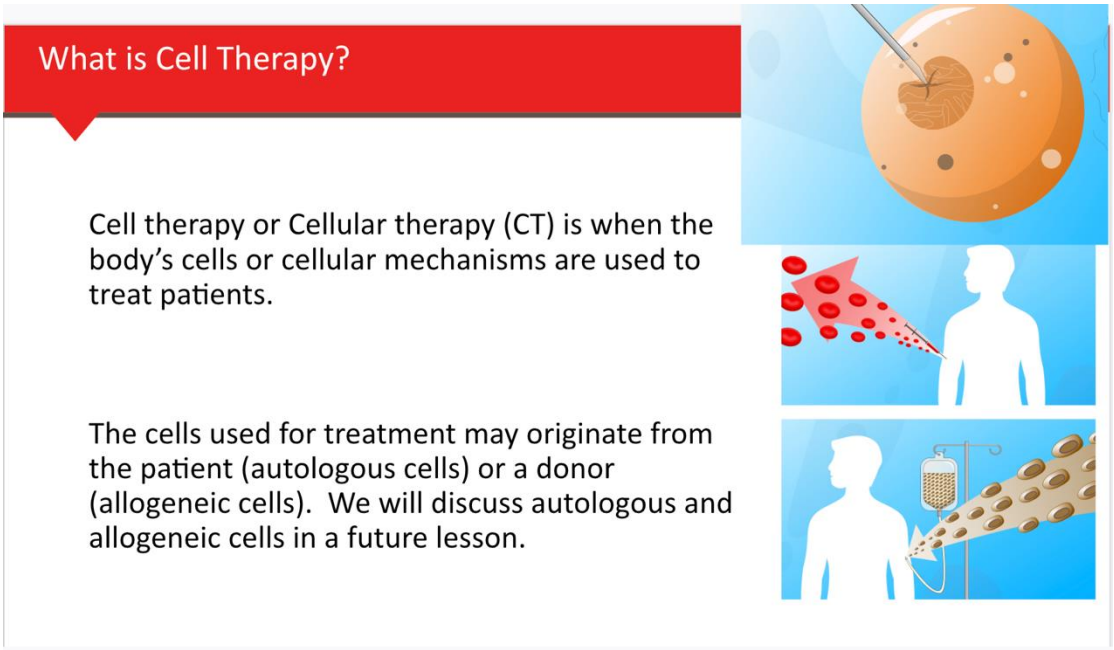
Lessons	Topics to Cover
Lesson 1: Overview	• Definition of cell and gene therapy • History of cell and gene therapies • Distinction from other biotherapeutics • First approved product and subsequent approvals • Cell and gene therapy pipeline
Lesson 2: Cell and Gene Therapy Platforms	Types of gene and cell therapy platforms • Stem cells • CAR T • CRISPR • DNA/RNA based therapies: RNAi. • Viral vectors What types of diseases can be treated by cell and gene therapy?

	• Hematology/blood disorders like sickle cell disease • Neurological disorders that affect the brain and spinal cord • Musculoskeletal diseases • Retinal disorders • Oncology (Blood cancers) • Cystic Fibrosis
Lesson 3: Product Development Overview	Development as compared to other biologics • "Process is the product" • Data collection and consistency • Site standardization • CMC • Manufacturing • Long term follow-up
Lesson 4: Production Early-Stage Developmental Challenges	• Supply chain [autologous vs. Allogeneic] • Raw materials for cell therapy: considering variability; supply issues related to vectors; lot number and associated validation challenges; the availability of reagents and use of research reagents instead of manufacturing reagents; The quality of the starting materials; Qualification processes and data for key starting materials; animal-derived materials (Source and economy of origin) • Analytics: development of potency assays; standard assays for: o Viral vector post translational modification (lack of uniform analytical tools) o Viral vector production: baculovirus and multi-plasmid transfection-based processes.
Lesson 5: Manufacturing Late-Stage Developmental Challenges	Manufacturing/scale • Comparability • *Challenges in CMC as compared to biologics Aseptic Qualification, Environmental Monitoring, and Contamination Control:* • Viral vector production capacity • Storage conditions: GMP status of the storage facilities, impact of the recommended storage conditions on container components, including any leachables and extractables. • Process Controls and Validation • Vectors, cells, Reagents, and excipients
Lesson 6: Postproduction Challenges	• Adverse reactions/Pharmacovigilance • Long term follow-up: Data challenges (Managing a radically new form of clinical trial that could span decades)

	○ Economy guidelines FDA guidelines, up to 15 years follow up https://www.fda.gov/media/113768/download EMA https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-follow-patients-administered-gene-therapy-medicinal-products_en.pdf PMDA https://www.pmda.go.jp/files/000216530.pdf
Lesson 7: Manufacturing Innovations	• Flexible facilities • Process Analytic Technology (PAT) for manufacturing and scale up challenges.

