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BIRS Course: RNA Vaccine Manufacture and Assessment of Regulatory Documents for RNA Vaccines

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Abstract

This paper is in three segments: (A) Segment on Vaccine Manufacture; (B) Segment on Ready to Use (RTU) Fluid Path for Compounded Sterile Preparations, mRNA Vaccines, and Phage Therapy, (C) Segment on Competency Framework for Addressing Regulatory Review These segments can be used separately or in combination. Additionally, they can be presented in any order. The time devoted to each segment depends on the depth of the course coverage. These segments are interrelated and describe how to make vaccines, how to manufacture vaccines with a point-of-care system built from ready-to-use parts; and how to regulate vaccines. This is a timely review because of the importance of vaccines for the treatment of diseases. It is hoped that it will lead to new approaches to vaccine manufacture and regulation.

Description of Course and Course Segments

This course sequence consists of three major segments:

A. Segment on Vaccine Manufacture
B. Segment on Ready to Use (RTU) Fluid Path for Compounded Sterile Preparations, mRNA Vaccines, and Phage Therapy
C. Segment on Competency Framework for Addressing Regulatory Review

These segments can be used separately or in combination. Additionally, they can be presented in any order. The time devoted to each segment depends on the depth of the course coverage.

A. Segment on Vaccine Manufacture

Vaccine manufacture is a complex, high-technology endeavor [1, 2]. Vaccine manufacturing is typically built on 4 competencies [3]:

1. the manufacturing process that defines how the product is made;
2. the compliance of the organization to successfully complete that process;
3. the testing of the product and supporting operations; and
4. the regulatory authorization to release and distribute the product.

In early September 2022, BIRS delivered an on-site symposium addressing core scientific and technical competencies critical for professionals in regulatory science at its Fall symposium in Arusha, Tanzania. About 75 MS students and 35 Ph.D. students attended and participated. The session included opportunities for experiential learning and project activities focused on quantitative thinking with applications in pharmacokinetics and design of experiments for manufacturing, leadership and systems thinking, and biotechnology innovation through the design and presentation of business canvas strategy for an mRNA vaccine manufacturing organization.

The scaffolded session on mRNA vaccines addressed basic concepts in plasmid manufacture, mRNA vaccine manufacture using lipid nanoparticles, establishing a company, and developing a strategy canvas

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for a business plan. This experience resulted in a summary of the competencies to build capacity for manufacturing mRNA vaccines in Africa.

The outcomes of this Purdue BIRS capacity-building vaccine program are:

- Ability to review dossiers
- Ability to design and carry out lot release and testing
- Ability to carry out GMP audits and inspections
- Ability to support vaccine manufacture and fill/finish operations
- Ability to design and implement a vaccine regulatory program
- Ability and competency for vaccine manufacture
- Ability and competency for sterile product manufacture

The BIRS capacity-building program can work at many levels, including certificate, MS, and Ph.D. In general, this program would be delivered in a flexible, hybrid format as a mixture of both online and in-person sessions.

The BIRS capacity-building program for vaccine manufacture focused mostly on mRNA vaccines but also addressed foundational concepts for the manufacture of vaccines in general.

Foundational Course Segments and Concepts for Initial BIRS Program

- Vaccine discovery and development, including introduction, history, immunology, and foundational science topics such as biochemistry, microbiology, and molecular biology
    - Risk in vaccine discovery and development
    - USP documents and other documents establishing standards, including
        - Biologics chapter
        - Viral vaccines
        - Polysaccharide and Glycoconjugates
        - Analytical including vaccine assay, and vaccine impurities
        - Lipids
- Manufacture of vaccines
    - RNA upstream
    - RNA downstream
    - Solid Lipid Nanoparticle RNA and DNA vaccines
    - Sterile products, including microbiology and pyrogens
    - Equipment – including equipment used for vaccine manufacture
    - Support fill and finish for manufacturing
    - Lot release and testing
    - Hands-on training
- Biomanufacturing Company Structure
    - Six systems
        - Production
        - Materials
        - Facilities and equipment
        - Lab
        - Packaging and labeling
        - Quality system
- Biomanufacturing Regulatory and GMP for manufacturing
    - GMP for six systems
    - Fundamentals of Biomanufacturing regulatory
    - QA, QC, QbD
    - Good Regulatory Practices for Vaccines
        - Preclinical

        - Clinical
        - GMP and common deficiencies
        - Sterile products
        - Review Dossiers
- Quality, audits, and inspections for vaccines
    - Critical quality attributes
    - Support GMP inspection
    - Supply chain, including cold chain and incoming supplies
    - Data integrity
    - Physicochemical
- Vaccine and Biopharmaceutical distribution
    - Cold chain

Intended Teaching Setting

The teaching setting is a symposium-style seating with students in round tables. Lectures are provided using slides but in discussion style with frequent stops for discussions of concepts. The material for the initial course can be covered in six hours of class time.

Slide Decks for Instructing Learners

Slide decks that describe details of vaccine manufacture, with emphasis on RNA vaccines and other relevant aspects of vaccine quality.

Slide Deck Number and Title	Brief Summary of Content
01 Introduction and Vaccine Manufacture	Summary of upstream and downstream manufacturing
02 mRNA vaccine upstream focus	Focus on the mRNA manufacture
03 Six systems and Sterile Manufacture Large Scale	Review of six systems for forming a vaccine company and Sterile Manufacture at Large Scale

EPARs and EPAR Case Study

These course offerings were supplemented by case studies. For example, the below case study compares and contrasts EPAR documents on the two approved mRNA vaccines for Covid. In this case study the learners were asked to:

- Find the epars for Comirnaty (Pfizer's vaccine) and Spike Vax (Moderna's vaccine)
- Find the following sections in each epar:
    - Quality Aspects
        - Introduction
        - Active Substance
        - Finished Medicinal Product
        - Discussion of chemical, pharmaceutical, and biological aspects
        - Conclusions on chemical, pharmaceutical, and biological aspects
        - Recommendations for future quality development

- Compare the stability information for both vaccines using the Formulation Development sections of the epar.
- Compare the Manufacture of the product, process controls and product specification for

each vaccine.

- Use the CQA document as a resource. Suggest two CQAs for each vaccine. Explain your choice.

B. Segment on Ready to Use (RTU) Fluid Path for Compounded Sterile Preparations, mRNA Vaccines, and Phage Therapy

With the advent of the SARS-CoV-2 vaccine and its rapid introduction along with the rapid introduction of monoclonal antibody therapies for SARS-CoV-2, there has been heightened interest in sterile compounding and the ability to rapidly manufacture sterile drug products. The availability of ready-to-use (RTU) sterile components and supplies for commercial manufacturing can facilitate sterile compounding as well as the availability of laminar flow hoods and isolators. USP 797 clearly describes guidelines for sterile compounding, providing additional support to the process that is aligned with aseptic manufacturing requirements[4].

This paper reports a small-scale economic sterile manufacturing/compounding system made from commercially available RTU components. This system has wide potential use, including compounding sterile preparations, preparing sterile products for clinical trials, preparing mRNA vaccines, preparing phage drug products including nasal sprays, continuous manufacturing of sterile products including mRNA vaccines, and a multitude of other uses as described later in this paper. This system can provide "on-demand" sterile products, reduce material wastage, and eliminate requirements for costly ultra-low temperature storage (<-80C).

Concerning liposomes and micelles, the Burgess group has described a platform for the continuous processing of polymeric micelles using a continuous precipitation process [5]. The Burgess group has also described using QbD principles for liposomal drug products containing hydrophilic API [6]. Shaw has discussed advanced manufacturing of liposomes using processes that translate to large-scale production. They also addressed regulatory issues [7]. Nag described a platform for manufacturing pharmaceutical-grade LNPs with a desired particle size using DOE methods [8]. In a related study, Daniel described a QbD method for enabling RNA platform production processes and addressed CQAs for RNA production and control [9]. In a very interesting paper, Sheybanifard described liposome manufacturing under continuous flow conditions [10]. They reported that this approach produced remarkable advantages for industrial processes.

This segment focuses on the design of easily implemented sterile compounding and continuous manufacturing systems for RNA vaccines; Figure 1 shows the simplest design of a sterile compounding system from commercially available ready-to-use parts.

The system in Figure 1 is made of commercially available single-use components. The sterile solutions are filled into vials and maybe held for up to 24 hours at room temperature, 72 hours stored refrigerated and 45 days when frozen per USP 797 [1]. The static mixer, which is optional, allows for in-line mixing of the formulated solution. The double sterile filters are 0.22 microns and integrity tested to ensure sterility. All operations are performed in a laminar flow hood or gloved isolator. As stated, the system is assembled and sterilized before use. This system can be used for monoclonal antibodies and numerous other sterile products. This system can also be used to prepare clinical supplies.

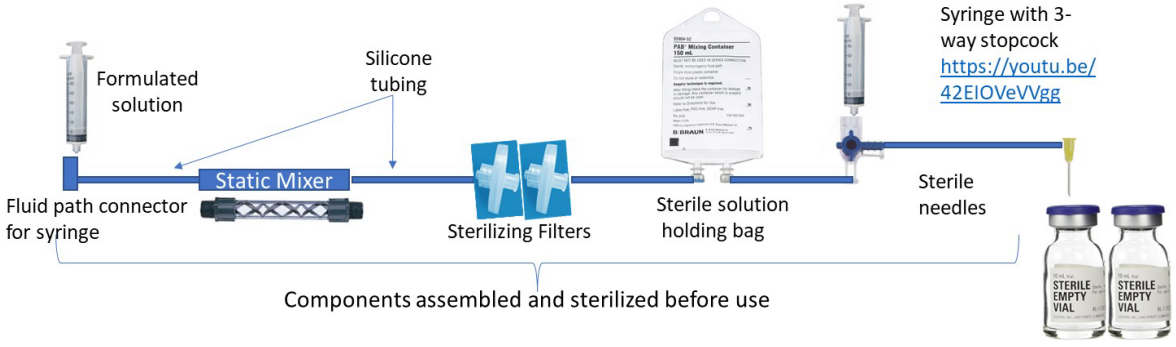

Figure 1. Basic Sterile manufacturing line for small scale preparation

Figure 2 shows a modification of the system in Figure 1 to make mRNA vaccines. As with the system above, all components are sterilized before use. USP 797 “High Risk Compounding” does not require the incoming components, the RNA, and the lipids to be sterile, paving the way for the utilization of this system. The two opposing syringes could easily be replaced with a commercial mixing system, including a microfluidics-based mixer.

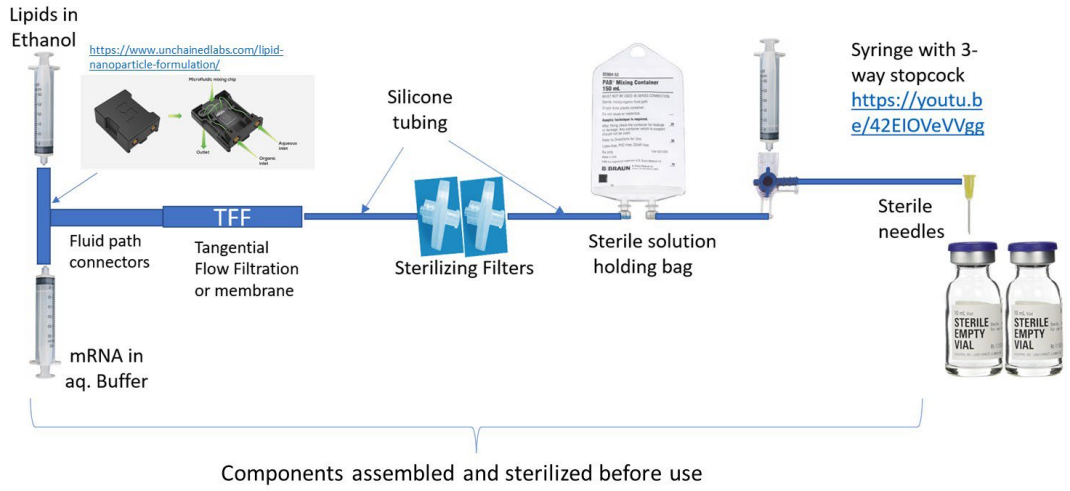

Figure 2. Sterile manufacturing system for mRNA vaccines or Phage therapeutics.

The TFF is to remove the ethanol and add formulation excipients (i.e., tonicity and buffering agents), but other systems could be used there. The formulated solution could be held and tested before forward processing. From then on, it’s the same as in Figure 1. The sterile filters mean the nanoparticles need to be less than 0.2 microns, but that should be acceptable. In addition, there might need to be a pH control stream and even pumps at various places to ensure proper fluid flow, which are controls consistent with commercial manufacturing processes.

This system would allow the manufacture of clinical supplies and produce products that can be stored and administered within 72 hours when stored refrigerated. Of course, for vaccines, it would be critical to immediately store the vials at -20 ºC and administer the product within 45 days of preparation as required by USP 797.

The system, when coupled with testing, would allow the determination of batch-to-batch consistency and exploration of variability in the manufacturing process. The process parameter is the flow rate. The material properties are solute concentration, solution viscosity, surface tension, ratio of lipid components, solubility, TFF system, and filter variability.

This system would allow the exploration of various formulations containing different lipids, cationic lipids, and other variations. The system would require only small amounts of the components such as SM-102, DSPC, cholesterol, and PEG lipid. In addition, new mRNA entities can be quickly explored and evaluated in clinical trials.

The system would also allow method validation studies without consuming large amounts of components. It would also allow the determination of the comparability of the CQAs of the product providing important information on the robustness of the manufacturing method. It would also allow studies of warehousing and temperatures. For example, the structure of the SLN could be evaluated, as well as the loading of the nanoparticles.

Importantly such a system would allow the testing and development of inline sensors, including inline particle size, spectroscopy, mass spectrometry, and sterility. However, it is important to remember that under USP 797 as long as the filters are operative, the environment controlled and the process qualified

by media fill simulations, the vials can be used within 48 to 72 hours without waiting for any further testing.

The system would also make product that could be studied for stability and pH effects further to explore formulation, composition, and manufacturing variations. Likewise, the products could be studied for impurities and compositional and content uniformity variation. These studies would provide information on degradation products and lipid-RNA adduct impurities present in addition to impurities.

With information on the flow and all of the other input parameters it should be possible to develop a digital twin that would simulate the CQAs of the output vaccine under different conditions, and flow rates. It is important to discuss the digital twin strategy in the classes and symposia that address mRNA vaccines.

Continuous Vaccine Manufacture

The system in Figure 2 can be easily converted into a continuous end-to-end manufacturing line where the input would be the mRNA and the lipids, and the output would be the vaccine. By adding flow sensors and controllers to control the input of the lipids in ethanol and the mRNA in buffer the flow can be controlled, and vials can be filled. Continuous operation would require filling RTU open vials, stoppers, caps and a vial changer and capper. A labeling system would also be required. This type of equipment is readily available.

This line could also be connected to another line that would continuously make mRNA. The lipids would be added as other formulation components, such as buffers.

A system that operates continuously could produce vaccines at a nearly fixed rate, and patients could be vaccinated at that same rate avoiding the need for stockpiling large amounts of vaccine. Technically, USP 797 would not require extensive QC testing of the final product for sterility assurance. USP 797 assumes process media fill simulations, control of compounding components and the compounding environment, and strict controls for material storage and use, provide sterility assurance for the compounded product. USP 797 assumes the formulation and stability of the drug product are well defined and small-scale manufacturing under control. Online sensors testing particle size, spectroscopy, and the use of closed systems for sterility assurance would be welcome additions to the testing so that the quality of the product could be assured. The digital twin for the process would help with compliance under USP 797.

As mentioned above, the CQAs would be monitored to assure a quality product. Some of these would be product identity, particulate matter, any sensor-based measurements, and perhaps confirmatory testing on one in ten of the produced vials. A small-scale continuous manufacturing line would also allow the testing of various concepts for a large-scale continuous manufacturing system.

Laboratory Instruction for Capacity Building

There is a critical need for capacity building in sub-Saharan Africa, where Moderna is reportedly installing a vaccine manufacturing facility in Rwanda, and Biontech is installing a second vaccine manufacturing facility in Kenya. The Purdue Biotechnology Innovation and Regulatory Science (BIRS) Center is linked to the Medical Missionaries of Mary in Arusha, Tanzania, and near both the Moderna and Biontech facilities. It is anticipated that scientists working in these facilities will need education on the mRNA vaccine, and regulators in East Africa and beyond will need education on vaccine submissions and best review practices. In addition, there is also a need for capacity building in Central Asia, where the BIRS Center has also provided capacity building in areas related to the mRNA and good review practices. The BIRS Center has numerous publications on capacity building in Africa [11], a few of the publications include studies of mentoring practices [12], staff training [13], regulatory compliance [14], and knowledge sharing [15]. There are several additional publications describing the BIRS master's degree in sub-Saharan Africa at the Purdue Libraries Site [16].

