

**APEC LSIF RHSC**  
**Training Centers of Excellence**  
**for Regulatory Science**

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**Operating Model and Guidelines**

January 2018



**Asia-Pacific  
Economic Cooperation**

**Regulatory Harmonization  
Steering Committee**



**Life Sciences  
Innovation Forum**

# **APEC LSIF RHSC Training Centers of Excellence for Regulatory Science - Operating Model and Guidelines**

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## **I. Background Summary**

The Regulatory Harmonization Steering Committee (RHSC) was formed in June 2009 under the auspices of the Asia-Pacific Economic Cooperation (APEC) Life Sciences Innovation Forum (LSIF) to promote a more strategic approach to regulatory harmonization by undertaking activities of greatest value to regulatory authorities and regulated industries. RHSC efforts have been guided by a Strategic Framework and vision to promote greater regulatory convergence<sup>1</sup> by 2020. Roadmaps based on gap analyses have been developed for several Priority Work Areas (PWAs). Working in partnership with the APEC Harmonization Center (AHC), the RHSC has established linkages with other harmonization/convergence initiatives, training institutions and key players in order to avoid duplication of effort, promote complementary action and make maximum use of resources.

Beginning in 2012, the RHSC turned its focus on how to implement a sustainable model for long-term efforts to implement the road maps to facilitate regulatory convergence. The RHSC agreed in February 2013 to explore the establishment of an APEC Multi-Regional Clinical Trials (MRCT)Regulatory Science Center of Excellence network as a means to provide quality continuing training, starting with a pilot workshop in Singapore in March 2014. The three day program took place March 17-19, 2014, hosted by Duke-National University of Singapore (NUS). The pilot affirmed the anticipated value of an ongoing training program offered through establishing Centers of Excellence (CoE).

## **II. Purpose**

This paper is intended to describe an operating model for CoEs that will carry out the training objectives of the RHSC in a long-term, sustainable manner.

Several primary objectives exist:

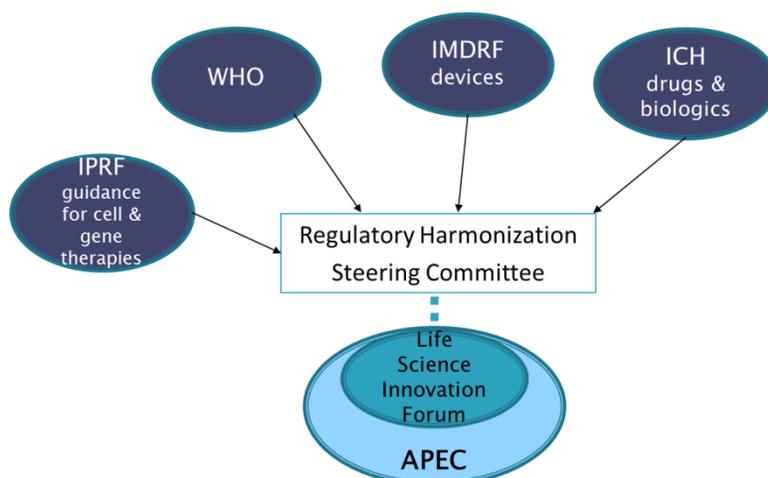
- Build skilled human capacity in regulatory sciences to bring safe, efficacious and quality medical products to patients as rapidly as possible.
- Promote dialogue with a view towards sharing understanding in science and best practices.
- Achieve a model of sustainable operation that includes periodic updates to maintain regulatory relevancy of materials and ensures continued value to all participating entities.

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<sup>1</sup> Convergence, a broader term, was defined to include the concept of harmonization.

- Do not duplicate efforts – leverage work that already exists, and work that already has a level of convergence.

## Leverage Significant Harmonization Work – Don't Reinvent



Key benefits expected from the implementation of CoEs are listed below:

- Delivery of training will be done and/or supported by training experts as well as regulatory Subject Matter Experts (SME) as appropriate
- Reliance on shrinking APEC money is reduced
- Enables long-term continuous training in the science and best practice(s) in the topic area(s)

### III. Vision and High Level Approach

The RHSC's vision with the CoE model is to implement a sustainable platform for promoting regulatory convergence<sup>2</sup>, capacity and cooperation in topic areas relevant to medical product regulation. The focus of convergence would be in science and best practices.