The cell and gene therapy online module was developed on Rise platform to allow for flexibility. The Rise teaching tool allows for multi-template story board with video capability. See Figure 2 below.

Figure 3



Once complete, the online modules were simultaneously launched for registered regulators to complete at their own pace but before the launch of the synchronous webinar. These modules served as the prerequisite for the remainder of the training and provided the basis for more in-depth learning in the synchronous webinar series and in-person training. Marketing fliers (Appendix A) were circulated to the APEC Regulatory Harmonization email list of approximately 200 contacts. The online modules were attended by 60 participants (see Appendix B). The online training remains available for APEC regulators to access at their own pace.

Synchronous Webinar: Shortly after the launch of the online modules- approximately four months- Northeastern University launched the 8-hour synchronous webinar. The

webinar delved deeper into the topics touched on in the online modules. The topics included the basics and fundamentals of biotherapeutics approvals including biosimilars, post approval considerations for biologics, cell and gene therapy basics and their difference from other therapeutics, regulatory considerations for cell and gene therapies and cell and gene therapy product development and unique challenges. Detailed outline for the webinar is presented in Figure 4 below.

Figure 4

	Biotherapeutics Basics and Fundamentals of Approvals
	Biotherapeutics Basics Regulators became familiar with the different types of biotherapeutics and how they are different from other molecules. This included an understanding of biosimilars and their distinction and how biotherapeutics differ from cell and gene therapy platforms. Regulators were also provided with training on the key ICH and various other guidelines regulating originator biotherapeutics.
	Fundamentals of Biotherapeutics Approval: Case study Regulators learned application of ICH Q5 A-E in approving biotherapeutics, and how risk-based approaches can be used for approving a recombinant biotherapeutics product. Regulators reviewed public assessment reports (e.g., EMA EPAR) and identified issues that were raised. Regulators also learned how authorities can facilitate reliance approaches.
	Biosimilar Assessment: Case study Regulators gained an understanding of how biosimilars are different from originator biologics by reviewing assessment reports from Stringent Regulatory Authorities (e.g., EMA, PMDA and FDA) and learned when the assessment of other trusted regulatory authorities can be utilized in approving these products. Regulators learned about CTD development for originator biologics vs. biosimilars (including CMC elements, Structure Function Studies, clinical pharmacology, immunogenicity) and learned the importance of clinical trials in the evaluation of the benefit-risk balance of biosimilars.
	Post approval considerations for Biologics (excluding vaccines) Regulators were exposed to various post approval considerations for all biotherapeutic products by overviewing various guidelines and standards including ICH Q12 guidelines, WHO post approval changes guidance, comparability protocols [FDA and EMA guidelines], EMA post approval change management document. Included in the discussion were lessons learned from COVID 19 (e.g., PPQ/PV comparability and stability approach), accommodations for post approval site transfers, divergent data requirements, etc. and how these lessons can be utilized by regulatory authorities.

	Overview of APEC's Advanced Therapy Roadmap, its goals, and objectives
	What are Gene and Cell Therapies and how are they different from other therapeutics? Regulators learned the characteristics of cell and gene therapies including definitions of allogeneic cell therapy, autologous cell therapy, the distinction between in vivo gene therapy, CAR-T as well as COVID19 vaccines vs. cancer vaccines. Examples included definition of cell and gene therapies from European Medicines Agency, TGA Australia and US FDA, and their distinction from each other and from other biotherapeutics by providing specific examples and descriptions of platforms and products including: 1. Tissue engineered products. 2. Unique nature of CAR T 3. Genome editing 4. Gene editing which is gene therapy 5. mRNA product for prophylactic purposes vs treatment 6. mRNA product for treatment of cancer
	Regulatory considerations for cell and gene therapies Regulators learned the applicable guidelines and points for consideration in the approval of cell and gene therapies including: 1. ICH M6, S12, and other relevant guidelines 2. IPRP materials (existing and upcoming guidelines) 3. Other economy guidelines (US FDA, EMA, PMDA etc.) Regulators also learned when reliance on other regulatory authorities should be considered and is appropriate.
	Cell and Gene Therapy Product Development Regulators were presented with a high-level view of product development for cell and gene therapy products including an overview of product manufacturing.
	Unique Challenges in Cell and Gene Therapy: An Overview Regulators were presented with a broad overview of the unique challenges associated with the development of cell and gene therapies. The areas of challenges included: 1. Overview of Nonclinical and Clinical challenges taking into consideration issues around Animal models; dosing; follow-up 2. An overview of the manufacturing challenges associated with cell and gene therapy taking into consideration GMP issues with product development (different regulatory authorities' perspective on GMP, CMC issues associated with accelerated timelines and scaleup; and sterility and shelf life including compendial challenges.