In addition, the identical BIRS master's degree has been involved in capacity building for over 15 years. The forerunner of the BIRS program was founded at Purdue University 20 years ago with the help of Lilly and AbbVie (originally known as Abbott). The BIRS Center is currently developing courses and a competency framework for capacity building in the US and sub-Saharan Africa.

The systems could be used for undergraduate and master's students in the US, Africa, Central Asia and worldwide. It would be reasonable to educate and train all students involved in vaccine manufacture on these systems. In the Purdue Biotechnology Innovation and Regulatory Science (BIRS) courses, we plan to provide instruction on mRNA vaccine manufacture, CQAs for vaccines, and control and regulatory approval of vaccines.

The BIRS center is currently focusing on the competencies needed for vaccine manufacture. Figure 3 shows the overall high-level competencies identified by the BIRS center. The three competencies

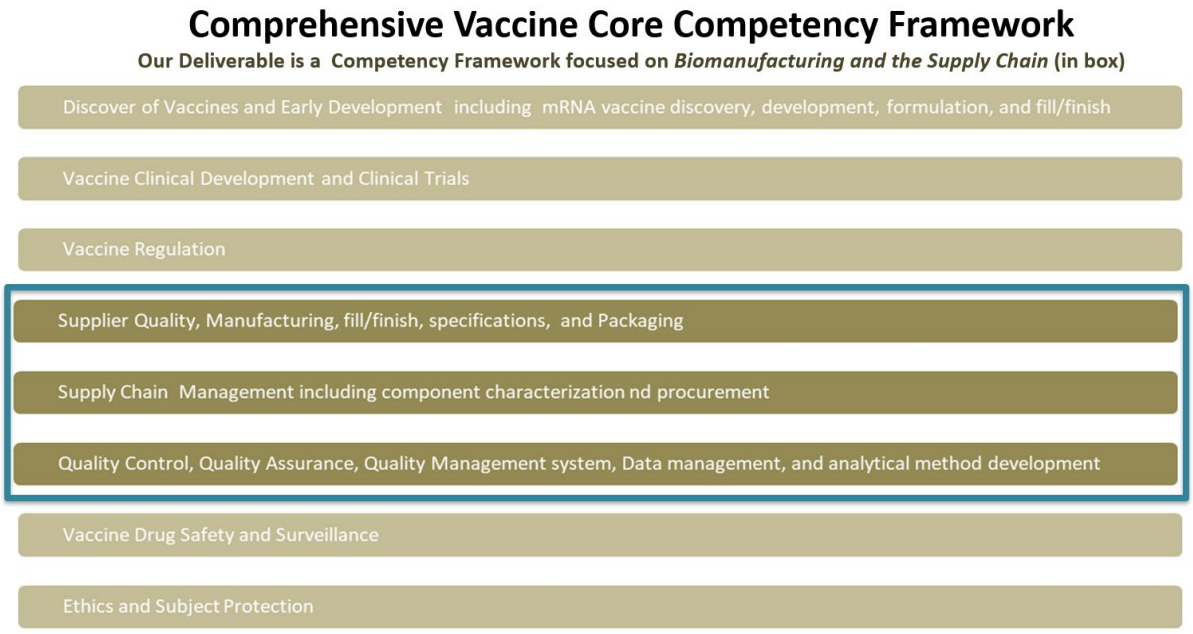

Figure 3. BIRS comprehensive competency framework for mRNA vaccines

Shown in the center of the diagram are the first ones addressed:

- Supplier quality, manufacturing, fill/finish, specifications, and packaging
- Supply chain management, including component characterization and procurement
- Quality control, quality assurance, quality management system, data management, and analytical method development

The vaccine manufacturing line in Figure 2 can easily be used to illustrate the importance of these competencies. Supplier quality, manufacturing, fill/finish, specifications, and packaging are all apparent as steps required to make vaccines, and variations in these parameters would obviously cause the failure of the line or even harm patients.

Similarly, because the system uses supplies from other sources, Supply chain management, including component characterization and procurement, is critical to ensure quality. In some cases, testing of incoming supplies would be required.

Finally, quality control, quality assurance, quality management system, data management, and analytical method development are all essential to ensure product quality.

One of the most important aspects of education and training on vaccines is understanding the CQAs and possible CQAs for the product. These manufacturing lines (Figures 1 and 2) and literature on the mRNA vaccine provide initial information on vaccine CQAs. In addition, these lines will allow the exploration and determination of new CQAs. Table 1 lists a comparison of some of the CQAs, specifications, and requests derived from the epar reviews of both SpikeVax and Comirnarty. The parameters mentioned in

this table are all candidates for CQAs and should be evaluated in the systems shown in Figure 2 and the continuous manufacturing system for vaccines.

Drug Substance - mRNA

	SpikeVax	Comirnaty
Release Specifications (noted differences in **bold**)	Appearance (**visual**)	Appearance (**clarity, coloration** (Ph. Eur.))
	pH (Ph Eur)	pH (Ph.Eur.)
	RNA content (UV)	RNA content (UV)
	ID (RT-Sanger sequencing)	**Identity of Encoded RNA Sequence (RT-PCR)**
	Purity (RP-HPLC)	
	Product-related impurities (RP-HPLC)	
	None	**RNA Integrity (Capillary Gel Electrophoresis)**
	5' Capped (RP-UPLC)	5'- Cap (RP-HPLC)
	PolyA tailed RNA (**RP-HPLC**)	Poly(A) Tail (**ddPCR**)
	Residual DNA template (qPCR)	Residual DNA template (qPCR)
	No dsRNA release spec (this was noted as a request)	**dsRNA (Immunoblot)**
	Bioburden (Ph. Eur.).	Bioburden (Ph. Eur.).
	Bacterial Endotoxin (Ph. Eur.)	Bacterial Endotoxin (Ph. Eur.)
Acceptable?	Yes	Yes

Drug Product

	SpikeVax	Comirnaty
In-Process Specifications (noted for SpikeVax only based on manufacture of the mRNA-loaded LNP intermediate)	Appearance mRNA identity (reverse transcription/Sanger sequencing) Total RNA content (AEX) Purity and product-related impurities (RP-HPLC) % RNA encapsulation (absorbance assay) Mean particle size and polydispersity (DLS) Lipid identity, content, and impurities (UPLC-CAD) pH (Ph. Eu.) Osmolality (Ph. Eu.) Bacterial endotoxins (Ph. Eu.) Bioburden (Ph. Eu.)	N/A
Release Specifications (noted differences in **bold**)	Appearance (Visual)	Appearance (Visual)
	Particulate Matter (Ph. Eur.)	**Appearance (Visible Particulates)** Subvisible Particles (Ph. Eur.)
	pH (Ph. Eur.)	pH (Ph. Eur.)
	Osmolality (Osmometry)	Osmolality (Osmometry)
	Mean particle size and polydispersity (DLS)	LNP Size (Dynamic Light Scattering)
		LNP Polydispersity (Dynamic Light Scattering)
	RNA encapsulation (absorbance assay)	RNA Encapsulation (Fluorescence assay)
	Total RNA content (AEX)	RNA content (Fluorescence assay)
	Lipid identity (UPLC-CAD) Lipid content for SM-102, cholesterol, DSPC, PEG2000- DMG (UPLC-CAD) **Lipid impurities** by UPLC-CAD (% individual impurities and sum of impurities)	ALC-0315 content (HPLC-CAD) ALC-0159 content (HPLC-CAD) DSPC content (HPLC-CAD) Cholesterol content (HPLC-CAD) Lipid identities (HPLC-CAD)
	N/A, SpikeVax did not contain overage	Extractable volume (Ph. Eur.)
	mRNA identity (reverse transcription/Sanger sequencing)	Identity of encoded RNA sequence (RT-PCR)
	In Vitro translation (methionine labelling)	**Potency / in Vitro Expression (Cell-based flow cytometry)**
	No equivalent	**RNA Integrity (Capillary Gel Electrophoresis)**

	SpikeVax	Comirnaty
	Bacterial Endotoxin (Ph. Eur.)	Bacterial Endotoxin (Ph. Eur.)
	Sterility (Ph. Eur.)	Sterility (Ph. Eur.)
	Container Closure Integrity (Dye incursion)	Container Closure Integrity (Dye incursion)
	Purity and product-related impurities (RP-HPLC)	**No equivalent**
Acceptability	The analytical methods used have been adequately described and (non-compendial methods) appropriately validated in accordance with ICH guidelines.	The analytical methods used have been adequately described and (non-compendial methods) appropriately validated in accordance with ICH guidelines.
Requests	• Risk assessment for elemental impurities in the drug substance • Tighten specifications for many release tests • Provide an updated LNP and finished product appearance testing description including characterization of potentially occurring visible particles • Demonstrated that the proposed detection wavelength is suitable for the quantification of lipid-RNA species	• Risk assessment for elemental impurities in the drug substance • Further evaluation of lipid-related impurities in the drug product

Table 1. Possible CQAs and Parameters of interest for SpikeVax and Comirnaty

Beyond the BIRS Center, the mRNA vaccine manufacturing line and the continuous mRNA vaccine manufacturing line could be invaluable as part of an effort to build capacity and train the workforce in mRNA manufacture and control. These small-scale systems would allow students to become immersed in the processes needed to make mRNA vaccines and make some mRNA vaccines of their own. It would also provide important instruction to students on sterile manufacturing.

Phage Manufacture

The BIRS biotechnology courses use phage isolation and purification as an instructional tool and capacity-building effort to inform students about genes, sequences, and related issues. In one of the laboratories, the students isolate phages and identify new phages based on their DNA. [17, 18]

Phages can be purified and separated from their bacteria host using filtration through a 0.22 micron filter. This is the same filter used in the standard and continuous manufacturing lines shown in Figures 1 and 2. Thus these lines could be utilized to prepare sterile solutions containing phages for either injection or as sterile nasal sprays. For phages, it is unlikely that TFF would be required unless ethanol was utilized in the process.

This type of manufacturing process would allow preparation of sterile therapies for the use of phages for the treatment of resistant organisms either by injection or as a nasal spray [19, 20]. To prepare products safe for human use and lacking variability several CQAs should be addressed. These include many of those outlined in Table 1. In particular, it is important to control the downstream manufacture of the phages themselves. Additionally, the formulation and other components in the formulation would need to be controlled. Of course, the concentration of the phage in the final product is critical. The packaging and labeling of the final products for injection could likely be similar to the mRNA vaccine.

Distributed Manufacture

Distributed manufacture has been described as the Factory of the Future [21]. In its report entitled “Lessons Learned from the COVID-19 Outbreak,” the Rand corporation described the advantages of distributed manufacture of medicines [22]. Myerson [23] described on-demand continuous flow production of medicines which is an obvious advantage of small-scale vaccine manufacturing lines like that described in Figures 1 and 2. Clearly, the ability to manufacture vaccines in a distributed manner using systems like that shown in Figure 2 would be important in future pandemics.

Standardizing the equipment in Figures 1 and 2 would facilitate developing a distributed manufacturing system for vaccines using identical units.

As currently conceived in Figures 1 and 2, the manufacturing outlined addresses only downstream manufacture of SLN-containing mRNA. An additional small-scale system for manufacturing the mRNA would be needed or the mRNA required for manufacture could be shipped to the distributed manufacturing sites where it is further converted to vaccines safe for injection.

Regardless of the strategy, it is clear that the manufacturing lines described in Figures 1 and 2 would be useful for distributed manufacture of vaccines in Africa.

Hands-on Instruction

The system described in Figures 1 and 2 along with the associated discussion including possible a Digital Twin can be used to instruct students on the importance of all of the parameters discussed above on vaccine manufacture and sterile product manufacture.

C. **Segment on Competency Framework for Addressing Regulatory Review**

Additional Author: M. Hynes

For this course segment, the class can be divided into one of four groups depending on job functions. Alternatively, all students can be required to take all four areas. In addition, the first course described here addresses the initial level competencies in each area. Advanced level competencies are

summarized in the appendix where the entire competency framework is presented including competencies at the advanced level.

Vaccines and biologics are complex biological products derived from living organisms or synthesized from complex lipid systems and are quite different from chemical pharmaceutical products. Vaccines are also typically injectable products requiring attention to sterility and the assurance of quality is difficult and complex. The NRAs have the responsibility for licensing facilities where vaccines are manufactured, review of submissions for clinical trials and registration documentation, inspection of facilities for clinical trial, development, manufacture and control of vaccines and biologics, independent lot-release and post licensure monitoring (vigilance). In some cases, the NRAs work with National Control Laboratories who perform testing on the submitted products.

This competency framework describes knowledge and behaviors that a regulatory professional is expected to demonstrate with respect to vaccines and biologicals. The framework is divided into levels of proficiency. In this case - entry level proficiencies are summarized. The document in the Appendix addresses all levels of proficiency. Four areas are addressed in this framework:

1. Reviewers
2. Inspectors
3. Lab analysts
4. Vigilance (Pharmacovigilance)

This competency framework for vaccines and biologics may help guide curriculum development, and training (academic and, more specifically, on-the-job training) of regulatory staff. It could also provide a unified framework for capacity building activities offered by various stakeholders and ensure systematic professional development and recognition of regulatory professionals.

This document was prepared by first reviewing model competency frameworks for medical products including those from the WHO and RAPS. Then the relevant activities and competencies for each role and the entry-level, mid-level, and senior level were defined by a broad and diverse team of subject matter experts from the Purdue Biotechnology Innovation and Regulatory Science community.

Table of relevant activities for each role

Relevant Activities for Each Role	
Reviewers	A. Conducting a clinical trial in conformance with the good clinical practices (GCPs): Execution of clinical trials as a part of the overall drug development plan B. Management of data generated in a clinical trial C. The review of safety and efficacy data generated during the conduct of a clinical trial: Reviewing the safety and efficacy data utilized in an application for marketing authorization and post approval changes ensuring its integrity and quality D. Design of clinical trial protocols E. Safety of clinical trial participants: Ensuring patient safety throughout the execution of a clinical trial

	F. Quality Management System: Consideration of techniques for monitoring and improving quality functions, processes and products G. Review of Risk Management: Risk management processes and procedures utilized throughout the conduct of a clinical trial H. Development of regulatory documents I. Utilization of investigational drug product in a clinical study: Rules and regulations governing the use of investigational drug product during the execution of a clinical trial J. Approved therapeutic products; maintenance of their approval and registration status: management of the regulatory processes that govern approved drug products including periodic reviews, regulatory actions, or withdrawals due to noncompliance K. Information contained on the product label and in package insert L. Drug Product Quality M. Decision making on regulatory matters: regulatory decision making on matters related to documentation, inspections, and laboratory testing N. Reliance strategy: Able to assess other regulatory authority O. Training: Able to evaluate training materials and train others P. Capacity building: Able to evaluate training materials and train others
Inspectors	A. Inspects data integrity and all other data acquisition and data processing activities B. Documentation inspection activities C. Review of manufacturing records as part of lot release: Reviews all data, documents, and batch records related to batch release. Reviews all data from contract laboratories and regulatory agencies D. Established quality system for inspectorate function E. Development of technical regulatory documents F. Carries audits and inspections based on current ICH and ISO quality guidelines G. Product Quality: inspects for all aspects related to product quality including vaccine starting materials, cell banks, and intermediates as applicable H. Supervision of vaccine disposal and destruction: Applies scientific biosafety regulatory and environmental requirements to ensure proper collection, management and disposal of vaccines and vaccination waste I. Investigation of product quality complaints: investigates complaints related to vaccines and biologics quality J. Import examination and screening

	K. Overall Regulatory Approaches: Develops regulatory approaches and strategies based on quality audits and inspections L. Sampling of products from the market: identifies and assesses the quality vaccines and biologics in the supply chain system; identifies vaccines and biologics, based on the risks associated with manufacturing complexity, dosage form, storage and stability; Assesses the quality of vaccines and biologics received at the ports of entry and border posts M. Provision of technical guidance (capacity building for stakeholders): Participates in capacity-building activities N. Training of regulatory personnel and industry: Applying new scientific innovation, technologies, and research to build a pool of competent workforce in the development, manufacturing and distribution of vaccines and biologics and the regulatory sector O. Enforcement: Enforces GMP guidelines for vaccines and biologics, seize any counterfeit, adulterated, bad or fake vaccine or biologics, based on surveillance and intelligence gathering, issue invitation letter or arrest suspect P. Reviews batch records of active medicinal Substance and finished medicinal product to ensure lot-to-lot consistency
Laboratory Analysts	A. Applies standards and International best practices: Ensure application of national, regional and international standards, guidelines and best practices in quality control laboratory for safety, efficacy and quality of vaccines and biologics B. Establishes and implements policies, guidelines, and procedures to ensure quality control laboratory operates in a safe environment and prevent health hazards to the personnel C. Establishes and sustains a maintenance program for laboratory systems and equipment's to ensure a high standard of performance and generate results/data which is accurate and precise (have minimal variations or errors) D. Outlines and implements analytical methods for vaccines and biologicals E. Ensures establishment specifications and methods consistent with ICH guidances for vaccines and biologics and conducts investigations of out of specifications (OOS) and CAPA F. Establishes and implements guidelines, procedures, and programs for qualification of laboratory equipment's to ensure accuracy and integrity of equipment's to generate reliable and accurate data G. Quality system for analysis laboratory H. Establishes accuracy of analytical reports and data management I. Participation in Research
Vigilance	A. PV assessment for marketing drugs and vaccines B. PV during the drug development process C. PV system strengthening D. Updating of market status

I. Reviewers

A. Conducting a clinical trial in conformance with the good clinical practices (GCPs): Execution of clinical trials as a part of the overall drug development plan.