A CoE is guided by those who worked on the Priority Work Area's (PWA) roadmap, with the PWA's Champion Economy(ies) as the lead advisor(s) to ensure that the core curriculum and resulting training programs are consistent with the roadmap. **PWA CoE Program Committees**, comprised of the Champion

<sup>2</sup> According to the RHSC's Operating Procedures (revised June 26, 2013) "regulatory convergence" represents a *voluntary process* whereby the regulatory requirements across economies become more similar or "aligned" over time as a result of the gradual adoption of internationally recognized technical guidance documents, standards and scientific principles (harmonization) and common or similar practices and procedures. It *does not* represent the harmonization of laws and regulations, which is not necessary to allow for the alignment of technical requirements and for greater regulatory cooperation.

Economy(ies) and other interested RHSC members, work with the hosting institution and its collaborative partners to ensure that training programs include the core curricula and are consistent with the roadmap, and provide support and oversight to the CoE to ensure its successful continued performance. The CoEs report to and final decisions are ratified by the LSIF through the RHSC.

Some key terms are defined here:

- **Training objectives** – the desired behavior changes for the intended audience
- **Core Curriculum** – the required curriculum elements that are needed in order to meet the training objectives; for instance, prerequisites to understanding certain concepts. The PWA’s CoE Program Committee, led by the PWA Champion Economy(ies), develops this and provides it, along with the training objectives, to the hosting institution. A hosting institution may collaborate in this effort.
- **Training program** – the full curriculum, training materials and training plan that the hosting institution develops to meet the PWA training objectives. This incorporates the core curriculum, and is developed in coordination with the PWA CoE Program Committee.

The approach to implement CoEs will be through partnerships among academia, regulators, industry and science organizations to deliver and maintain topic-focused program(s). CoEs must yield sufficient benefit to all partners to ensure long-term support and sustainability. RHSC, supported by AHC, an organization committed to harmonization and capacity building in the APEC region, will provide any oversight and periodic assessment necessary to ensure that performance continues to meet APEC objectives.

There is general agreement that the RHSC should adopt a pragmatic, step-wise approach in establishing one or more CoEs. Experience gained from the initial CoEs can be used to refine the operating model.

## **IV. The Operating Model**

Following is a high-level summary of the operating model:

### **A. Topics for a CoE**

The RHSC agreed in January 2015 on the following PWAs that will serve as initial candidates for (CoEs):

- Multi-regional Clinical Trials (MRCT), merged with Good Clinical Practices (GCP) Inspection
- Medical Product Quality and Supply Chain Integrity
- Biotherapeutics
- Good Review Practices (GRevP), merged with Good Submission Practices
- Pharmacovigilance

These candidates were selected based upon RHSC consideration of the level of maturity in the key areas below, also agreed to in January 2015:

- Science and practices in the topic area are fairly well established
- Global guidelines have already been developed in the PWA
- Sufficient progress has been made in defining key challenges to convergence that can be effectively addressed through ongoing training
- The core curriculum has been sufficiently developed to establish a CoE
- Significant level of interest and commitment from government, industry, academia and other stakeholders to establish and support a CoE for the PWA

Part of the work of the PWA CoE Program Committees, with support from the AHC, is to identify where relevant training already exists and not duplicate it in CoEs. Instead, the PWA CoE Program Committee should make sure that CoE activity is complementary with existing training where practical.

In the future, the primary experts to consider whether a topic area is a good candidate for CoEs, and the scope within the topic area, should include:

1. The RHSC and Champion Economy(ies)
2. Stakeholder regulators who have implemented or are implementing existing guidelines and/or best practices in the topic area
3. Regulated industry through their relevant RHSC industry coalition representatives

It is understood that more than one CoE may be best suited to satisfy the needs of a PWA.