	**Links of interest: EMA assessment reports (European public assessment reports):* https://www.ema.europa.eu/en/medicines/field_ema_web_categories%253Aname_field/Human/ema_group_types/ema_medicine https://www.who.int/biologicals/areas/biological_therapeutics/Annex_3_WHO_TRS_1011_web-7.pdf?ua=1 Webinars, Presentations, and Articles | FDA https://www.ema.europa.eu/en/human-regulatory/overview/biosimilar-medicines-overview **Links of interest:* FDA Drug Topics: Biosimilar and Interchangeable Products in the U.S.: Scientific Concepts, Clinical Use, and Practical Considerations – December 10, 2018, | FDA FDA Overview of Biosimilar Products; *Helpful link for comparability protocols* https://www.semanticscholar.org/paper/Comparability-Protocols-for-Biotechnological-Schlegel-Bobinnec/334184833841c7fd34994b9f317d186609e51865 *Helpful link for lessons learned in manufacturing.* https://www.icmra.info/drupal/en/covid-19/7-8july2021/video-recording *Helpful link for definitions and treatment of these products in various economies:* https://admin.iprp.global/sites/default/files/2021-09/IPRP_CTWG-GTWG_Frameworks_2021_0811_1.pdf *Advanced reading*: IPRP Table of Guidances and Guidelines for 13 economiesmr *Link to ICH consideration documents* https://www.ich.org/page/consideration-documents *IPRP on gene therapy* http://www.iprp.global/working-group/gene-therapy *IPRP on cell therapy* http://www.iprp.global/working-group/cell-therapy https://admin.iprp.global/sites/default/files/2021-09/IPRP_CTWG-GTWG_Frameworks_2021_0811_1.pdf *Helpful document:* https://cdn.ymaws.com/www.casss.org/resource/resmgr/cell&gene_therapy/cgtp_2020/Kwilas_Anna_Slides.pdf

The webinar employed the Zoom platform with transcription and translation of the event, and was developed simultaneously with the launch of the online modules with faculty drawn from the advisory committee, APEC regulators, industry, and academia. Marketing materials (Appendix B2) and biographies of faculty/speakers (Appendix B3.1 and Appendix B3.2) were sent to the APEC RHSC list of 200+ individuals The webinar took place September 13-22, 2022, with two hours on each September 13, 15, 20 and 22 covering biotherapeutics and cell and gene therapy related regulatory issues. The 8-hour webinar was attended by 58 participants from Thailand, Peru, Mexico, Malaysia, Indonesia, Singapore, and Chile.

In Person Training: The final phase of the training, an in-person 3-day training, was to take place in a selected APEC economy in the Latin American region (Mexico, Peru, Chile). This portion of the program is directly related to the goal of the original project proposal and the RHSC Vision 2030 to explore the feasibility of implementing a sustained CoE in the Latin American region. To aid in this effort, the Advisory committee conducted a careful review of the capabilities of APEC Latin American economies in the biotherapeutics and cell and gene therapy space. This was done through detailed discussions and the experience of advisory committee members in their dealings with local institutions. After careful review of the capabilities of the region

in the areas mentioned, it was decided that the in-person training would take place in Santiago Chile at the University of Chile where training facilities existed.

The in-person portion of the training also included the collecting and compilation of case studies pertaining to specific agenda items. These case studies served to provide real world examples of issues that regulators would face in reviewing submissions. A detailed outline of the 3 day in-person training is represented in Figure 5 below.