RA-1 Clinical trial protocol design in conformance with the overall drug development strategy	
Explain how to design and execute a clinical trial	
Early Level Professional	Able to explain the design, purpose, and conduct of trial as it relates to the new intervention Screens the submitted documents against the guideline requirements to identify gaps
RA-2 Auditing of clinical trials	
Conducting audits of a clinical study in order to assess compliance with GCP's	
Early Level Professional	Demonstrates understanding of the GCP audits Screens submitted documents/applications for completeness
RA-3 Ensuring compliance with good clinical practices	
Ensuring that the design in conduct of a trial is in compliance with good clinical practice guidelines	
Early Level Professional	Demonstrates understanding of the Good Clinical Practice guidelines, clinical trial protocol requirements Reviews the clinical trial protocol and supporting documentation for completeness
RA-4 Appropriate management of investigational drug product	
Best practices for the storage, dispensing, and accountability for investigational product during the conduct of a clinical study	
Early Level Professional	Demonstrates understanding of the manufacturer's instructions regarding storage and dispensing of the product Participates in review of deviations from product storage, transportation, and dispensing
RA-5 Identification of safety issues and their management in conformance with regulatory requirements	
Methodology employed in the identification and reporting of safety issues identified during the conduct of a clinical trial	
Early Level Professional	Understands the potential safety issues associated with the product being investigated
RA-6 Assessment of adverse events during the conduct of a clinical trial	
Categorizing adverse events that occur during the conduct of a clinical trial and reporting to IRB's sponsors and regulatory authorities	
Early Level Professional	Collates and report of AEs
RA-7 Utilization of clinical trial monitors	
The role and responsibility of ongoing clinical trials	
Early Level Professional	Maintains schedules for clinical trial monitoring
RA-8 Protection of the rights, welfare, and well-being of human subjects	

Ensure that clinical research is carried out with the highest ethical standards, and in an environment where the rights, welfare and well-being of subjects is protected	
Early Level Professional	Exhibits a command of the various regulations that apply to conducting clinical research that protects human subjects Understands the role of the institutional review board in making sure that the research that is being conducted meets the appropriate ethical guidelines before enrolling patients
RA-9 Good clinical practice requirements for the clinical investigator team	
The role and responsibility of the clinical team in the execution of the trial, ensuring conformance with the protocol	
Early Level Professional	Verifies submitted protocol for compliance with GCP Verifies that the staff has been trained in good clinical practice Verifies the protocol has been reviewed and approved by the IRB

B. Management of data generated in a clinical trial

RB-1 Management of data generated in a clinical trial; analysis and reporting	
Utilization of case report forms to collect manage and manage data generated during the execution of a clinical trial	
Early Level Professional	Verifies that documents are compliant with standards and best practices when collecting, capturing, managing, analyzing and reporting data during clinical research process
RB-2 Management of data generated during the execution of a clinical trial	
Collection and management of data collected during the course of a clinical trial	
Early Level Professional	Verifies and categorizes data sources contributing to a clinical study and understands appropriate industry standards used in data handling Explains origin and flow of data from clinical trial protocol to case report forms to the clinical study report
RB-3 The role of quality assurance in the management of clinical trial data	
Early Level Professional	Ensure that there is a quality assurance in monitoring group to oversee data quality Ensure that quality assurance is checking to make sure that data is accurate, legible, attributable, original ,complete, and contemporaneous Ensures that data is verifiable Ensures that data is recorded appropriately on the case report forms
RB-4 The utilization of informatics and statistics in the analysis of clinical trial data	
Employing statistics and informatics in the analysis of data generated during the execution of a clinical trial	

Early Level Professional	Verifies collectable data relevant to statistical study in clinical studies

C. RC-1 The review of safety and efficacy data generated during the conduct of a clinical trial: Reviewing the safety and efficacy data utilized in an application for marketing authorization and post approval changes ensuring its integrity and quality

Early Level Professional	Reviews applications to assess safety and efficacy

D. Design of clinical trial protocols

RD-1 Clinical trial data analysis	
Analysis of the result generated during the conduct of a clinical trial	
Early Level Professional	Ensures that the data to be utilized in the statistical analysis process is accurate
RD-2 Design of the clinical trial protocol	
Design of the clinical trial protocol in conformance with good clinical practices	
Early Level Professional	Verifies that the elements and correct principles and processes underpin the design of a clinical study
RD-3 Application of biomedical science to a clinical trial protocol	
Ensures that the principles of biomedical science are appropriately applied to drug development protocols	
Early Level Professional	Applies scientific principles to discovery and development of investigational products
RD-4 The hypothesis to be tested during the conduct of the clinical trial	
Highlight the scientific questions that are to be tested during the execution of the clinical trial in an effort to substantiate the research hypotheses	
Early Level Professional	Formulates the research question

E. Safety of clinical trial participants: Ensuring patient safety throughout the execution of a clinical trial

RE-1 Protection of the clinical trial participants during the conduct of the study	
Utilization of international and national regulations to ensure the safety and protection of human subjects, throughout the execution of the clinical development plan	
Early Level Professional	Verifies that national and international principles of Subject safety and ethical considerations including care, protection are maintained throughout the study
RE-2 Risk benefit analysis	
Analysis of the risk benefit ratio through the selection and management of clinical trial subjects	
Early Level Professional	Recognizes the risks and benefits for a clinical trial with a given investigational drug product Ensures that trial participants understand the risk benefit ratio
RE-3 Utilizing the concepts of clinical equipoise and the therapeutic misconception during the management of a clinical trial	
Ensuring the protection and safety of human subjects during the execution of a clinical study	

Early Level Professional	Recognizes the concepts of clinical equipoise and therapeutic misconception in clinical studies
RE-4 Clinical trial inclusion and exclusion criteria	
Establishing inclusion and exclusion criteria for a clinical trial protocol to ensure human subject protection	
Early Level Professional	Ensures the appropriate application of inclusion criteria, as well as exclusion criteria in the clinical trial protocol Ensures that the inclusion and exclusion criteria captured in the clinical trial all right here to inpatient selection Ensures that the inclusion and exclusion criteria captured in the clinical trial protocol are adequate to ensure patient safety
RE-5 Application of ethical and cultural considerations to the commercial aspects of clinical trial research	
The application of ethical and cultural considerations to the commercial aspects of clinical trial research during the drug development process	
Early Level Professional	Highlights all cultural and ethical considerations relating to commercial aspect of the dossiers Screens the dossiers according to regulation and policies related to cultural and ethical issues relating to commercial aspects Proposes suggestions to be moved further to the mid-level and senior level reviewers
RE-6 The application of the principles of informed consent	
Understanding the key principles of informed consent, their origin, as well as their application in the conduct of a clinical study	
Early Level Professional	Screens the elements and principles of the Informed consent in the submitted applications for appropriateness, and completeness; (IC)
RE-7 The protection of vulnerable patient populations during the conduct of clinical research	
Establishing the appropriate ethical standards and safeguards for vulnerable patient populations	

Early Level Professional	Verifies the various safeguards for vulnerable populations are in place Screens the dossiers for completeness of safeguards elements for vulnerable populations Ensures that the clinical trial staff has been trained on how to recognize vulnerable subjects Ensure that the clinical trial staff identifies individuals whose willingness to participate in the clinical trial may be unduly influenced by expectations of benefits associated with participation

F. RF 1 Quality Management System: Consideration of techniques for monitoring and improving quality functions, processes, and products

Early Level Professional	Ensures that the organization has a robust quality management system in place Ensures that the quality management system is kept current with evolving standards of good clinical practices, good laboratory practices, good manufacturing processes, as well as good Pharmacovigilant practices Ensures that a robust training plan is in place throughout the organization Ensures that training on the quality system is documented Conducts routine assessments of the quality system Drives improvements in the quality system based upon ongoing assessments of its effectiveness

G. RG-1 Review of Risk Management: Risk management processes and procedures utilized throughout the conduct of a clinical trial

Early Level Professional	Ensures that the organization conducting the clinical trial has the appropriate risk management, policies, and procedures in place Ensures that the organization conducting the clinical trial follows there, risk management, policies, and procedures in the execution of a clinical trial

H. Development of regulatory documents

RH-1 Development of regulatory documents	
Early Level Professional	Develops basic documents based on review Utilizes appropriate software Communicates with peers and clients Develops communications Applies appropriate guidelines to documents
RH-2 Utilization of standard of care in the study of an investigational product	
Early Level Professional	Demonstrates understanding of the difference between the Standard of Care and Clinical Trial of the drugs presented Screens dossiers according to existing regulations

I. **Utilization of investigational drug product in a clinical study**: Rules and regulations governing the use of investigational drug product during the execution of a clinical trial

RI-1 The global aspects of vaccine/biological drug development and approvals	
The regulations that apply to the development and approval of new therapeutics developed globally	
Early Level Professional	Appraises the regulatory issues related to the increase in regulations of vaccines and biologicals
RI-2 Historical considerations in the development of global regulatory environment	
The role of key historical events in the formulation of global regulations governing the development of new pharmaceuticals	

Early Level Professional	Organizes and manages registration, renewal of vaccines and biologics preparations (human and veterinary) Reviews promotional and advertising documents of vaccines and biologics Inspects pharmaceutical manufacturing facilities Assesses the safety, efficacy and biologicals and vaccines Issues marketing authorization Monitors vaccine and biologics marketed products to assure compliance with regulations Manages all regulatory aspects for vaccines and biologics preparations Reviews approaches to tracking of biologics and vaccines to reduce fraud
RI-3 Key processes for gaining marketing approval	
The phases of drug development that must be executed in order to gain regulatory approval to market a new vaccine or biologic	
Early Level Professional	Reviews and assists applicants with preclinical and clinical applications and authorization applications
RI-4 Establishment of roles and responsibilities for institutions participating in clinical trials	
Institutional roles and responsibilities during the development of an investigational drug product	
Early Level Professional	Reviews and identifies responsibilities of applicants including CROs and companies
RI-5 Reporting safety concerns	
Detailed knowledge of the regulations governing the development of vaccines and biological products	

Early Level Professional	Reviews documents according to the guidelines for safety reporting requirements, the adverse events

J. RJ-1 Approved therapeutic products; maintenance of their approval and registration status: management of the regulatory processes that govern approved drug products including periodic reviews, regulatory actions, or withdrawals due to noncompliance

Early Level Professional	Reviews the approved product register and ensuring it is up to date

K. RK-1 Information contained on the product label and in package insert

Early Level Professional	Sets basic labelling requirements of Health Products & Technologies in relation to vaccines and other biologics Compares the product labelling vice versa innovator product

L. RL-1 Drug Product Quality

Early Level Professional	Ensures the basic structures of the product quality sections are in place Reviews safety data on Active Substance and Medical Product Reviews the nonclinical aspects and toxicology and assures safety of the drug product

M. Decision making on regulatory matters: regulatory decision making on matters related to documentation, inspections, and laboratory testing

RM-1 Making regulatory decisions
The ability to make and execute regulatory decision

Early Level Professional	Holds a degree in a relevant scientific field, such as pharmacology or toxicology, as well as experience in regulatory affairs and knowledge of relevant regulations and guidelines Evaluates the safety, quality, and effectiveness of products in accordance with regulatory guidelines and standards

N. RN-1 Reliance strategy: Able to assess other regulatory authority

Early Level Professional	Assesses submitted applications using reports and results obtained by another regulatory authority, typically in another jurisdiction, to inform its own decision-making process, based on agreed upon reliance strategies and procedures

O. RO-1 Training: Able to evaluate training materials and train others

Early Level Professional	Evaluates the effectiveness of the training provided to healthcare professionals (HCPs) who will be administering the product

P. RP-1 Capacity building: Able to evaluate training materials and train others

Early Level Professional	Evaluates an organization's capacity to comply with regulatory requirements. This may involve reviewing training programs, assessing the expertise of staff, and evaluating the effectiveness of policies and procedures

II. Inspectors

A. I-A Inspects data integrity and all other data acquisition and data processing activities

Early Level Professional	Screens documentation using the principles of data integrity “ALCOA+”. before and during an inspection at sites Maintains accurate and objective records of facts and observations made during audits/inspections

B. I-B Documentation inspection activities

Early Level Professional	Reviews all documents including licensing applications and all other documents including biologicals related documents Uses checklists and guidelines to screen submitted applications

C. I-C Review of manufacturing records as part of lot release: Reviews all data, documents, and batch records related to batch release. Reviews all data from contract

laboratories and regulatory agencies

Early Level Professional	Understands the principles and reasons for Specifications Understands ICH Q5E (Especially Comparability protocols) Understands of the product and laboratory control methods Understands of vaccines and biologics manufacturing processes and control methods Understands of the Standard Operating Procedures (SOPs) for summary protocol review

D. I-D Established quality system for inspectorate function

Early Level Professional	Develops quality manual for inspectorate system Addresses audits and inspections

E. I-E Development of technical regulatory documents

Early Level Professional	Awareness and understanding of the regulatory frameworks, guidelines, standard operating procedures (SOPs) and tools for regulation of vaccines and biologics Develops draft regulatory frameworks, guidelines, standard operating procedures (SOPs) and tools for regulation of vaccines and biologics Awareness of stakeholders and key players involved in the development, manufacture, distribution and regulation of vaccines and biologics

F. I-F Carries audits and inspections based on current ICH and ISO quality guidelines

IF-1 Inspections based on good clinical practices guidelines

Early Level Professional	Understands basic legal and administrative aspects of clinical trials (GCP) inspections for vaccines and biologics Assesses applications for GCP inspection for vaccine and biologics by clinical research organizations performing clinical studies Performs GCP inspections as an observer
IF-2 Inspections based on GDP guidances	
Early Level Professional	Assesses applications for GCP inspection for vaccine and biologics by distributors/wholesalers Understands of how to read and interpret vaccine vial monitor device Performs GDP inspections as an observer Understands national and international guidelines on GDP for vaccines and biologics
IF-3 Inspections based on guidances for good laboratory practices	
Early Level Professional	Understands national and international guidelines on GLP for vaccines and biologics Assesses applications for GCP inspection for vaccine and biologics by laboratories in non-clinical research and drug development and bioanalytical laboratories Performs GLP inspections as an observer
IF-4 Inspections based on guidances for good manufacturing practices	
Early Level Professional	Assures all GMP requirements are met Understands national and international guidelines on GMP for vaccines and biologics Assesses applications for inspection of biologics active substances and finished products

G. I-G Product Quality: inspects for all aspects related to product quality including vaccine starting materials, cell banks, and intermediates as applicable

Early Level Professional	Evaluates biosafety requirements and procedures for vaccine and biological manufacturing as governed by different regulatory bodies Reviews all requirements related to biomanufacturing equipment and facilities Reviews all QC and QA methods used

H. I-H Supervision of vaccine disposal and destruction: Applies scientific biosafety regulatory and environmental requirements to ensure proper collection, management and disposal of vaccines and vaccination waste

Early Level Professional	Assesses application of national policy, regulations, and procedures for the disposal of expired, substandard, and poorly stored vaccines Assesses application of national policies, regulations, and procedures for disposal of equipment used for vaccination including used vials, ampoules or syringes placed in a proper, puncture-resistant “sharps” box

I. I-I Investigation of product quality complaints: investigates complaints related to vaccines and biologics quality

Early Level Professional	Understands the critical quality attributes (CQAs) for vaccines and biologics in the marketing authorization (MA) Understands the SOPs for handling (receiving, documenting, investigating and preparation of final report) product quality complaints Receives, documents, and communicates product complaints to the responsible person for investigation.