As of August 2018, the current list of RHSC approved PWA's includes:

1. Multi-regional Clinical Trials (MRCT), merged with Good Clinical Practices (GCP) Inspection
2. Medical Product Quality and Supply Chain Integrity
3. Biotherapeutics (Biotechnological Products)
4. Good Registration Management (Good Review Practices (GRevP), merged with Good Submission Practices)
5. Pharmacovigilance
6. Advanced Therapies
7. Medical Devices

## **B. Selecting a Hosting Institution for a CoE**

CoEs are physically hosted and managed by institutions including academia, regulatory, industry, and science organizations who supply faculty, staff and material support; additional experts are identified and recruited to augment staff where the topic area warrants it.

In January 2015 the RHSC agreed on the following selection considerations for a CoE hosting institution in principle. In August, 2015, the considerations were reviewed and updated based on input from candidate academic institutions:

- Trusted global educational/regulatory/science-setting organizations
- Ability to develop and deliver training program against priorities set by the APEC RHSC
- Willingness to provide a full or part-time Director and appropriate staff to manage the CoE
- Ability & commitment to achieve objectives as agreed in operating guidelines
- Ability to fund the administrative overhead over the life of the agreement (minimum 5 years)
- Credibility in the topic area
- Location that provides easy access by participants
- Ability to provide qualified faculty; this could be visiting regulatory staff or other experts as required by the training program
- Ability to receive funding to support specific aspects of CoE training (for instance, to fund student travel)

A single hosting institution may be a CoE for more than one PWA topic. An analogy would be schools within a university system – e.g., school of business, school of pharmacy, etc.

Institutions interested in hosting a CoE Pilot Program should submit a CoE Pilot application form to the RHSC. The RHSC, with AHC support, will examine the application by the hosting institution against the agreed criteria above and inform the institution of the results.

To become a formal CoE, the hosting institution submits a Formal CoE application form to the RHSC, indicating its successful completion of at least one CoE pilot.

### **C. CoE Collaboration**

The RHSC encourages the concept of collaboration among CoEs within, and across, topic areas. The AHC will maintain an awareness of CoEs and facilitate collaboration if needed. All CoEs should model the basic CoE framework described in the guidelines in this document.

The core curriculum and training objectives (not necessarily the training program itself) should be the same across all CoEs for a given topic area, but training materials and delivery may be different from organization to organization. There may also be local or regional differences such as language, constraining regulations, etc. It is the responsibility of the PWA CoE Program Committee to ensure that the core curriculum and training objectives are provided to each CoE providing training for the topic area. It is the responsibility of the hosting institution for the CoE to ensure that this core curriculum and training objectives are incorporated into the training program.

### **D. Training Expectations**

The RHSC agrees that training should focus on higher level principles of how science is applied to regulatory actions and not the specifics of any one agency's approach. A universal core curriculum of regulatory science, and training objectives, shall be developed for each PWA that articulates

common principles. Resulting training programs could and should involve interactive elements such as hands on, concrete case studies, using the MRCT pilot as an example. While the RHSC may expect diversity in the training approach as noted above, RHSC will not specify to the CoE hosting institutions how they deliver training programs, except to the extent that the training program meets the PWA CoE Program Committee's training objectives and incorporates the core curriculum.

PWA CoE Program Committees will develop the core curriculum and training objectives. The core curriculum and training objectives shall be presented to and endorsed by the RHSC. RHSC, the PWA CoE Program Committee, and other stakeholders including already approved CoEs will periodically review the core curriculum to ensure that it is still relevant and current. Any changes will be presented to and endorsed by the RHSC. Changes to the core curriculum and training objectives are anticipated to be infrequent.

In order to effectively engage in development and oversight of a training program at an appropriate level, RHSC representative(s) should participate on the hosting institution's Program Committee overseeing training program development. The number of RHSC participants should be kept small to enable their integration into the hosting institution's process. Representatives are typically members of the PWA CoE Program Committee. The PWA CoE Program Committees shall review and approve each training program. They will also endeavor to review the speakers' materials, whenever possible, prior to their delivery in partnership with CoE hosting institution

When there are multiple CoEs under one PWA, RHSC and the PWA CoE Program Committee should make such efforts as to facilitate the exchange of experiences and training materials among the CoEs in order to minimize the trainings' excessive divergence. RHSC and the PWA CoE Program Committee, with the help of AHC, shall encourage, and help facilitate, coordination and collaboration between CoEs in the same PWA.