Figure 5

Session 1: Regulatory Agility in Biotherapeutics
Leveraging learnings to manage regulatory capacity: • ***Reliance*** Full or partial reliance on assessment reports of regulatory authorities from other regions to enable approval and implementation of post-approval changes (PACs), reduce the complexity and regulatory burden associated with lifecycle management. • ***Accelerated assessments*** (early access programs; conditional approvals; expedited access). • ***COVID learnings***-COVID changing paradigm for accelerating vaccine development.
Expedited Regulatory Programs A look at existing facilitated regulatory pathways as well as accelerated approvals developed as a result of dealing with the COVID pandemic. For example: • Establishment of quick, frequent, and **continuous communications**/engagement between regulators and manufacturers, convergence of regulatory requirements and expectations • Acceptance of **alternate process qualification/validation** approaches, such as leveraging of platform data and prior knowledge, concurrent validation, decoupling DS and DP validation, and/or continuous process verification • Acceptance of alternate approaches, shifting regulatory evaluation of process validation data to **inspections/facility assessments** can further expedite post-approval site transfers and create resources efficiencies for regulators and manufacturers. **Rolling submissions**, Approval of post-approval changes in the absence of full data with certain data provided later.
Session 2: Key Challenges in Biotherapeutics
Role of Qualified Laboratories for Local Made Products and Products on the Market Explore the role of qualified laboratories for local made products and reliance on trusted regulatory authorities to waive import retesting. Explore the role of regulatory authorities in Latin America for local made products taking into consideration minimum capacity requirements. Explore the expectation of products already in market vs. those products in the registration process.

Accelerated Development and Product Lifecycle for Biotherapeutics

An overview of the lifecycle of biotherapeutics from the initial marketing application to post-approval activity.

Review of a case-study demonstrating acceleration strategies implemented, and their impact on the post-approval landscape. Explore how to minimize global post-approval complexity, accelerate approvals, and drive toward regulatory convergence.

CMC topics include:

- Acceleration strategies and the impact to lifecycle
- Pre- and post-approval comparability
- Divergence of approval timelines and economy-specific requirements, including stability data expectations
- ICH Q12 and the impact on post-approval change control and lifecycle management

Session 3: Cell and Gene Therapies Development

Case Study: Integrating QBD Principles in Gene Therapy CMC Programs

A look at regulatory considerations, standards in gene therapy, generation of quality target product profile, process development using quality by design principles, upstream and downstream processing, the drug product, process control strategies, and comparability in relation to cell and gene therapies.

Explore the biggest challenges to cell and gene therapy CMC. Explore the realities of manufacturing that affect gene therapy product development.

The Use of Standards for Regulatory Purposes and Product development

How standards support development of cell and gene therapies and how they can be used in a regulatory submission. Some standards discussed ISO and ASTM standards. (American Society for Testing Materials)

Unique Nonclinical and Clinical Considerations for AAV-based Gene Therapy Products:

Explore the unique nonclinical and clinical considerations around cell and gene therapy products, in particular for AAV-based Gene Therapy products.

Nonclinical: Challenges with Potency assays; considerations for preclinical studies including toxicology studies, animal selection, etc.; biodistribution and shedding studies including learnings from ICH S12 guideline; translatability of nonclinical to clinical data; and current thinking on integration and insertional mutagenesis analysis.

	Clinical: Considerations on innovative clinical trial designs, immunosuppression and corticosteroid use, benefit-risk assessment, immunogenicity, and use of companion diagnostic, developing strategy for long term follow up.
	Cell and Gene Therapy Manufacturing
Session 4: Gene Therapy Manufacturing	
	Case Study: GMP for Cell and Gene Therapies Case studies of mock facilities with guidance on acceptable practices with reference to specific quality guidelines.

	Manufacturing: Cell and Gene Therapy Supply Chain Challenges Learn about controls for data governance in cell and gene therapies and differences in data governances and controls in conventional areas and new and emerging areas such as cell and gene therapies. Examples include a comparison of data controls for monoclonal antibodies vs. gene therapy products. Learn what to expect during a site visit for cell and gene therapy products, handling of cell therapy products (including gene modified cells) including chain of identity in autologous therapies; product and raw material including apheresis product integrity; other issues. Key critical points in the vector manufacturing process and plasmid and vector quality guidances.