J. I-J Import examination and screening

Early Level Professional	Understands the regulatory requirements and SOPs for inspection of vaccines and biologics at the port of entry Performs screening of imports for vaccines and biologics

K. I-K Overall Regulatory Approaches: Develops regulatory approaches and strategies based on quality audits and inspections

Early Level Professional	Understands the regulations related quality, safety and efficacy of vaccines and biologics Understands the standard operating procedures (SOPs) applicable to inspection of vaccines and biologics across the supply chain Understands the vaccines and biologics regulatory inspection outcomes that informs decision making

L. I-L Sampling of products from the market: identifies and assesses the quality vaccines and biologics in the supply chain system; identifies vaccines and biologics, based on the risks associated with manufacturing complexity, dosage form, storage, and stability; Assesses the quality of vaccines and biologics received at the ports of entry and border posts

Early Level Professional	Understands of the guidelines and procedures for surveillance and sampling of vaccines and biologics in the supply chain Understands the sampling techniques for vaccines and biologics Understands the handling, storage and transportation of sampled vaccines and biologics

M. I-M Provision of technical guidance (capacity building for stakeholders): Participates in capacity-building activities.

Early Level Professional	Understands of capacity building guidelines for capacity building of stakeholders in vaccine manufacturing Understands of what kind of questions to ask Understands of stakeholder's engagement techniques Understands of areas of engagement and collaboration with stakeholders in vaccine manufacturing initiatives

N. I-N Training of regulatory personnel and industry: Applying new scientific innovation, technologies, and research to build a pool of competent workforce in the development, manufacturing and distribution of vaccines and biologics and the regulatory sector

Early Level Professional	Understands the regulatory guidelines for vaccines and biologics Conducts training needs assessment for the industry and regulators

O. I-O Enforcement: Enforces GMP guidelines for vaccines and biologics, seize any counterfeit, adulterated, bad or fake vaccine or biologics, based on surveillance and intelligence gathering, issue invitation letter or arrest suspect

Early Level Professional	Identifies counterfeit or substandard vaccine products

P. I-P Reviews batch records of active medicinal Substance and finished medicinal product to ensure lot-to-lot consistency

Early Level Professional	Understands the importance of batch records Is familiar with typical batch records

III. Laboratory Analysts

L-A1: Applies standards and international best practices: Ensures application of national, regional, and international standards, guidelines, and best practices in quality control laboratory for safety, efficacy, and quality of vaccines and biologics

Early Level Professional	Implements standards and best practices, including current Good Laboratory Practices (cGLP), Good Microbiological Laboratory Practices (GMLP), and current good manufacturing practices (cGMP)as applicable to quality control laboratories for vaccines and biologics Understands national and regional, as well as international standards, guidelines, and best practices (cGLP, cGMP) for vaccines and biologics (i.e., Bioanalytical Laboratory) Initiates development of written standards for specific products, such as mRNA vaccines, and aligns written standards to regional as well as international best practices Ensures that the principles of reliance and harmonization are included in written standards Defines certification /accreditation scheme for assuring the safety, quality, and efficacy of vaccines and biologics Ensures the autonomy of the quality control laboratory to ensure independent, authoritative, and impartial decisions on safety, efficacy, and quality of vaccines and biologics Identifies laws pertaining to the operation of quality control laboratories Participates in proficiency and competency assessment of quality control, laboratories, and quality control personnel Initiates exchange of information on safety, efficacy, and quality of vaccines and biologics among NRAs

L-B1. Establishes and implements policies, guidelines, and procedures to ensure quality control laboratory operates in a safe environment and prevent health hazards to the personnel

Early Level Professional	Develops and implements policies, guidelines, and procedures on laboratory safety, and handling of biohazardous materials Develops and implements standard operating procedures for handling biohazardous materials and usage of personal protective equipment (PPE), including labeling and equipment used Implements Laboratory Safety Programs for the quality control laboratories personnel Documents all safety related incidents and reports to appropriate authorities Participates in safety trainings and drills as required Ensures implementation of relevant safety policies, guidelines, and regulations related to laboratory safety within the quality control labs Ensures that appropriate safety information and documents, such as safety data sheets, are available on all chemicals, reagents, drugs, vaccines, biologics, and other applicable materials that are utilized in the quality control laboratories Ensures use of relevant PPE whilst working in the quality control labs Promotes health and safety by encouraging adherence to quality control policies and procedures within the organisations quality control labs

L-C1: Establishes and sustains a maintenance program for laboratory systems and equipment to ensure a high standard of performance as well as to generate results/data which are accurate and precise (with minimal variations/errors)

Early Level Professional	Develops written policies and procedures for maintenance of laboratory systems, equipment, and all other items utilized in a laboratory Follows United States Pharmacopeia (USP) or International Organization for Standardization (ISO) procedures for all measurements and repair of equipment, including HVAC equipment, including Design Qualification (DQ), Installation Qualification (IQ), Operational Qualification (OQ), Performance Qualification (PQ) Implements the Laboratory Quality Management System that supports the analytical lifecycle Creates and adheres to Standard Operating Procedures for the quality control laboratories

L-D1: Participates in the design and development of analytical and verification methods and procedures for various vaccines and biologics. Works to facilitates method transfer of analytical and verification methods and procedures for various vaccines and biologics

Early Level Professional	Understands national, regional, and international guidelines for analytical procedures and methods validation for vaccines and biologics Understands quality attributes of mRNA, DNA, Inactivated Viral Vector, Protein Subunit, virus-like particle, and attenuated vaccines Provides guidance to pharmaceutical industry on analytical methods development for vaccines and biologics including critical parameters such specificity, linearity, limits of detection (LOD), limits of quantitation (LOQ), range, accuracy, and precision Understands various bioassays applicable to vaccines (animal-based biological assays, cell culture based biological assays, and biochemical assays) Develops verification protocol for analytical procedures Participates in analytical method validation Participates in developing analytical method verification, validation, and method transfer protocol Develops tools and checklist to guide inspection of pharmaceutical industries on analytical methods used for various vaccines and biologics Prepares verification report for analytical methods for vaccines and biologics

L-E1: Ensures establishment of scientifically sound and appropriate specifications, standards, and test procedures. Specifications, standards, and test procedures are designed to ensure components, containers and closures, in-process materials, and finished vaccines and biologics, conform to the established standards

Early Level Professional	Understands national, regional, and international regulations and guidelines on investigation of out-of-specification (OOS) results Plans and participates in out-of-specification and failure investigations Addresses and resolves issues arising from the investigation of OOS results as well as failure investigations Plans and participates in CAPAs with the goal of eliminating recurrences

L-F1: Establishes and implements guidelines, procedures, and programs for qualification of laboratory equipment to ensure accuracy and integrity of equipment to generate reliable and accurate data

Early Level Professional	Understands national, regional, and international guidelines and procedures for qualification of laboratory equipment Develops policies, procedures, and guidelines for equipment qualification on non-sophisticated laboratory instruments, e.g., weighing balance, conductivity meter, and pH meter Performs calibration and verification of laboratory equipment Documents and maintains records of equipment qualification activities in approved report Troubleshoots non-sophisticated equipment as a facilitation to their qualification process Guides pharmaceutical manufacturing on development of plans and protocols for laboratory equipment calibration taking into account design qualifications (DQ), installation qualifications (IQ), operational qualification (OQ) and performance qualification (PQ)

L-G1: Quality system for Analysis Laboratory

Early Level Professional	Establishes quality system for Analytical Laboratory Utilizes ISO Documents to set up quality laboratory Adheres to ISO documents and quality manual Performs analysis of samples

L-H1: **Establishes accuracy of analytical reports and data management**

Early Level Professional	Confirms that all required data and reports are submitted for review Devises and implements master data management processes for specific subsets of data Maintains and implements information handling procedures for analytical data Enables the availability, integrity, and searchability of information through the application of formal data and metadata structures as well as protection measures

L-I: Participation in Research

Early Level Professional	Understands the research and development of vaccines as well as biological products Demonstrates a thorough understanding of the regulations that govern the development of drugs, vaccines, and biological products Demonstrates basic understanding of scientific research methods, study designs, and the different sources of data utilized in the development of drugs, vaccines, as well as biological products Understands the purpose, concept, and topic of a scientific study Possesses ability to pose relevant research questions

IV. Vigilance Professionals

A. Pharmacovigilance (PV) assessment for marketing drugs and vaccines

VA-1 Robust assessment of safety signals	
Collection and evaluation of adverse events from numerous sources	
Early Level Professional	Categorization of ADRs/AEFIs from reports Extract authentic vaccine or biologics effects from medical and patient Identify and report idiosyncrasies and new reactions associated with vaccines and biologics Maintain list of AEFIs and sources
VA-2 Individual case safety reporting for vaccines and pharmaceutical products	
Reporting of individual case, safety data to the appropriate regulatory authorities for both drugs and vaccines/biologics	
Early Level Professional	Conducts trend analysis of locally received ADRs/AEFIs for identification of probable/possible safety concerns and signal and reports/shares data within and outside the NRA for further investigations Understands the difference between individual case study reports for drugs versus that for vaccines/biologics Understands how to submit data to VAERS and FAERS
VA-3 Utilization of PV centers to detect medication errors, substandard, and counterfeit	

drugs, vaccines, and biologics	
Detection of medical errors, substandard and counterfeit drugs, vaccines, and biologics through the establishment of robust PV systems and processes	
Early Level Professional	A thorough understanding of PV systems and processes, and a thorough understanding on how to detect medical errors for substandard and counterfeit drugs, vaccines, and biologics
VA-4 Ongoing risk assessment	

Assessment and communication of risk utilizing a PV system	
Early Level Professional	Ensures that risk management, tools, and techniques are in place to monitor safety and evaluate risk benefit ratios on an ongoing basis Ensures that all of the risk management policies and procedures are codified in SOPs Conducts initial reviews of risk management plans and summarizes key components for further decision-making Monitors all products and conducts post-market evaluations to ensure drug safety Applies professional knowledge on risk associated with continuous exposure Ensures that the good pharmacovigilance practices (GVP) are followed Ensures that staff are trained on PV regulatory requirements Ensures that the sponsor submits a risk management plan at the time of applying for market authorization Ensures risk management plans distill technical detail into information that the general public can understand Ensures that the risk management plan is modified and updated on an ongoing basis as new risk information becomes available Ensures that the risk benefit ratio is modified and updated as new information on risk becomes available, as the updated risk benefit ratio should reflect either increases or decreases in risk as new data becomes available
VA-5 Detection of safety signals	

Early Level Professional	Collates and upload causality reports on database Participates in analyzing an ICSR
VA-6 Separation of signal versus noise	
Differentiation of safety signals from background noise	
Early Level Professional	Ensures that the organization monitors ADR and AEFI for vaccines and biological products Ensures that after appropriate medical and scientific evaluation of the ARD and /or AEFI the appropriate communication ensues to healthcare professionals, patients, as well as regulators
VA-7 Periodic Safety Update Reports (PSURs) or Periodic Benefit-Risk Evaluation Report (PBRERs). Both reports are authored to provide a periodic evaluation of risk to benefit ratio	
Early Level Professional	Reviews and analyzes the appropriateness/completeness of PSURs and PBRERs as per national regulations and international set standards (i.e., the International Conference on Harmonization [ICH]) Reviews and analyzes ICSRs, to ensure that they include signal detection, signal validation, and signal management, and risk minimization as described in VA-5 (Detection of safety signals) Is proficient in the uses of search engines, medical databases, and study registers to assist in the identification and processing of ADR's or AEFI
VA-8 Advertisement/medical products promotion	
Knowledge, skills to enable one to judge if advertisement/promotional information is fit for consumption by either public or health care professionals	

Early Level Professional	Reviews promotional material related to vaccines and biological products Reviews potential adverse reactions for drugs, vaccines, as well as biological products from a variety of different sources, including publications, social media reports, healthcare professionals, and ongoing clinical research Retrieves all relevant data on potential adverse reactions related to drugs, vaccines, as well as biological products Ensures that the relevant data is appropriately reviewed by medical and scientific staff Ensures that data relevant to adverse reactions is subject to statistical analysis where appropriate Critically appraises clinical trials publications and other studies/literature published to justify claims made on promotional materials/advertisement and explore the limitations of such studies to authenticity and generalizability of generated evidence Assesses appropriateness of advertisements/promotional material to the targeted audience considering rational use of the vaccine/biological product

B. BV-1 PV during the drug development process

Early Level Professional	Ensures that appropriate criteria such as the Bradford Hill criteria or adverse drug reaction probability scale are used in the analysis of adverse event reports on drugs, vaccines, as well as biological products to determine causation

C. PV system strengthening

VC-1 Capacity Building	
Knowledge and skills that enable horizontal cooperation	
Early Level Professional	Adapts/develops PV training materials for various audiences Facilitates/conducts PV training for healthcare professionals Conducts PV awareness/sensitization campaigns for the general public
VC-2 Maintaining public health through the use of a PV system	
Utilizes the data from PV to maintain and approve public health	

Early Level Professional	Ensures that there is a robust PV system in place to detect adverse events for marketed drugs/vaccines/biological products
Mid-Level Professional	Designs procedures and tools for detection and reporting of ADRs/AEFIs by the public Communicates risk from vaccines and biological products to the public and highlights products of public health concern, like those with potential for abuse
Senior Level Professional	Builds scientific evidence based on safety by identifying trends and anomalies based on the presented scientific problems to reduce the risk or anticipate problems Develops and incorporates risk communication in public health campaigns for vaccines
VC-3 PV System Development	
Early Level Professional	Understands the principles of GVP and the importance of an organization being in compliance with GVP Has a foundation in systems' thinking and approaches as well as understands how this system impacts safety monitoring and vice versa Understands risk management including risk identification, risk assessment, risk mitigation, and tools associated with the risk system Understands the quality system that resides within the PV system Understands the importance of policies and procedures in place and in use
VC-4 PV regulations and guidelines	
Compliance with GVP	
Early Level Professional	Knowledgeable of local/regional regulatory requirements governing PV activities Understands and applies GVP Understands and complies with policies and procedures to comply with PV regulatory guidance Participates in audits and inspection activities and has a strong understanding of these areas Articulates why record management is important in PV and follows record management procedures and best practices

D. Updating of market status

VD-1 Responses to the PV signal	
Ensures that the organization has the appropriate policies and procedures in place to support any action required as a result of a PV review. The outcome of a PV review could include communication with the public, communication with healthcare providers, or recalling products	
Early Level Professional	Advises consumers on where they can find additional information (i.e., NRA's website, consulting with pharmacist) for vaccines or biologics on recall list Ensures proper documentation and accountability for recalled products Writes technical reports for simpler applications or cases Records observations and/or data obtained in the course of one's duties in a timely manner to prevent loss of relevant information Prepares general documentation in relation to the role Ensures proper application of laws, regulations, and guidelines for regulatory decisions Provides rationale for regulatory decisions Ensures adequate application of good regulatory practices in regulatory actions
VD-2 Routine auditing of the quality system to ensure continued compliance with GVP	
Early Level Professional	Participates in internal and external audits of PV systems for the NRA, industry, and sponsors Assists in compiling of data for inspection reports Supports external compliance monitoring with PV obligations Drafts and writes inspection and audit reports
VD-3 Dissemination of information related to the risk benefit ratio	
Communication with regulators, medical professionals, patients, journalists, and the general	

public regarding changing risk benefit ratios	
Early Level Professional	Ensures that safety communications deliver relevant, clear, and accurate information to the right audiences Ensures that safety communications are tailored to the appropriate audience, i.e., healthcare professional versus professionals Ensures coordination and cooperation among the different parties involved in issuing safety communications Ensures that information on risks be presented in the context of risk to benefit ratios Ensures that safety communications comply with all relevant regulations Coordinates with regulatory authorities regarding the need and content of any press releases Ensures that safety information disseminated online via social media is accurate Ensures that procedures are in place for the communication of safety information Ensures that safety communications are subject to quality control reviews to ensure their accuracy and clarity prior to release
VD-4 Quality Management System (QMS)	
Early Level Professional	Strong understanding of, and commitment to, the QMS and the associated activities Participates in delegated QMS activities
VD-5 PV Intelligence	
Applies Pharmacovigilance Intelligence in regulatory strengthening	
Early Level Professional	Gathers information-related changes in regulatory landscape related to PV Applies the global safety regulations for vaccines and biologics
VD-6 Use of Apps for PV	
Utilization of smart phone mobile applications for adverse drug reaction/reporting	

Early Level Professional	Reviews the utility of smart phone applications for adverse drug reporting with the staff of the PV center Evaluates the utility of smart phone applications for adverse drug reporting Creates awareness on availability of smart phone applications for adverse drug reporting Participates in the review of existing smart phone applications for adverse drug reporting and selects the best application for the PV center

General References to Competency Frameworks

Numerous references contributed to the concepts and statements in the Competency Framework. It was not possible to link many of the references to a specific statement but instead to a concept included in the competency framework. The reader is directed to a review of all of these documents to provide a complete picture of the background.