For pilot Center of Excellence programs, organizations can apply for funding support from the AHC via their website. Funding is not guaranteed and is at the discretion of AHC. Officially recognized CoEs are responsible for all operational costs associated with running the Center, and may raise funds through grants, private and public donors, running "open" training programs for a fee, and other means.

## **E. CoE Operating Guidelines**

A CoE is formally established by the creation of a memorandum of understanding (MOU) between APEC LSIF and the hosting institution. The terms "party" and "parties" in this document refer to the parties included in the MOU for any particular CoE.

The Operating Guidelines outline expectations of the parties in the MOU for the operation and performance of the CoE. These Operating Guidelines acknowledge the intent of each party to make best efforts to meet the objectives as outlined below in the CoE collaboration.

Key Operating Guidelines are listed below:

### **1. Training Program Development**

- The hosting institution should obtain the training objectives and core curriculum such as prerequisites, from the PWA CoE Program Committee and develop a suitable timeline in achieving the milestones in agreement with the RHSC.
- The hosting institution will develop the training program (including identifying appropriate speakers and approving speaker materials), working with PWA CoE Program Committee to address any issues; and ensure that the proposed training program meets the training objectives.
- The hosting institution should ensure RHSC representatives (typically from the PWA CoE Program Committee) are present on its program committee for the development and oversight of its CoE training programs.
- The hosting institution should obtain final approval from the RHSC for the training program, before conducting any training events.

### **2. Participant Selection and Registration**

- The participant registration and selection process, and any travel subsidy for participants, is within the purview of the hosting institution and will be implemented as the hosting institution determines best.
- Hosting institutions will limit registration to those who meet the prerequisites for a training session.
- Hosting institutions will make the registration process easily accessible.
- Hosting institutions will ensure that participant selection is fair and impartial and that core curriculum and training objectives have been addressed.
- Hosting institutions may open registration beyond participants from APEC member economies; however, participants from APEC member economies will be given priority.
- Hosting institutions will send registration announcements to the RHSC Secretariat for circulation to all RHSC members and for the AHC to post to the AHC website. Announcements should be sent at least 60 days prior to the training program.
- Hosting institutions will clearly communicate the application process and deadlines to apply for travel subsidies<sup>3</sup>, if available.
  - Hosting institutions will make every effort to distribute travel subsidies, if available, to the broadest possible number of travel eligible economies, recognizing that funding sources or governmental constraints may prohibit a hosting institution from funding travel from participants from certain economies.

### **3. Delivery and Certification of Training**

- The hosting institution agrees to use qualified staff to deliver training (this may be faculty, regulatory staff, industry, or other experts in the field as necessary based on the content).

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<sup>3</sup> According to paragraph 9-19 of the APEC Guidebook, the following eleven APEC member economies are considered “travel-eligible” economies and may receive travel subsidies: Chile; China; Indonesia; Malaysia; Mexico; Papua New Guinea; The Philippines; Peru; Russia; Thailand and Viet Nam.

- The hosting institution will establish a “Certificate of Participation” for the training which might later be used in a certification process by regulators. This document may be co-signed by a representative of the hosting institution and RHSC leadership.
- The hosting institution ensures that the training program includes a significant interactive element (e.g., dialogue among students and instructors as a whole; case studies and problem solving; role playing, opportunities for small-group learning, hands-on laboratory based experiences).
- Where feasible, the hosting institution may provide remote training.
- The hosting institution will make a significant amount of training material available online as feasible.

#### **4. Periodic Assessments**

- A CoE is assessed on its own merits, based on the performance of the programmes and the outcomes meeting the applicable objectives, and independent of other CoEs
- RHSC, through the AHC and PWA CoE Program Committees, maintains an overarching view of the content of all CoEs for incompatibilities, and provides updates or information to hosting institutions as needed.
- The hosting institution will develop an operational report of the CoE program for presentation and discussion with the RHSC.
- The hosting institution shall agree to assessment conducted by the RHSC every 3 years, which could include but is not limited to a review of the following: the extent to which the CoE meets the needs of all parties; the ability of the CoE to achieve sustained knowledge transfer; the effectiveness of the training programs in meeting the training objectives and expectations of the trainees; and the currency of the content and training programs.
  - If the periodic assessment indicates that the program is not effective or not meeting the training objectives, the parties will collaborate to resolve the issues. If issues cannot be successfully resolved within a reasonable time (to be agreed by the parties), either party may choose to exit the MOU.
- The hosting institution shall update materials as required by the PWA CoE Program Committee and RHSC based on changes to the core curriculum and training objectives.