	Case Study: FDA and EMA Approval of gene therapy product Adeno-associated virus (AAV) is widely used as a delivery vector for gene therapies in clinical studies. Several AAV gene therapies are also approved in US and EU. Learn the development and regulatory perspectives for AAV therapies including considerations of all phases of AAV gene therapy development, before clinical trials, during clinical development, marketing authorization and post-marketing. Discuss regulatory guidance, precedents, and case studies with a deep dive on the recent European Commission (EC) Conditional marketing authorization (CMA) of Roctavian – AAV gene therapy for severe hemophilia A.

The 3-day in person training (December 5-7, 2022) was attended by 19 Chilean regulators from ISPCH and included faculty from Korea MFDS, US FDA, Health Canada, and Brazil ANVISA.

Appendix D lays out the complete program for the in-person training at the University of Chile in Santiago. Appendix D2 provides a comprehensive list of participants at the event.

4. Key Outputs

Key outputs from the year-long training program included a

I. A training program in Biotherapeutics and Advanced Therapies consisting of:

1) Online basic cell and gene therapy online module and biotherapeutics online module. Introduction to Biological Medicines (instructure.com)
https://skillstacklogin.sites.northeastern.edu/
Cell and Gene Therapy International Regulatory Sciences (instructure.com)
https://skillstacklogin.sites.northeastern.edu/

2) Comprehensive Training PowerPoint Presentations Webinar (recorded for future viewing)
https://drive.google.com/drive/folders/1vn4XZXh_gPNqg63dPX67DDL3NQcQ_0sY?usp=share_link

3) Comprehensive Training PowerPoint Presentations In Person Training
https://drive.google.com/drive/folders/1qHmFti-JmpiLsHHXji49CQ1ZNmNn8kYx?usp=share_link

**The agendas for each aspect of the training were developed using the approved Asia-Pacific Economic Cooperation (APEC) Life Science Innovation Forum (LSIF) Regulatory Harmonization Steering Committee (RHSC) core curriculums for Biotherapeutics and Advanced Therapies, experts from industry, governments, and academia to develop and deliver the content.*

II. A survey of the training measuring content appropriateness and effectiveness, and future needs. The survey was conducted after the completion of the in-person training. See Appendix E for raw survey results.

5. Key Outcomes

The first combined biotherapeutics and cell & gene therapy training program was held in three parts (virtually and in person) throughout 2022. Overall, based on the number and demographic makeup of those in attendance and the survey results, the program was successful.

Attendance and Demography: Table 1 below measures the actual numbers vs planned numbers for specific indicators. The overall goal of the training was to train 12 economies in relation to workshops and case studies (Webinar and in person) of those 6 being travel eligible economies. The webinar and in person training had 7 economies in attendance and of those 7 all were from travel eligible economies. While the total number of participants was not met (60 actual attendees vs 100 planned), the number of travel eligible economies exceeded that indicated. The training took place just as the COVID 19 pandemic was subsiding. In view of the COVID pandemic which resulted in overburdened regulatory offices, many regulators were not able to travel for training programs. It is highly probable that this was a main reason several APEC economies did not attend the training resulting in missed targets. In addition, it is likely that the in-person location of the event (University of Chile in Santiago) made it difficult for many

of the APEC economies located in the Asian region to attend the in-person training. Given the nature of the online module, it was difficult to assess how many were from APEC economies. Accordingly, the data reflects participation in the webinar and in the in-person training. Table 1 below provides details about the list of indicators and whether or not the targets for the indicators were met.

Inclusion of women in APEC programs and programming is a major priority of APEC. Table 2 demonstrates that the outreach to women for the yearlong training program was successful in that most participants in all aspects of the program were women.

TABLE 1 (Indicators)

Indicators	**# planned**	**# actual**
# workshops / events	3	3
# economies attended	12	7
# participants (M/F)	100	60
# participants from travel-eligible economies (M/F)	21	19
# participants funded by APEC (M/F)	3	0
# speakers/experts engaged (M/F)	15	24
# APEC-funded speakers/experts (M/F)	3	3
# other organizations engaged	6	4
# businesses and/or academic organizations engaged	10	10
# surveys	1	1
Other outputs (websites, etc) :	2	2

TABLE 2 (Participants/Speakers Summary Table)

Economy (of Participants) *(Insert rows as needed)*	**# male**	**# female**	**Total**
Chile	9	10	19
Mexico	3	6	9
Indonesia	1	4	5
Thailand	2	3	5
Peru	0	8	8
Singapore	4	4	8
Malaysia	3	3	6
Participants (Total)	22	38	60
Economy (of Experts) *(Insert rows as needed)*	**# male**	**# female**	**Total**
USA		3	3
Singapore	1		1
Korea		2	2

Canada	1		1
Brazil		1	1
Speakers/Experts (Total)	2	6	8

Overall, the data above indicates that the training was very near its target goal for attendance for the yearlong project.