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Conclusion

The tree segments of this BIRS course can be taught individually or together

A. Segment on Vaccine Manufacture
B. Segment on Vaccine Regulatory Review
C. Segment (including possibly hands-on experimentation) on point-of-care vaccine manufacture

In general, each segment would be divided into modules containing: (1) On-line or live lectures; (2) Quizzes to focus on important points; and (3) Laboratory experiments with vaccine manufacturing and sterile products manufacture. In some courses, case studies using groups or individuals should be assigned to further enhance the student's learning.

By combining the courses with actual manufacturing establishments, it should be possible to manufacture vaccines in Africa by Africans.

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APPENDIX

COMPETENCY FRAMEWORK FOR REGULATORS OF VACCINES

Provided by BIRS Center, Purdue University

Professor Kari Clase, Director
Professor Stephen Byrn, Co-Director

June 28, 2023

Table of Contents

I. List of Acronyms

ADRs Adverse drug reactions
AEFIs Adverse events following immunization
ALCOA Attributable, Legible, Contemporaneous, Original, Accurate
CAPA Corrective and preventative action
cGMLP current Good Microbiological Laboratory Practices
cGMP current Good Manufacturing Practices
DQ Design qualification
EU European Union
FMEA Failure Modes and Effects Analysis
GRP Good research practices
GVP Good Pharmacovigilant practices
HCPs Health care professionals
HVAC Heating Ventilation and Air Conditioning
ICH International council for harmonization
ICSR Individual case study reports
ICSRs Individual case study reports
IMP Investigational medical product
IQ Installation qualification
IRB Institutional review board
ISO International Organization for Standardization
NRA National regulatory agencies
OOS Out of Specifications
OQ Operational qualification
PPE Personal Protective Equipment
PBRER Periodic benefit risk evaluation report
PIL Package information leaflet
PMDA Pharmaceutical and medical device agency
PQ Performance qualification
PSUR Periodic safety update report
PV Pharmacovigilance
QMS Quality management system
RCA Root Cause Analysis
RMP Risk management program
SOPs Standard operating procedures
US United States
USP United States Pharmacopoeia
WHO World health organization

II. Introduction

Vaccines and biologics are complex biological products derived from living organisms or synthesized from complex lipid systems and are quite different from chemical pharmaceutical products. Vaccines are also typically injectable products requiring attention to sterility and the assurance of quality is difficult and complex. The NRAs have the responsibility for licensing facilities where vaccines are manufactured, review of submissions for clinical trials and registration documentation, inspection of facilities for clinical trial, development, manufacture and control of vaccines and biologics, independent lot-release and post licensure monitoring (vigilance). In some cases, the NRAs work with National Control Laboratories who perform testing on the submitted products.

This competency framework describes knowledge and behaviors that a regulatory professional is expected to demonstrate with respect to vaccines and biologicals. The framework is divided into levels of proficiency. In this case - entry level, mid level and senior level. These levels allow readers and educators to differentiate the level of training the potential learner has and the amount of instruction required to achieve this level. Four areas are addressed in this framework:

5. Reviewers
6. Inspectors
7. Lab analysts
8. Vigilance (Pharmacovigilance)

This competency framework for vaccines and biologics may help guide curriculum development, and training (academic and, more specifically, on-the-job training) of regulatory staff. It could also provide a unified framework for capacity building activities offered by various stakeholders and ensure systematic professional development and recognition of regulatory professionals.

This document was prepared by first reviewing model competency frameworks for medical products including those from the WHO and RAPS. Then the relevant activities and competencies for each role and the entry-level, mid level, and senior level were defined by a broad and diverse team of subject matter experts from the Purdue Biotechnology Innovation and Regulatory Science community.

III. Table of relevant activities for each role

Relevant Activities for Each Role	
Reviewers	Q. Conducting a clinical trial in conformance with the good clinical practices (GCPs): Execution of clinical trials as a part of the overall drug development plan R. Management of data generated in a clinical trial S. The review of safety and efficacy data generated during the conduct of a clinical trial: Reviewing the safety and efficacy data utilized in an application for marketing authorization and post approval changes ensuring its integrity and quality T. Design of clinical trial protocols U. Safety of clinical trial participants: Ensuring patient safety throughout the execution of a clinical trial V. Quality Management System: Consideration of techniques for monitoring and improving quality functions, processes and products W. Review of Risk Management: Risk management processes and procedures utilized throughout the conduct of a clinical trial X. Development of regulatory documents Y. Utilization of investigational drug product in a clinical study: Rules and regulations governing the use of investigational drug product during the execution of a clinical trial Z. Approved therapeutic products; maintenance of their approval and registration status: management of the regulatory processes that govern approved drug products including periodic reviews, regulatory actions, or withdrawals due to noncompliance AA. Information contained on the product label and in package insert BB. Drug Product Quality CC. Decision making on regulatory matters: regulatory decision making on matters related to documentation, inspections, and laboratory testing DD. Reliance strategy: Able to assess other regulatory authority EE. Training: Able to evaluate training materials and train others FF. Capacity building: Able to evaluate training materials and train others
Inspectors	Q. Inspects data integrity and all other data acquisition and data processing activities R. Documentation inspection activities S. Review of manufacturing records as part of lot release: Reviews all data, documents, and batch records related to batch release. Reviews all data from contract laboratories and regulatory agencies T. Established quality system for inspectorate function U. Development of technical regulatory documents V. Carries audits and inspections based on current ICH and ISO quality guidelines W. Product Quality: inspects for all aspects related to product quality including vaccine starting materials, cell banks, and intermediates as applicable X. Supervision of vaccine disposal and destruction: Applies scientific biosafety regulatory and environmental requirements to ensure proper collection, management and disposal of vaccines and vaccination waste Y. Investigation of product quality complaints: investigates complaints related to vaccines and biologics quality Z. Import examination and screening AA. Overall Regulatory Approaches: Develops regulatory approaches

	and strategies based on quality audits and inspections BB. Sampling of products from the market: identifies and assesses the quality vaccines and biologics in the supply chain system; identifies vaccines and biologics, based on the risks associated with manufacturing complexity, dosage form, storage and stability; Assesses the quality of vaccines and biologics received at the ports of entry and border posts CC. Provision of technical guidance (capacity building for stakeholders): Participates in capacity-building activities DD. Training of regulatory personnel and industry: Applying new scientific innovation, technologies, and research to build a pool of competent workforce in the development, manufacturing and distribution of vaccines and biologics and the regulatory sector EE. Enforcement: Enforces GMP guidelines for vaccines and biologics, seize any counterfeit, adulterated, bad or fake vaccine or biologics, based on surveillance and intelligence gathering, issue invitation letter or arrest suspect FF. Reviews batch records of active medicinal Substance and finished medicinal product to ensure lot-to-lot consistency
Laboratory Analysts	J. Applies standards and International best practices: Ensure application of national, regional and international standards, guidelines and best practices in quality control laboratory for safety, efficacy and quality of vaccines and biologics K. Establishes and implements policies, guidelines, and procedures to ensure quality control laboratory operates in a safe environment and prevent health hazards to the personnel L. Establishes and sustains a maintenance program for laboratory systems and equipment's to ensure a high standard of performance and generate results/data which is accurate and precise (have minimal variations or errors) M. Outlines and implements analytical methods for vaccines and biologicals N. Ensures establishment specifications and methods consistent with ICH guidances for vaccines and biologics and conducts investigations of out of specifications (OOS) and CAPA O. Establishes and implements guidelines, procedures, and programs for qualification of laboratory equipment's to ensure accuracy and integrity of equipment's to generate reliable and accurate data P. Quality system for analysis laboratory Q. Establishes accuracy of analytical reports and data management R. Participation in Research
Vigilance	D. PV assessment for marketing drugs and vaccines E. PV during the drug development process F. PV system strengthening G. Updating of market status

IV. Reviewers

Q. Conducting a clinical trial in conformance with the good clinical practices (GCPs): Execution of clinical trials as a part of the overall drug development plan.

RA-1 Clinical trial protocol design in conformance with the overall drug development strategy	
Explain how to design and execute a clinical trial	
Early Level Professional	Able to explain the design, purpose, and conduct of trial as it relates to the new intervention Screens the submitted documents against the guideline requirements to identify gaps
Mid Level Professional	Identifies the link between developing a new intervention and the interrelated trial goals and design (by reading and comprehending a clinical trial protocol) Reviews submitted documents for absence of gaps Recommends changes to the design and conduct of the clinical study
Senior Level Professional	Provides guidance on regulatory requirements for the product type under clinical trial Advises/approves study design and purpose to fit the new intervention
RA-2 Auditing of clinical trials	
Conducting audits of a clinical study in order to assess compliance with GCP's	
Early Level Professional	Demonstrates understanding of the GCP audits Screens submitted documents/applications for completeness
Mid Level Professional	Applies the good clinical practices during the conduct of a clinical site audit to ensure all of the regulations are being followed in the conduct of the study Reviews the informed consent documents, protocol, SOP's, etc. to ensure the site is conforming with all appropriate regulations regarding human subject participation Reviews screened applications for completeness and make necessary recommendations Applies the appropriate level of scrutiny to the conduct of routine audits of clinical trial sites as well as those performed for cause
Senior Level Professional	Applies risk assessment in determination of acceptability of clinical trial audit applications Implements risk Advanced level skills in risk assessment are essential for clinical trial auditors Approves recommendations in the clinical trial audit applications
RA-3 Ensuring compliance with good clinical practices	
Ensuring that the design in conduct of a trial is in compliance with good clinical practice guidelines	
Early Level Professional	Demonstrates understanding of the Good Clinical Practice guidelines, clinical trial protocol requirements Reviews the clinical trial protocol and supporting documentation for

	completeness
Mid Level Professional	Reviews and approve the clinical trial protocol Explains applicable regulations and following established processes in place to ensure compliance Assesses compliance with good clinical practices (WHO, ICH, FDA) by carefully examining clinical study protocol, case report forms, study databases, as well as statistical analysis of study data In order to ensure the integrity in the accuracy of study data
Senior Level Professional	Provides guidance to the clinical site staff to ensure that they have the appropriate policies and procedures in place to execute a clinical trial in conformance with appropriate regulations and guidelines Reviews and approves all policies and procedures at the clinical trial site Ensures that appropriate training programs are in place, and that trial staff have completed all of the necessary training in conformance with their roles and responsibilities in the execution of the trial Reviews the job descriptions, educational background, CVs and training of all study staff to ensure that they are qualified to perform the duties outlined in their job description
RA-4 Appropriate management of investigational drug product	
Best practices for the storage, dispensing, and accountability for investigational product during the conduct of a clinical study	
Early Level Professional	Demonstrates understanding of the manufacturer's instructions regarding storage and dispensing of the product Participates in review of deviations from product storage, transportation, and dispensing
Mid Level Professional	Identifies the life cycle of an investigational product that includes transport, storage and handling and accountability Interprets and understands data submitted to support related to the product life cycle and ensure that it makes scientific sense Reviews deviations associated with product storage, transportation and dispensing to ensure they are appropriately investigated, and patient safely is maintained
Senior Level Professional	Develops regulatory requirements for control, storage and dispensing of investigational products to ensure patient safety Monitors CAPAs to ensure issues or problems that are identified in the handling of investigational products to limit future deviations
RA-5 Identification of safety issues and their management in conformance with regulatory requirements	
Methodology employed in the identification and reporting of safety issues identified during the conduct of a clinical trial	
Early Level Professional	Understands the potential safety issues associated with the product being

	investigated
Mid Level Professional	Identifies safety issues that are observed during the conduct of the clinical trial and ensures they are reported to the appropriate regulatory authorities in a timely fashion
Senior Level Professional	Reviews all safety procedures to ensure that the correct procedures are in place to ensure the accurate and timely reporting of adverse events should they occur Ensures that the staff at the clinical trial site are appropriately trained on all safety procedures Given the overall importance of compliance with safety procedures, works with staff to make sure that the procedures are appropriately implemented and followed Ensures that a robust Pharmacovigilance plan is in place and rigorously followed
RA-6 Assessment of adverse events during the conduct of a clinical trial	
Categorizing adverse events that occur during the conduct of a clinical trial and reporting to IRB's sponsors and regulatory authorities	
Early Level Professional	Collates and report of AEs
Mid Level Professional	Reports an SAE during a clinical trial to appropriate entity within appropriate timeline Reviews the reporting requirements of an SAE
Senior Level Professional	Works to harmonize the reporting requirements for SUSARs across a variety of different regulatory organizations Works to implement the harmonized reporting requirements within their organization
RA-7 Utilization of clinical trial monitors	
The role and responsibility of ongoing clinical trials	
Early Level Professional	Maintains schedules for clinical trial monitoring
Mid Level Professional	Ensures that monitors are in place throughout the duration of the trial Ensures that the monitors are appropriately trained and qualified for their responsibilities Ensures that a robust monitoring plan is in place and rigorously followed Identifies any outstanding and unresolved issues from monitoring activities Ensures a corrective plan is in place for any deficiencies identified as a result of ongoing monitoring activities Ensures that the appropriate corrective action have been taken in response to any deficiencies identified by the study monitors Ensures that the monitoring plan is current, up-to-date improve by the

	sponsor
Senior Level Professional	Rigorously executes the monitoring plan
RA-8 Protection of the rights, welfare, and well-being of human subjects	
Ensure that clinical research is carried out with the highest ethical standards, and in an environment where the rights, welfare and well-being of subjects is protected	
Early Level Professional	Exhibits a command of the various regulations that apply to conducting clinical research that protects human subjects Understands the role of the institutional review board in making sure that the research that is being conducted meets the appropriate ethical guidelines before enrolling patients
Mid Level Professional	Makes sure that the clinical trial being conducted is done with the highest ethical standards and in conformance with the expectations of the various regulations governing the conduct of clinical research designed to ensure the privacy, rights, welfare, and well-being of the clinical subjects Makes sure that the clinical trial is being conducted in order to meet all of the expectations of the IRB related to the welfare of the subjects enrolled in a clinical trial program
Senior Level Professional	Guides local, clinical staff in authoring standard operating procedures that clarify, the processes necessary to ensure the rights, welfare, and well-being of all clinical trial subjects Guides local clinical staff in authoring appropriate standard operating procedures that ensure compliance with IRB expectations Works with local clinical staff to ensure appropriate training is provided to all staff on the various policies, procedures, and guidelines that ensure patient rights, welfare, and well-being Works with clinical trial site key personnel to ensure that all SOP's related to patient rights, welfare and well-being are followed
RA-9 Good clinical practice requirements for the clinical investigator team	
The role and responsibility of the clinical team in the execution of the trial, ensuring conformance with the protocol	
Early Level Professional	Verifies submitted protocol for compliance with GCP Verifies that the staff has been trained in good clinical practice Verifies the protocol has been reviewed and approved by the IRB
Mid Level Professional	Reviews the protocol to ensure that the role of the site team members including the PI is clearly stated, as required by GCP Verifies that the team have job descriptions that clearly defined their roles and responsibilities Verifies the team have the appropriate qualifications to execute their roles and responsibilities, Verifies that all appropriate training on the part of the clinical trial staff

	has been completed and documented Verifies that protocol training has been completed by all team members Verifies that all clinical trial team members have read the clinical investigational brochure Verifies that all clinical research records have been stored in accordance with good clinical practice requirements
Senior Level Professional	At the completion of the trial ensures that the trial has been completed in compliance with good clinical practice regulations and all institutional requirements At the completion of the clinical trial ensures that all trial documentation has been appropriately retain At the completion of the clinical trial ensures that all relevant parties have been informed of the trial outcomes, both in terms of safety and efficacy