#### **5. Operations**

- The parties will make good faith efforts to meet the commitment of the signed MOU; however, any party may discontinue participation in the CoE collaboration with 180 days advance notice.
- The hosting institution funds and provides the training venue, program administration and administrative costs. The hosting institution may receive grants, donations, tuition and other funding sources for supporting a CoE; the institution may use any received funding related to the CoE as they determine most suitable to support the CoE.
- The hosting institution may secure, collect and distribute financial and in-kind resources sufficient to support the CoE’s objectives (including travel subsidy for travel eligible participants) and to recover its operating costs.

- The hosting institution may also provide periodic closed regulator training sessions as needed and agreed between the collaborating parties. Faculty for closed sessions may include private sector experts taking into consideration any conflicts of interest.
- The hosting institution will identify a Program Director to oversee all CoE program operations, serve as primary point for information sharing with RHSC and AHC, coordinate an annual review of the CoE's performance in meeting its objectives, and present the results of the review in the form of financial and operations annual reports to the RHSC.

AHC will maintain an overall awareness of agreements or memos of understanding for all CoEs, for instance, the signed MOUs between hosting institutions and LSIF. An original signed MOU is maintained by each signing party.

## **F. Intellectual Property and Sharing Training Materials**

Each CoE institution may wish to hold intellectual property rights to its training materials and approaches. Parties may wish to explore establishing agreements between organizations to share material. Some training delivery does not lend itself to remote learning, for instance hands-on labs and case studies. If hands-on labs and case studies are not part of the training program, and depending on the PWA topic scope to be covered by a CoE, it may not be possible to make the full training available via remote learning.

It is expected that the CoE make some set of training material publicly available at their CoE sites. The AHC also has the capability to post publicly available training materials on their website, and/or will have an awareness of locations of publicly available material. It is not common for all classes to be video-taped, but it should be noted that making these tapes public will require that all participants agree to them being publicly available. RHSC and the hosting institution will determine whether this is necessary, and the means to accomplish it.

## **G. Periodic CoE Review and Assessment**

A periodic assessment would be performed for each CoE to ensure that the CoE is still functioning as expected. AHC will coordinate this process. The Champion Economy(ies) and RHSC would periodically review training objectives and core curriculum to ensure that it is still relevant and current based on current regulatory science. Changes to the core curriculum are anticipated to be infrequent.

Training objectives and core curriculum assessment and CoE assessment should occur at the same time. It is expected that the periodic assessment would occur every three (3) years. However, if an improvement is deemed necessary due to changes in regulatory science or other reasons, this assessment may occur more frequently.

CoE assessment could include the following:

- Is the CoE training program meeting the needs of all parties
- Is the CoE active and effective

- Is the material still current or does it need to be updated

CoEs should be assessed on their own merits, not compared to other CoEs.

## **H. Key Roles – RHSC and PWA CoE Program Committee**

The Key roles of the RHSC and the PWA CoE Program Committees are detailed below:

- Define core curriculum and training objectives
- Endorse core curriculum and training objectives (RHSC)
- Establish CoE assessment requirements (through the AHC and PWA CoE Program Committees)
- Maintain high level political support
- Periodically evaluate progress on convergence (RHSC through the AHC and PWA CoE Program Committees)
- Periodically evaluate the need for changes to core curriculum due to changes in science and best practices
- Endorse revised core curriculum and training objectives (RHSC)

## **I. Key Roles – AHC**

The key roles of the AHCs as a coordinator of CoEs are detailed below:

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- Maintain a public website to provide information on APEC CoEs in general, as well as information on current and previous CoE programs
- Maintain an online system for the receipt of APEC CoE applications
- Manage written communications regarding APEC CoE operations, including approval letters, MoUs, assessment documents, etc., and will maintain a repository of CoE operating documents and templates
- Convene CoE Executive Directors annually to discuss operations, challenges, issues of concern, and report progress and recommendations to RHSC
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## **V. Appendix A – Additional Background**