Satisfaction: A survey conducted after the completion of the in-person training (December 5-7, 2022) demonstrated satisfaction with the course topics and materials. The survey had a high response rate with 18 of the 19 participants responding. All respondents were regulators with mixed expertise in CMC, clinical trials, GMP, and safety and efficacy. Participants ranged in experience from 1-20 years, with the majority having more than a decade of experience in regulatory approvals.

According to the survey, the content of the training met the needs of 80 percent of the respondents with ten percent indicating more training on GMP issues associated with Advanced therapies. In addition, more than 70 percent of the respondents indicated that the information provided during the presentations was appropriate while approximately 30 percent indicating that the information was too advanced.

The survey also fleshed out the topics that regulators would like to see in future trainings, including more detailed information about GMP for advanced therapies, more training relating to pharmacovigilance for advanced therapies and vaccines, more training on clinical design studies for rare diseases and cell and gene therapies among others.

Future Training: The yearlong, multifaceted training program demonstrated that in addition to the significant gap in capacity regarding cell and gene therapy competency in the Latin American region, there is a great appetite for training in this space. The project also demonstrated that while there is competency for regulating biotherapeutics products, there is still a need for streamlining certain elements of the regulatory approval process in the Latin American region. In particular, there is a need for training in ICH Quality guidelines as they relate to biotherapeutics.

6. Overall Impact and Lessons Learned

Despite its delay due to COVID-19 pandemic, the yearlong Capacity Building in Biotherapeutics and Cell/Gene Therapies in Latin America training program was well received by regulators. All Chilean regulators responsible for cell and gene therapy approvals attended the in-person training program and regulators from 6 other economies as well as Chile attended the online and webinar portions of the training. The project demonstrated the need for a regulatory sciences CoE for the Latin American region to fill the existing regulatory gaps in both biotherapeutics and cell/gene therapy. The project also demonstrated that Latin American economies recognize the gap in capacity and are willing to invest training time to fill those gaps. The yearlong training program demonstrated the overlap in certain aspects of cell/gene therapy training which can be combined with/or overlayed on, biotherapeutics training.

7. Conclusions and Next Steps

The COVID19 pandemic changed the way we do our work. During the pandemic, regulatory reviews became more flexible, and meetings and trainings took place virtually.

Some of the lessons learned from the pandemic carry over to how we do business today. To be prepared for the next pandemic, the role that training programs play in ensuring the approval of safe, effective, and high-quality drugs in the most efficient way is more important than ever. LSIF 01 2020 was designed to build the capacity of participants through workshop activities such that they can apply risk-based, science-based approaches to their drug review. In this program which used the Latin American region as its basis, also sought to include lessons learned from COVID in regulatory techniques and sought to identify a potential CoE in the Latin American region.

In short, the overall goal of the program was to train regulators, particularly those in the Latin American region, to enable them to be ready to approve only biotherapeutics and advanced therapies of the proper quality hit the market using the most effective training techniques. This stated objective of the yearlong project was met.

The project resulted in the training of more than 60 regulators in APEC with a specific focus in the Latin American region, at basic levels to mid-level in cell and gene therapy and mid to advanced level in biotherapeutics. The training program included state of the art regulatory techniques and directed regulators to consider where reliance might be appropriate. The project also created a template for training in the region with requisite training materials and identified a potential CoE for the Latin American region (University of Chile in Santiago).

Based on the information gleaned from the training, we recommend further collaboration with University of Chile to enhance training capacity primarily through funding. We also recommend that APEC consider future trainings either at individual domestic regulatory authorities, or regionally employing the template created through LSIF 01 2020.

In addition, based on survey responses from the participants on topics regulators would like to see in the future, APEC should consider more training relating to pharmacovigilance for advanced therapies and vaccines, more training on clinical design studies for rare diseases and cell and gene therapies, Good Manufacturing Practices for advanced therapies, and an in depth look at cell and gene therapy manufacturing and inspections.