R. Management of data generated in a clinical trial

RB-1 Management of data generated in a clinical trial; analysis and reporting	
Utilization of case report forms to collect manage and manage data generated during the execution of a clinical trial	
Early Level Professional	Verifies that documents are compliant with standards and best practices when collecting, capturing, managing, analyzing and reporting data during clinical research process
Mid Level Professional	Verifies that the reporting of clinical trial information is carried out by the principal investigator of the clinical trial, as well as the study sponsor. Verifies that the data is reported to the appropriate oversight bodies, including the IRB as well as local and global regulators were appropriate Verifies that the appropriate study personnel are involved in the collection and handling of all study data Ensures that highly qualified statisticians are engaged in the analysis and reporting of the data generated during the conduct of the clinical trial Ensure that the study protocol include a description of appropriate statistical methods Verify that the statistical methodology mentioned in the study protocol are utilized in the analysis and reporting of the data
Senior Level Professional	
RB-2 Management of data generated during the execution of a clinical trial	
Collection and management of data collected during the course of a clinical trial	
Early Level Professional	Verifies and categorizes data sources contributing to a clinical study and understands appropriate industry standards used in data handling Explains origin and flow of data from clinical trial protocol to case

	report forms to the clinical study report
Mid Level Professional	Organizes data Verifies that all data is captured in the case report form accurately Verifies that all data are reported accurately and are legible as well as attributable Ensures, appropriate verification of data occurs prior to data analysis, Ensures that all data, integrity, policies, and procedures are in place and followed Verifies that all data is being stored according to GCP standards, local policies, and procedures Verifies that data is being retained for the required storage Ensures data is being retained in appropriate storage facilities to prevent theft, fire, or water damage
Senior Level Professional	Implements QA Analyzes data using appropriate statistics Interprets and uses data to make informed decisions
RB-3 The role of quality assurance in the management of clinical trial data	
Early Level Professional	Ensure that there is a quality assurance in monitoring group to oversee data quality Ensure that quality assurance is checking to make sure that data is accurate, legible, attributable, original ,complete, and contemporaneous Ensures that data is verifiable Ensures that data is recorded appropriately on the case report forms
Mid Level Professional	Verifies compliance with data quality related SOPs Verify is that the appropriate SOPs are in place that govern data capture in quality Verifies that staff have been trained on the SOPs governing data capture Verifies that staff are appropriately following their training on data capture
Senior Level Professional	Brings any issues related to the data integrity to the attention of appropriate personnel, for example, chief clinical investigator, institutional review board Works with chief clinical investigator to ensure any data quality issues are appropriately managed
RB-4 The utilization of informatics and statistics in the analysis of clinical trial data	

Employing statistics and informatics in the analysis of data generated during the execution of a clinical trial	
Early Level Professional	Verifies collectable data relevant to statistical study in clinical studies
Mid Level Professional	Works with the statistician to ensure a robust statistical plan to analyze the data from the clinical trial is in place prior to the start of the clinical trial Verifies the necessary data is called for in the study protocol Verifies that the necessary data for the statistical plan is captured in the case report forms Ensures that methods employed in the conduct of the clinical trial, such as randomization, stratification, or crossover design is appropriately executed and documented Verifies that the appropriate statistical methods have been utilized to analyze study data Ensures that the data used in statistical analysis has been reviewed, cleaned, and verified prior to statistical analysis Works with the statistician to ensure an adequate number of subjects are utilized to achieve statistical significance Ensures that the proper statistical analysis is included in the final study report
Senior Level Professional	

S. RC-1 The review of safety and efficacy data generated during the conduct of a clinical trial: Reviewing the safety and efficacy data utilized in an application for marketing authorization and post approval changes ensuring its integrity and quality

Early Level Professional	Reviews applications to assess safety and efficacy
Mid Level Professional	Evaluates clinical trial data to be utilized in regulatory submissions to ensure its accuracy and completeness Evaluates pharmacokinetics, biosimilarity, in vitro and in vivo studies with different end points Reviews proposed vaccine and biologics labels to determine whether they contain truthful claims about the product's effectiveness, appropriate warnings and precautions about the product's safety, and adequate directions for the product's use Reviews risk management plans Plans and coordinates the submissions and review process Reviews a broad range of application types as a first or primary reviewer Evaluates clinical data (safety and efficacy) for clinical trials or for

	marketing authorization for simpler molecules
Senior Level Professional	Leads the analysis and evaluation of submitted data in specific disciplines/specialty area Evaluates the impact of vaccines and biologics on clinical practice and public health Assesses applications within their field to understand a range of issues, both unique and complex, to ensure product and regulatory compliance Evaluates clinical data (safety and efficacy) for clinical trials or for marketing authorization for all types (complexity) of products Evaluates data on product quality for all types (complexity) of applications for clinical trials or marketing authorization

T. Design of clinical trial protocols

RD-1 Clinical trial data analysis	
Analysis of the result generated during the conduct of a clinical trial	
Early Level Professional	Ensures that the data to be utilized in the statistical analysis process is accurate
Mid Level Professional	Analyzes of clinical trial results Ensures that the data to be utilized in the statistical analysis is accurate and has been verified Ensures that the data has been properly documented in the case report forms Ensures the appropriate maintenance of randomization-codes and trial blinding Ensures that appropriate procedures are in place for unwinding in the case of medical emergencies. Ensures that there's full documentation, filing on blading in the case of a medical emergency Works with the investigator to make sure that safety reporting is done in conformance with all appropriate procedures Recognizes the importance of reporting all adverse events in a timely fashion Gives special attention to ensuring that serious and unexpected events are reported to sponsor, IRB and regulatory authorities as required
Senior Level Professional	Relates the study results to the study questions and purpose
RD-2 Design of the clinical trial protocol	
Design of the clinical trial protocol in conformance with good clinical practices	
Early Level Professional	Verifies that the elements and correct principles and processes underpin the design of a clinical study
Mid Level Professional	Determines types of testing to conduct during the design and premarket

	stage, and appropriate regulatory pathway Participates in the design of the clinical trial protocol to ensure good clinical practices are followed Ensures that the protocol is followed during the execution of the clinical trial Ensures that the clinical staff has been trained in the clinical trial protocol Ensures that protocol training has been appropriately documented Ensures a good alignment between the clinical trial protocol, and the case report forms Ensures that the clinical trial protocol has been reviewed and approved by the appropriate authorities Ensures that the appropriate information as required under GCP's has been captured in the protocol (e.g., protocol's title name, address of sponsor name, address of monitor name, and address of responsible parties) Ensures that the appropriate inclusion and exclusion criteria are contained within the protocol Ensure that withdrawal criteria are contained in the clinical study protocol Ensures the protocol describes how efficacy in safety will be assessed Ensures the protocol captures the statistical methods Ensures that the protocol describes how data will be handled and how the records will be retained over time Ensures there is a description of the quality control in the quality assurance procedures that will be used to maintain quality during the conduct of the trial
Senior Level Professional	
RD-3 Application of biomedical science to a clinical trial protocol	
Ensures that the principles of biomedical science are appropriately applied to drug development protocols	
Early Level Professional	Applies scientific principles to discovery and development of investigational products
Mid Level Professional	Ensures that sound scientific principles are applied to the design, an execution of the clinical trials Ensures that sound scientific principles are followed during the design, an execution of the clinical trials

	Ensures that sound scientific principles are utilized in case study report forms, as well as statistical analysis, plan, Ensures that sounds scientific principles are utilized in the analysis and reporting of data Ensures the final study report documents, the adherence to principles of scientific writing
Senior Level Professional	
RD-4 The hypothesis to be tested during the conduct of the clinical trial	
Highlight the scientific questions that are to be tested during the execution of the clinical trial in an effort to substantiate the research hypotheses	
Early Level Professional	Formulates the research question
Mid Level Professional	Ensures that the clinical trial protocol clearly states the research hypothesis to be tested Ensures that the hypothesis being tested, provides appropriate justification for the clinical trial Ensures that the hypothesis tested will provide adequate data on whether the outcome of the clinical trial is positive or negative Ensures that the clinical research protocol adequately formulate the research question
Senior Level Professional	

U. Safety of clinical trial participants: Ensuring patient safety throughout the execution of a clinical trial

RE-1 Protection of the clinical trial participants during the conduct of the study	
Utilization of international and national regulations to ensure the safety and protection of human subjects, throughout the execution of the clinical development plan	
Early Level Professional	Verifies that national and international principles of Subject safety and ethical considerations including care, protection are maintained throughout the study
Mid Level Professional	Works with the clinical trial investigator to and IRB ensure ethical principles are adhere to during the recruiting and treatment of clinical research participants Ensures that all clinical trials staff has been appropriately trained in the ethical principles of conducting clinical research, including the Nuremberg code, declaration of Helsinki, Belmont report, and all relevant standards Ensures that the seven main principles of conducting ethical research adhere to including social and scientific values, scientific validity, fair subject selection, favorable risk benefit ratio, independent review, informed consent, and respect for potential and enrolled patients Identifies, and applies ethical issues and implications for research Applies relevant national and international principles of human subject

	protections and privacy throughout all stages of clinical study Compares the requirement for human subject protection and privacy under different national and international regulations Ensures implementation of appropriate throughout all phases of a clinical development
Senior Level Professional	Describes the ethical issues involved when dealing with vulnerable populations Ensures that additional safeguards are in place for vulnerable populations
RE-2 Risk benefit analysis	
Analysis of the risk benefit ratio through the selection and management of clinical trial subjects	
Early Level Professional	Recognizes the risks and benefits for a clinical trial with a given investigational drug product Ensures that trial participants understand the risk benefit ratio
Mid Level Professional	Applies risk benefit methodology in the selection of clinical trials subjects
Senior Level Professional	Approves the methodology utilized in balancing risk versus benefits Provides organization with training on risk detection, and risk mitigation in the conduct of clinical trials Ensures the organization, including the management, team or appropriately, trained in the concepts of risk identification, risk prioritization, and risk mitigation
RE-3 Utilizing the concepts of clinical equipoise and the therapeutic misconception during the management of a clinical trial	
Ensuring the protection and safety of human subjects during the execution of a clinical study	
Early Level Professional	Recognizes the concepts of clinical equipoise and therapeutic misconception in clinical studies
Mid Level Professional	Reviews and ensures that the concept of clinical equipoise is applied to guarantee safety of patients and avoid therapeutic misconception
Senior Level Professional	Participates in the design and execution of training programs for the clinical trial staff around the principles of clinical equipoise and therapeutic misconception Ensures that appropriate training on these topics is delivered to the staff and documented Approves the reviews of clinical equipoise and therapeutical misconception on patient safety
RE-4 Clinical trial inclusion and exclusion criteria	
Establishing inclusion and exclusion criteria for a clinical trial protocol to ensure human subject protection	
Early Level Professional	Ensures the appropriate application of inclusion criteria, as well as exclusion criteria in the clinical trial protocol

	Ensures that the inclusion and exclusion criteria captured in the clinical trial all right here to inpatient selection Ensures that the inclusion and exclusion criteria captured in the clinical trial protocol are adequate to ensure patient safety
Mid Level Professional	Ensures that clinical trial staff are appropriately train on the inclusion and exclusion criteria capture in the protocol Ensures that the inclusion and exclusion criteria were carefully follow during the execution of the clinical trial Determines that the appropriate inclusion, exclusion, and other criteria are included in a clinical protocol to ensure subject protection
Senior Level Professional	Reviews and approves the inclusion and exclusion criteria included in the clinical trial protocol Ensures that the clinical trial protocol inclusion and exclusion, criteria are appropriate for patient protection Ensures that the inclusion and exclusion criteria are based upon sound medical rationale Ensures that the rationale for the inclusion and exclusion criteria included in the clinical trial protocol have been documented and thoroughly reviewed by the medical team
RE-5 Application of ethical and cultural considerations to the commercial aspects of clinical trial research	
The application of ethical and cultural considerations to the commercial aspects of clinical trial research during the drug development process	
Early Level Professional	Highlights all cultural and ethical considerations relating to commercial aspect of the dossiers Screens the dossiers according to regulation and policies related to cultural and ethical issues relating to commercial aspects Proposes suggestions to be moved further to the mid level and senior level reviewers
Mid Level Professional	Reviews the highlighted cultural and ethical issues that are related to the commercial aspect of the vaccines and biologics Ensure alignment throughout the dossiers and evoke discussions around the cultural and ethical considerations that could be presented to the Level III reviewer
Senior Level Professional	Ensures that answering the key questions in the clinical trial protocol are sufficiently important to justify exposing subjects to the risk of the trial Answers to the research questions being asked in the protocol should contribute to the scientific understanding of human health Ensure that the key scientific questions being answered are useful for the

	prevention, treatment or curing of disease Ensure that society will gain useful information to justify, exposing human subjects to risk, as well as the burden of the study conduct
RE-6 The application of the principles of informed consent	
Understanding the key principles of informed consent, their origin, as well as their application in the conduct of a clinical study	
Early Level Professional	Screens the elements and principles of the Informed consent in the submitted applications for appropriateness, and completeness; (IC)
Mid Level Professional	Reviews the informed consent document to ensure that is compliant with all appropriate regulations and guidelines Reviews that the issues of risk-benefit disclosure during the process of consent are discussed Reviews and ensures that the contents of the IC align with the information in other sections of the dossiers
Senior Level Professional	Ensures that the contents of the IC align with the information in other sections of the dossiers Ensures that individuals are not coerced into participation in the research Ensures that the informed consent document contains the purpose, methods, risk, benefits, and alternatives to the trial Ensures that the informed consent document communicates how the clinical research protocol relates to a subject's clinical situation Ensures that the informed consent document has been reviewed and approved by the appropriate institutional review board Ensures that the staff has been appropriately trained on the informed consent document Ensure the records of informed consent are appropriately stored and archived
RE-7 The protection of vulnerable patient populations during the conduct of clinical research	
Establishing the appropriate ethical standards and safeguards for vulnerable patient populations	
Early Level Professional	Verifies the various safeguards for vulnerable populations are in place Screens the dossiers for completeness of safeguards elements for vulnerable populations Ensures that the clinical trial staff has been trained on how to recognize vulnerable subjects Ensure that the clinical trial staff identifies individuals whose willingness to participate in the clinical trial may be unduly influenced by expectations of benefits associated with participation
Mid Level Professional	Ensure that the types of the various safeguards proposed for the

	vulnerable populations are appropriate
Senior Level Professional	Works with vulnerable patient populations to enable them to make the best decisions possible on participation in a clinical trial Understands the particular situation that impacts the engagement and vulnerable patients in clinical trials Ensures that the types of the various safeguards proposed for the vulnerable populations are appropriate Ensures that the information on the safeguards for the vulnerable population is aligned to the different sections of the quality and bioequivalence sections

V. RF 1 Quality Management System: Consideration of techniques for monitoring and improving quality functions, processes, and products

Early Level Professional	Ensures that the organization has a robust quality management system in place Ensures that the quality management system is kept current with evolving standards of good clinical practices, good laboratory practices, good manufacturing processes, as well as good Pharmacovigilant practices Ensures that a robust training plan is in place throughout the organization Ensures that training on the quality system is documented Conducts routine assessments of the quality system Drives improvements in the quality system based upon ongoing assessments of its effectiveness
Mid Level Professional	Ensures that the quality standards articulated in the quality system are followed during the execution of clinical trials, Works with clinical trial teams as they address quality issues encountered in conduct of going clinical studies
Senior Level Professional	Maintains a quality improvement plan for the organization Ensures that senior management is supportive and committed to supporting the quality system Ensures that the quality plan has identifies the major quality issues in the organization and has appropriate remediation plans in place Ensure the quality activities throughout the organization are appropriately resourced with the correct number of people having the appropriate expertise Ensures that quality remediation plans are executed in a timely and thorough fashion

	Ensures that the organization is in a constant state of compliance with all appropriate regulatory standards and guidelines, including but not limited to good laboratory practices, good, clinical practices, good manufacturing practices and good Pharmacovigilant practices Conducts routine assessments of the quality management system and drives necessary improvements

W. RG-1 Review of Risk Management: Risk management processes and procedures utilized throughout the conduct of a clinical trial

Early Level Professional	Ensures that the organization conducting the clinical trial has the appropriate risk management, policies, and procedures in place Ensures that the organization conducting the clinical trial follows there, risk management, policies, and procedures in the execution of a clinical trial
Mid Level Professional	Engages in the organizations development of risk management, policies, and procedures Ensures, the staff is trained on risk management, policies and procedures Ensures that risk management training is documented and kept current Monitors trial risk on an ongoing basis ensures that newly identified risks are appropriately captured in risk benefit ratios Monitors the effectiveness of risk management process and procedure
Senior Level Professional	Engages in the development and management of a risk management system Ensure that the organization is constantly scanning for potential new risks Ensures that were possible risk mitigation plans exist for identified risks Ensures that business continuity plan exist where there is appreciable risk to the organization, and therefore the conduct of the clinical trial Communicates relevant risk broadly throughout the organization