*RHSC: Vision to promote regulatory convergence by 2020*

The Regulatory Harmonization Steering Committee (RHSC) was formed in June 2009 under the auspices of the Life Sciences Innovation Forum to promote a more strategic, effective and sustained approach to regulatory harmonization by identifying and prioritizing work seen to be of greatest value to regulatory authorities and the regulated industries. APEC and the RHSC are well suited to undertake this work

given the high level political and economic policy framework that exists within APEC as well as the strong support of regulatory authorities and industry.

RHSC efforts have been guided by a Strategic Framework and vision to promote greater regulatory convergence<sup>4</sup> by 2020, and roadmaps for each of the Priority Work Areas (PWAs) was established by the RHSC. Working in partnership with the APEC Harmonization center (AHC), the RHSC has established linkages with other harmonization/convergence initiatives, training institutions and key players in order to avoid duplication of effort, promote complementary action and make maximum use of resources.

#### *RHSC Priority Work Areas (PWAs)*

PWAs have been established in a number of areas, representing a mix of medical product class, regulatory function or product development domains. The current PWAs include:

1. Multi-regional Clinical Trials (MRCT), merged with Good Clinical Practices (GCP) Inspection
2. Medical Product Quality and Supply Chain Integrity
3. Biotherapeutics (Biotechnological Products)
4. Good Registration Management (Good Review Practices (GRevP), merged with Good Submission Practices)
5. Pharmacovigilance
6. Advanced Therapies
7. Medical Devices

#### *PWAs Roadmaps*

All roadmaps follow a similar model essentially composed of three phases:

*Phase 1 - Gap analysis* to establish the extent of and key challenges to regulatory convergence. This has been accomplished through diagnostic workshops, surveys and expert opinion. Expected output includes a definition and ranking of challenges with recommendations on how to best address the challenges.

*Phase 2 - Addressing the gaps (“Implementation Phase”)*. Training serves the RHSC as the primary means of building human and institutional capacity in executing regulatory functions, and promoting common science and risk-based approaches based on international technical standards and best practices. Phase 2 training efforts are aimed at promoting a new skill, ability or behaviour.

Phase 3 activities may also include other implementation aids where appropriate, as exemplified by the development of draft Good Review Practices guidance for the WHO and toolkits associated with aspects of the Supply Chain roadmap, all of which in turn serve as a reference for training. The work

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<sup>4</sup> Convergence, a broader term, was defined to include the concept of harmonization.

undertaken is guided by the particular roadmap, the charge of the RHSC and complementary work being undertaken by other organizations and initiatives.

*Phase 4 - Evaluation.* A critical phase is to measure learning and competency development to demonstrate the effectiveness of training in areas of focus related to actual regulatory practice. Adjustments and updating of training activities and approaches may be based on evaluation findings. Performance indicators should enable the RHSC to progress of regulatory convergence over time.

*CoE Pilot in Singapore (2014)*

Beginning in 2012, with the progression of work under a number of the roadmaps, the RHSC started to focus on how to implement a sustainable model for the continued training efforts needed to facilitate regulatory convergence by and following 2020. The RHSC agreed in February 2013 to explore the establishment of an APEC MRCT Regulatory Science Center of Excellence (CoE), starting with a pilot workshop in Singapore in March 2014. The dual objectives of the pilot were:

- a. to build skilled human capacity in clinical trial regulatory science to facilitate MRCTs as well as enhance regulatory cooperation in the conduct and regulation of such trials, and
- b. to determine the best method(s) and configuration to deliver the training. In other words, to determine what type of training is most effective for the different components of the MRCT topic, what types of faculty are required for the different components, what level of effort is involved, and how extensive is the involvement of regulatory experts.

The three day program took place March 17-19, 2014, hosted by Duke- National University of Singapore (NUS). The pilot affirmed the anticipated value of an ongoing curriculum offered through a CoE. Furthermore, the pilot allowed organizers to assess the advantages of a team-based learning approach that involved remote preparatory work followed by in-person lectures and group work, including a case study and role playing.