X. Development of regulatory documents

RH-1 Development of regulatory documents	
Early Level Professional	Develops basic documents based on review Utilizes appropriate software Communicates with peers and clients Develops communications Applies appropriate guidelines to documents

Mid Level Professional	Addresses various problems with both scientific and regulatory documents Addresses stakeholder needs Knows best way to communicate regulatory conclusions with peers and stakeholders
Senior Level Professional	Develops complete, effective communication strategies Able to host a conference Utilizes best practices for communication strategies Works with junior staff to develop appropriate regulatory documents Formulating special considerations required for studies in vulnerable populations
RH-2 Utilization of standard of care in the study of an investigational product	
Early Level Professional	Demonstrates understanding of the difference between the Standard of Care and Clinical Trial of the drugs presented Screens dossiers according to existing regulations
Mid Level Professional	Determines that the appropriate Standard of Care is proposed for the Clinical Trials Assesses that there is an alignment throughout the dossiers with respect to the Standard of Care and Clinical trials
Senior Level Professional	Makes correct judgement that the appropriate Standard of Care vs. Clinical Trials are proposed Guides and trains early and mid level professionals

Y. Utilization of investigational drug product in a clinical study: Rules and regulations governing the use of investigational drug product during the execution of a clinical trial

RI-1 The global aspects of vaccine/biological drug development and approvals	
The regulations that apply to the development and approval of new therapeutics developed globally	
Early Level Professional	Appraises the regulatory issues related to the increase in regulations of vaccines and biologicals
Mid Level Professional	Utilizes best practices to develop polices and regulations for vaccines and biologicals
Senior Level Professional	Develops strategies for allowing growth of the utilization of curative biologicals and vaccines
RI-2 Historical considerations in the development of global regulatory environment	
The role of key historical events in the formulation of global regulations governing the development of new pharmaceuticals	
Early Level Professional	Organizes and manages registration, renewal of vaccines and biologics preparations (human and veterinary) Reviews promotional and advertising documents of vaccines and biologics

	Inspects pharmaceutical manufacturing facilities Assesses the safety, efficacy and biologicals and vaccines Issues marketing authorization Monitors vaccine and biologics marketed products to assure compliance with regulations Manages all regulatory aspects for vaccines and biologics preparations Reviews approaches to tracking of biologics and vaccines to reduce fraud
Mid Level Professional	Develops approaches to increase collaboration among regulators Supports policies that ensure a secure supply of good-quality vaccines and biologics, including vaccines and biologics Mutual recognition of legal framework and regional operationalization of the regulation of vaccine and biologicals
Senior Level Professional	Contributes to polices that increase the growth of the pharmaceutical industry in the home country Contributes to a country-wide vaccines and biologicals policy Review and encourage updating of policies for vaccines and biologicals
RI-3 Key processes for gaining marketing approval	
The phases of drug development that must be executed in order to gain regulatory approval to market a new vaccine or biologic	
Early Level Professional	Reviews and assists applicants with preclinical and clinical applications and authorization applications
Mid Level Professional	Reviews and assists applicants with regulatory submission (e.g., IND, BLA, NDA) Reviews and assists applicants with filing IND and NDA applications
Senior Level Professional	
RI-4 Establishment of roles and responsibilities for institutions participating in clinical trials	
Institutional roles and responsibilities during the development of an investigational drug product	
Early Level Professional	Reviews and identifies responsibilities of applicants including CROs and companies
Mid Level Professional	Reviews and assists stakeholders to determine roles and responsibilities of all persons involved in biologicals development and testing
Senior Level Professional	Develops country-wide approaches to encourage clinical trials and development of new biologicals and vaccines
RI-5 Reporting safety concerns	
Detailed knowledge of the regulations governing the development of vaccines and biological products	
Early Level Professional	Reviews documents according to the guidelines for safety reporting requirements, the adverse events
Mid Level Professional	Reviews the adverse event reports and other safety related documents
Senior Level Professional	Judges appropriateness of safety data

	Approves the assessment and interpretation of data on safety of products

Z. RJ-1 Approved therapeutic products; maintenance of their approval and registration status: management of the regulatory processes that govern approved drug products including periodic reviews, regulatory actions, or withdrawals due to noncompliance

Early Level Professional	Reviews the approved product register and ensuring it is up to date
Mid Level Professional	
Senior Level Professional	Determines various policies and contribute to enhancement as well as maintenance of approved product register

AA. RK-1 Information contained on the product label and in package insert

Early Level Professional	Sets basic labelling requirements of Health Products & Technologies in relation to vaccines and other biologics Compares the product labelling vice versa innovator product
Mid Level Professional	
Senior Level Professional	

BB. RL-1 Drug Product Quality

Early Level Professional	Ensures the basic structures of the product quality sections are in place Reviews safety data on Active Substance and Medical Product Reviews the nonclinical aspects and toxicology and assures safety of the drug product
Mid Level Professional	Reviews active substance data against ICH guidances Verifies sameness of Active Substance to reference standard if scientifically relevant Reviews physical, chemical, and biological properties of Active Substance Ensures the Active Substance Critical Quality Attributes meet specifications Reviews method of manufacture of Active Drug Substance and the ability of this procedure to meet critical quality attributes if appropriate Reviews defined Critical Quality Attributes and Certificate of Analysis of Active Substance and verifies their completeness and acceptability including identity, purity, potency, and sterility Review controls of Active Substance to ensure their completeness Review procedures for lot release of Active Substance including the adequacy of the Certificate of Analysis Reviews procedures for providing samples of Active Substance to regulatory agency for independent testing

Senior Level Professional	Reviews Development report on Active Substance and Finished Medical Product – ensures quality Makes recommendations for future quality development Reviews development report of Finished Medicinal Products and assesses its fitness for purpose Reviews how Active Medicinal Ingredient and excipients and adjuvants are incorporated into Finished Medicinal Product and how they combine to contribute to the safety, efficacy, and stability of the drug product Assures that all Critical Quality Attributes of the drug product are identified and assessed in the specifications as appropriate, Reviews manufacturing methods, data, and controls to ensure lot to lot consistency Reviews the analytical methods for drug substance and drug product and makes sure they are fit for purpose Reviews how the sterility of the Finished Medicinal Product is assured Reviews comparability protocols showing equivalence of Finished Drug Product and Active Drug Substance used in previously approved vaccines or biologicals anywhere in the world Reviews defined Critical Quality Attributes, Certificate of Analysis of Finished Medicinal Product and verifies their completeness and acceptability including identity, purity, potency, and sterility prior to release of each lot Reviews procedures for providing samples of Finished Medicinal Product to regulatory agency for independent testing Reviews submitted procedures for monitoring of safety signals on marketed vaccines looking for known and unknown safety risk; also reviews adequacy of these procedures Collaborates with inspectors to ensure adequate process facilities, manufacturing equipment, warehousing, labeling equipment, and all other equipment is adequate and properly controlled and maintained Collaborates with inspectors to ensure the supply chain system and procedures are adequate and ensure product quality until the product reaches the patient

CC. Decision making on regulatory matters: regulatory decision making on matters related to documentation, inspections, and laboratory testing

RM-1 Making regulatory decisions
The ability to make and execute regulatory decision

Early Level Professional	Holds a degree in a relevant scientific field, such as pharmacology or toxicology, as well as experience in regulatory affairs and knowledge of relevant regulations and guidelines Evaluates the safety, quality, and effectiveness of products in accordance with regulatory guidelines and standards
Mid Level Professional	Ensures regulatory reviewer competency, regulatory agencies often have specific requirements for the education, training, and experience of regulatory reviewers Understands of the science and technology underlying the product, as well as the regulatory framework in which it operates Critically evaluates scientific data, assess risk, and communicate their findings and recommendations effectively
Senior Level Professional	Weighs the benefits and risks of a product and make informed decisions that balance the interests of public health and safety with the needs of industry Ensures that products that are approved for use are safe, effective, and of high quality, and that regulatory decisions are made in a transparent, consistent, and scientifically rigorous manner

DD. RN-1 Reliance strategy: Able to assess other regulatory authority

Early Level Professional	Assesses submitted applications using reports and results obtained by another regulatory authority, typically in another jurisdiction, to inform its own decision-making process, based on agreed upon reliance strategies and procedures
Mid Level Professional	Applies the regulatory framework of both the relying on and receiving jurisdictions, as well as the scientific and technical issues involved in the assessment
Senior Level Professional	Evaluates and judge the suitability of reliance strategies

EE. RO-1 Training: Able to evaluate training materials and train others

Early Level Professional	Evaluates the effectiveness of the training provided to healthcare professionals (HCPs) who will be administering the product
Mid Level Professional	Understands of the regulatory requirements for training, as well as the scientific and clinical principles behind the product being evaluated Can critically evaluate the training materials to determine whether they are comprehensive, accurate, and effective
Senior Level Professional	Possesses excellent communication and analytical skills, as well as the ability to work collaboratively with industry representatives and other stakeholders

FF. RP-1 Capacity building: Able to evaluate training materials and train others

Early Level Professional	Evaluates an organization's capacity to comply with regulatory requirements. This may involve reviewing training programs, assessing the expertise of staff, and evaluating the effectiveness of policies and procedures
Mid Level Professional	Promotes effective capacity building experts

	Develops and delivers training programs that are tailored to the specific needs of the organization
Senior Level Professional	Promotes regulatory compliance and improving the overall performance of regulated organizations. As a regulatory reviewer, it is important to prioritize capacity building efforts and work collaboratively with stakeholders to ensure that individuals and organizations have the necessary knowledge and skills to meet regulatory requirements

V. Inspectors

Q. I-A Inspects data integrity and all other data acquisition and data processing activities

Early Level Professional	Screens documentation using the principles of data integrity "ALCOA+". before and during an inspection at sites Maintains accurate and objective records of facts and observations made during audits/inspections
Mid-Level Professional	Ensures that accurate and objective records of facts and observation are made and maintained during audits and inspections Reviews the processes and records of clinical research during audits/inspections
Senior Level Professional	Ensures provision of resources for storage of records of facts and observations made during audits/inspections Verifies and approves the manufacturer's policies, practices, and procedures for data lifecycle management Verifies and approves interoperability where there are heterogeneous information systems Verifies and approves that technical data validation of the Enterprise Resource Planning (ERP) System is based on the data in the Marketing Authorization

R. I-B Documentation inspection activities

Early Level Professional	Reviews all documents including licensing applications and all other documents including biologicals related documents Uses checklists and guidelines to screen submitted applications
Mid-Level Professional	Serves as second reviewer for all documents including licensing applications and all other documents including biologicals related documents
Senior Level Professional	Approves the discussion points and recommendations made for improvement Establish a risk-based approach for selection of facilities to be inspected from outcome of review of submitted documentation by manufacturers

S. I-C Review of manufacturing records as part of lot release: Reviews all data, documents, and batch records related to batch release. Reviews all data from contract laboratories and regulatory agencies

Early Level Professional	Understands the principles and reasons for Specifications Understands ICH Q5E (Especially Comparability protocols) Understands of the product and laboratory control methods Understands of vaccines and biologics manufacturing processes and control methods Understands of the Standard Operating Procedures (SOPs) for summary protocol review
Mid-Level Professional	Applies the knowledge of the principles of ICH Q6B (Title: Specifications: Test Procedures and Acceptance Criteria for Biotechnological/Biological Product) during inspection Applies the knowledge of the principles of ICH Q5E (Title: Comparability of biotechnological/biological products subject to changes in the manufacturing process) during inspection Understands the components of Lot Release Protocols Applies the knowledge of vaccines and biologics manufacturing processes and control methods during inspection Reviews quality attributes (identity, potency, purity, concentration, and particle size) in the analytical assays as applicable to the type of vaccine (inactivated, attenuated, subunit, DNA, mRNA, viral vector and VLP vaccines) Reviews the compendial test results (appearance, pH, osmolality/osmolarity, container closure integrity, container content for injections, sterility, bacterial endotoxins) for compliance with standards Reviews SOPs for summary protocol to assess compliance of the lot/batch with specification and MA Reviews of manufacturer's summary protocol to confirm compliance with specifications defined in the marketing authorization dossier Verifies compliance to the specifications Verifies security of databases used to capture information for a particular test or section of the protocol Documents and verifies any discrepancies, errors or OOS results found in the summary protocol submitted Evaluates National Control Laboratory (NCL) test results when independent testing is carried out as part of lot release for vaccines and biologics

	Uses all critical quantitative data from quality-control test results, especially potency test results from the manufacturer or other sources to perform trend analysis as an essential part of lot release
Senior Level Professional	Establishes of a quality management system (QMS) to support lot release of vaccines and biologics Relies on other regulatory agencies' lot release process Develops Checklist for summary protocol review Contributes to the establishment of procedure for selection of lots of vaccines/biologics for independent testing as part of lot release Establishes criteria for selection of tests for lots for independent testing of vaccines/biologics and percentage of lots to be tested Develops procedure for review of summary protocol that describes the acceptance criteria for completeness Develops SOP for tracking and trending of manufacturers' and, where available, the NCL's results Coordinates trending and analyses of all data from independent testing of lots performed at the NCL, including performance of reference standards and controls Compares of results from the NCL with those of the manufacturers to inform regulatory decisions

T. I-D Established quality system for inspectorate function

Early Level Professional	Develops quality manual for inspectorate system Addresses audits and inspections
Mid-Level Professional	Implements requirements for clean rooms, controlled environments, and activities within clean rooms as per ISO 14644-1:-2015 are maintained Verifies adequacy of cold chain and cold chain monitoring Verifies temperature equipment used in monitoring vaccine storage for adequacy and utilization
Senior Level Professional	Coordinates inspection activities Oversees the maintenance of information repositories Leads the implementation risk-related inspections Plans and allocates resources Coordinates the scheduling and conduct, as lead, of GLP,GCP and GMP inspections for vaccines and biologics

	o Confirms that the vaccines comply with market authorization o Provides support for other relevant activities of the vaccine's assessment and inspection teams

U. I-E Development of technical regulatory documents

Early Level Professional	Awareness and understanding of the regulatory frameworks, guidelines, standard operating procedures (SOPs) and tools for regulation of vaccines and biologics Develops draft regulatory frameworks, guidelines, standard operating procedures (SOPs) and tools for regulation of vaccines and biologics Awareness of stakeholders and key players involved in the development, manufacture, distribution and regulation of vaccines and biologics
Mid-Level Professional	Reviews and validates the draft regulatory frameworks, guidelines, standard operating procedures (SOPs) and tools for regulation of vaccines and biologics Develops Verifies standard operating procedures for vaccines/biologics storage are adequate and followed Ensures reports and records of regulatory functions are in line with the Quality Management Systems Contributes to updating the regulatory frameworks, guidelines, standard operating procedures (SOPs) and tools for regulation of vaccines and biologics in line with emerging issues Contributes to the development of information portal for the regulatory frameworks, guidelines, standard operating procedures (SOPs) and tools for regulation of vaccines and biologics for public use
Senior Level Professional	Approves regulatory frameworks, guidelines, standard operating procedures (SOPs) and tools for regulation of vaccines and biologics Ensures implementation and adherence to the regulatory frameworks, guidelines, standard operating procedures (SOPs) and tools for regulation of vaccines and biologics Ensures that all required documentation is present for imported vaccines Assists in developing CAPA and SOPs for the regulation of vaccines

V. I-F Carries audits and inspections based on current ICH and ISO quality guidelines

IF-1 Inspections based on good clinical practices guidelines	
Early Level Professional	Understands basic legal and administrative aspects of clinical trials (GCP) inspections for vaccines and biologics Assesses applications for GCP inspection for vaccine and biologics by clinical research organizations performing clinical studies

	Performs GCP inspections as an observer
Mid-Level Professional	Assesses the authorization of clinical trials and modifications Ensures trials safety reporting is carried out according to GCP principles Performs inspection of clinical studies to assess compliance with GCP requirements Reviews documentations for clinical evaluation of vaccine especially for assurance of immunogenicity, efficacy and effectiveness, and safety in compliance with GCP Reviews all documents related to clinical studies
Senior Level Professional	Evaluates quality systems of the clinical trial for vaccines and biologics Coordinates inspections of approved facilities for compliance over time Evaluates the risks/ impact of facility non-compliances or deviations on clinical practice and public health Leads the GCP inspection for vaccines and biologics Approves of GCP inspection reports and certification of approved Distributors after review of CAPA
IF-2 Inspections based on GDP guidances	
Early Level Professional	Assesses applications for GCP inspection for vaccine and biologics by distributors/wholesalers Understands of how to read and interpret vaccine vial monitor device Performs GDP inspections as an observer Understands national and international guidelines on GDP for vaccines and biologics
Mid-Level Professional	Assesses compliance with Good Storage and distribution practices (GSP & GDP) including personnel, premises, equipment, environment, documentation, distribution systems, transport and handling systems and recommend for certification for GDP compliance
Senior Level Professional	Identifies potential risks at each segment of cold chain, using risk-based approach to analyze them and designing control strategies to mitigate the risks Applies legal and regulatory frameworks to assess compliance to import, export and shipments of vaccines at regional and national level Approves GDP inspection reports and certification of approved distributors after review of CAPA
IF-3 Inspections based on guidances for good laboratory practices	
Early Level Professional	Understands national and international guidelines on GLP for vaccines

	and biologics Assesses applications for GCP inspection for vaccine and biologics by laboratories in non-clinical research and drug development and bioanalytical laboratories Performs GLP inspections as an observer
Mid-Level Professional	Inspects facilities, personnel, study animals' management, study protocols, SOPs, test drug product, data collection, documentation of results and quality assurance Reviews documentations for non-clinical evaluation of vaccine including assessment of all CQAs and compliance with GLP
Senior Level Professional	Leads GLP inspections of drug development research laboratories for vaccines and biologics and bioanalytical laboratories Assesses performance of bioanalytical laboratories based on regulatory requirements Verifies accreditation/ certification of bioanalytical laboratories to regional and international certifying bodies Identifies data integrity breeches in laboratory documents/records and risks associated with generation of results in the laboratories Approves GLP inspection reports and certification of approved laboratories after review of CAPA
IF-4 Inspections based on guidance for good manufacturing practices	
Early Level Professional	Assures all GMP requirements are met Understands national and international guidelines on GMP for vaccines and biologics Assesses applications for inspection of biologics active substances and finished products
Mid-Level Professional	Identifies GMP deficiencies and evaluating risk of the deficiency to the patient Understands of legislation on vaccines and biologics licensing and inspection of manufacturers, importers, retailers/pharmacies, healthcare facility dispensaries Applies sanctions for violation of drug legislation Performs all types of inspections such as routine, investigative, random inspections for vaccine and biologics
Senior Level Professional	Evaluates quality risk management plan of vaccines and biologics manufacturing plants, control strategy to minimize variability and preventive measures to avoid contamination and cross-contamination Evaluates purification and filtration techniques for vaccines and biologics and its impact to finished product

	Monitors approved vaccines and biologics manufacturing facilities to ensure their continued compliance to GMP requirements Identifies non-compliances or deviations, evaluating their impact, and issuing regulatory actions Applies regulatory actions (issue, vary, suspend, or withdraw licenses) for vaccines and other biologic products Oversees the quality of the vaccines and biologics

W. I-G Product Quality: inspects for all aspects related to product quality including vaccine starting materials, cell banks, and intermediates as applicable

Early Level Professional	Evaluates biosafety requirements and procedures for vaccine and biological manufacturing as governed by different regulatory bodies Reviews all requirements related to biomanufacturing equipment and facilities Reviews all QC and QA methods used
Mid-Level Professional	Identifies manufacturing procedures of vaccines and biologics including mRNA technology Analyzes bioanalytical techniques and assessing variability and its impact to product quality and consistency Evaluates control strategy for environmental contamination levels for high risk products or intermediates Interprets stability data of reference samples or retention samples of biological starting materials and finished products Determines if microbiological tests (sterility tests or purity checks) verify lack of contamination Determines if the vaccines and biologics manufacturer have traceability plan for proper use and storage of reference standards and that reference standards are stable through their shelf life. Determines if vaccine and biological manufacturer have sufficient knowledge about stability studies. Verifies lot-to-lots consistence of biological products and vaccines and reviews Comparability Protocols. Determines appropriateness of a given container closure system to maintain product integrity under the different storage conditions
Senior Level Professional	Evaluates pharmaceutical quality system (PQS) of vaccines and biologics Assesses quality risk management plans and control strategy

	Analyzes bioburden and endotoxin control measures in entire aseptic manufacturing process (e.g., Water sources, sterilization of final product) Predicts the potential quality issues given the characteristics of the starting materials and finished products Assesses the analytical methods meet all applicable ICH requirements

X. I-H Supervision of vaccine disposal and destruction: Applies scientific biosafety regulatory and environmental requirements to ensure proper collection, management and disposal of vaccines and vaccination waste

Early Level Professional	Assesses application of national policy, regulations, and procedures for the disposal of expired, substandard, and poorly stored vaccines Assesses application of national policies, regulations, and procedures for disposal of equipment used for vaccination including used vials, ampoules or syringes placed in a proper, puncture-resistant "sharps" box
Mid-Level Professional	Evaluates the implementation of the national policy, regulations, and procedures for the disposal of expired, substandard, and poorly stored vaccines along the supply chain Evaluates the implementation of the national policies, regulations, and procedures for disposal of equipment used for vaccination including used vials, ampoules or syringes placed in a proper, puncture-resistant "sharps" box Applies the acceptance/rejection criteria for vaccines lot release from the manufacturer/Health Authority in determining vaccines for disposal/destruction Determines if the vaccination sites have knowledge on management and disposal of unused vaccine (e.g., expired or spoiled), used syringes and needles, packaging materials & non-hazardous waste, personal protective equipment (PPE) and other wastes Determines if the vaccination site applies policies and procedures for waste segregation and collection
Senior Level Professional	Evaluates performance of the vaccination site on vaccination waste management including timely and proper packing, marking, storage and treatment/disposal of vaccines, vials/ampoules, sharps, and non-sharps waste Trains of staff at vaccination sites on disposal of unused vaccine (expired or spoiled) Conducts surveillance and inspection of disposal sites for unused, expired and substandard vaccines, used vaccines vials/ampoules, packaging/labelling materials to ensure adherence to the regulatory guidelines Leads inspection of documentation and records of disposed unused,

	expired, and substandard vaccines, used vaccines vials/ampoules, packaging/labelling materials, syringes, and non-hazardous waste Evaluates control strategies to prevent dispensing of expired and substandard vaccines and packaging/labelling materials in healthcare facilities Leads a team of regulators to supervise disposal/destruction of expired and substandard vaccines and packaging/labelling materials and other biowastes

Y. I-I Investigation of product quality complaints: investigates complaints related to vaccines and biologics quality

Early Level Professional	Understands the critical quality attributes (CQAs) for vaccines and biologics in the marketing authorization (MA) Understands the SOPs for handling (receiving, documenting, investigating and preparation of final report) product quality complaints Receives, documents, and communicates product complaints to the responsible person for investigation.
Mid-Level Professional	Conducts investigation of product quality complaints, preparing report of the investigation, and advising on regulatory action as appropriate. Educates the public on reporting product quality issues
Senior Level Professional	Takes regulatory actions based on outcome of the investigation of product quality complaints as appropriate Communicates product quality issues to the other regulatory functions and the public as appropriate Monitors global alerts related to product quality

Z. I-J Import examination and screening

Early Level Professional	Understands the regulatory requirements and SOPs for inspection of vaccines and biologics at the port of entry Performs screening of imports for vaccines and biologics
Mid-Level Professional	Conducts cold chain verification of imported vaccines and biologics at the port of entry/ storage facilities in line with regulatory requirements and approved procedures Prepares the report of the screening/ examination Prepares procedures for performance of screening and examination of vaccines and biologics imports
Senior Level Professional	Uses the report of the screening/examination to make regulatory decision Approves procedures for performance of screening and examination of vaccines and biologics imports

	Uses reports of screening and examination of vaccines and biologics to alert other regulatory functions for monitoring compliance

AA. I-K Overall Regulatory Approaches: Develops regulatory approaches and strategies based on quality audits and inspections

Early Level Professional	Understands the regulations related quality, safety and efficacy of vaccines and biologics Understands the standard operating procedures (SOPs) applicable to inspection of vaccines and biologics across the supply chain Understands the vaccines and biologics regulatory inspection outcomes that informs decision making
Mid-Level Professional	Develops regulatory approaches to vaccines and biologicals Recommends premises/clinical trial sites for issuance/suspension/withdrawal/modification or cancellation of licenses for vaccines/biologics or for importation and exportation of same based on applicable regulatory requirements Provides regulatory guidance to the applicants, sponsor, and manufacturers during regulatory correspondence
Senior Level Professional	Approves issuance/suspension/withdrawal/ modification or cancellation of licenses for vaccines/biologics or for importation and exportation of same based on applicable regulatory requirements Provides regulatory guidance to the leadership and the board/scientific committees Provides scientific evidence to inform on policy/regulatory reviews or changes to the leadership/the board Coordinates and communicating the outcomes of inspections of facilities for vaccines and biologics with other functions for decision making

BB. I-L Sampling of products from the market: identifies and assesses the quality vaccines and biologics in the supply chain system; identifies vaccines and biologics, based on the risks associated with manufacturing complexity, dosage form, storage and stability; Assesses the quality of vaccines and biologics received at the ports of entry and border posts

Early Level Professional	Understands of the guidelines and procedures for surveillance and sampling of vaccines and biologics in the supply chain Understands the sampling techniques for vaccines and biologics Understands the handling, storage and transportation of sampled vaccines and biologics
Mid-Level Professional	Validates the guidelines, protocol and procedures for surveillance and sampling of vaccines and biologics in the supply chain Validates the sampling techniques for vaccines and biologics based on

	risk-based approach and intelligence information Ensures proper handling, storage and transportation of sampled vaccines and biologics Organizes training on sampling techniques for vaccines and biologics and ensuring effectiveness of the training
Senior Level Professional	Ensures development and implementation of the sampling of the techniques and protocols for vaccines and biologics Determines survey sites based on geographical locations, complaints, disease prevalence, poor accessibility, population density and income level Establishes acceptance/ rejection criteria for freeze sensitive vaccines prior to sampling exercise Verifies proper handling, storage and transportation of sampled vaccines and biologics Uses the laboratory results to take regulatory decision and action Reports any relevant information to management for informed decision making

CC. I-M Provision of technical guidance (capacity building for stakeholders): Participates in capacity-building activities.

Early Level Professional	Understands of capacity building guidelines for capacity building of stakeholders in vaccine manufacturing Understands of what kind of questions to ask Understands of stakeholder's engagement techniques Understands of areas of engagement and collaboration with stakeholders in vaccine manufacturing initiatives
Mid-Level Professional	Assesses capacity needs and assets Shares of technical knowledge Identifies capacity indicators Identifies appropriate methodological approach and sources of data Integrates stakeholder engagement into appropriate systems
Senior Level Professional	Develops an implementation and dissemination plan Selects appropriate approaches and tools Motivates, supports, and incentivizing staff

	Excels in communication Understands how to evaluate impact risks associated with decision making Develops monitoring and evaluation framework for capacity building initiative

DD. I-N Training of regulatory personnel and industry: Applying new scientific innovation, technologies, and research to build a pool of competent workforce in the development, manufacturing and distribution of vaccines and biologics and the regulatory sector

Early Level Professional	Understands the regulatory guidelines for vaccines and biologics Conducts training needs assessment for the industry and regulators
Mid-Level Professional	Develops training materials for all stages in the vaccines and biologics lifecycle for the industry and regulators Trains regulators on all the regulatory functions as applicable Ensures training compliance across all the regulatory functions in the NRA Trains the industry on upcoming regulations
Senior Level Professional	Draws the training plan for vaccines and biologics manufacturing, control, release and distribution for the industry and regulators Approves the developed training materials and delivering the trainings for all stages in the vaccines and biologics lifecycle to the industry and regulators Oversees development of training policy for the NRA, onboarding/ ongoing training program for all functions and individual training plan for all personnel Performs quality assurance for all trainings across all the regulatory functions to verify the training effectiveness

EE. I-O Enforcement: Enforces GMP guidelines for vaccines and biologics, seize any counterfeit, adulterated, bad or fake vaccine or biologics, based on surveillance and intelligence gathering, issue invitation letter or arrest suspect

Early Level Professional	Identifies counterfeit or substandard vaccine products
Mid-Level Professional	Gathers information on counterfeit and substandard information form a range of sources
Senior Level Professional	Seizes and removes counterfeit vaccine or biologic Assists in arrest of suspect

FF. I-P Reviews batch records of active medicinal Substance and finished medicinal product to ensure lot-to-lot consistency

Early Level Professional	Understands the importance of batch records Is familiar with typical batch records
Mid-Level Professional	Can find problems with batch records Can Find inconsistencies in batch records
Senior Level Professional	Can communicate with persons on batch record inconsistencies Can initiate enforcement actions

VI. Laboratory Analysts

L-A1: Applies standards and international best practices: Ensures application of national, regional, and international standards, guidelines, and best practices in quality control laboratory for safety, efficacy, and quality of vaccines and biologics

Early Level Professional	Implements standards and best practices, including current Good Laboratory Practices (cGLP), Good Microbiological Laboratory Practices (GMLP), and current Good manufacturing practices (cGMP)as applicable to quality control laboratories for vaccines and biologics Understands national and regional, as well as international standards, guidelines, and best practices (cGLP, cGMP) for vaccines and biologics (i.e., Bioanalytical Laboratory) Initiates development of written standards for specific products, such as mRNA vaccines, and aligns written standards to regional as well as international best practices Ensures that the principles of reliance and harmonization are included in written standards Defines certification /accreditation scheme for assuring the safety, quality, and efficacy of vaccines and biologics Ensures the autonomy of the quality control laboratory to ensure independent, authoritative, and impartial decisions on safety, efficacy, and quality of vaccines and biologics Identifies laws pertaining to the operation of quality control laboratories Participates in proficiency and competency assessment of quality control, laboratories, and quality control personnel Initiates exchange of information on safety, efficacy, and quality of vaccines and biologics among NRAs
Mid Level Professional	Implements the process of standard development Develops and retains documentation to comply with quality regulations

	Ensures routine audits of quality control processes and systems Engages in the development of national standards to ensure they are based on sound scientific and regulatory guidance Explains certification /accreditation process for quality control, laboratories, and personnel Applies laws pertaining to the operating principles and procedures of the quality control labs Organizes proficiency as well as competency assessment for laboratory operations and personnel Analyzes components of the laboratory information management system to ensure they are compliant with regulatory standards Determines areas where existing processes should change resulting from audit findings Facilitates improvements to processes by changing approaches and working practices, typically using recognized models and standards Takes responsibility for controlling, updating, and distributing organizational standards Applies relevant risk regulations, policies, and procedures to noncomplex issues Identifies and assesses the impact as well as the likelihood of an organization's risks to achieving business objectives Monitors the effectiveness of actions taken to manage identified risks and intervenes as appropriate Understands, develops, and prepares risk reports Identifies risk to the quality control operations and codifies those risks in reports Designs and implements risk reporting systems in order to facilitate communications to senior management
Senior Level Professional	Evaluates the adequacy of the manufacturer's establishment and facilities, starting materials, production processes, control-test procedures, and product specifications to determine whether they meet international and/or national requirements Defines standards and best practices, including current Good Laboratory Practices (cGLP), Good Microbiological Laboratory Practices (GMLP), and current Good manufacturing practices (cGMP) as applicable to quality control laboratories for vaccines and biologics

	Evaluates the use of standards and best practices, including current Good Laboratory Practices (cGLP), Good Microbiological Laboratory Practices (GMLP), and current Good manufacturing practices (cGMP) as applicable to quality control laboratories for vaccines and biologics Develops and ensures adherence to standards and best practices including current Good Laboratory Practices (cGLP), Good Microbiological Laboratory Practices (GMLP), and current Good manufacturing practices (cGMP) for laboratory services Appraises national and international standards for those that apply to quality control laboratories and works with laboratories to ensure adherence to these standards Assesses certification/accreditation process for quality control laboratories Evaluates compliance with laws pertaining to the quality control laboratories Evaluates proficiency competency of personnel working in quality control laboratories Assesses the impact of the laboratory information management system Achieves and maintains compliance with all national and international standards that apply to quality control laboratories Prioritizes areas for quality improvement by considering strategy, business objectives, and results from internal and external audits Initiates the application of appropriate quality management techniques in the quality control laboratories Initiates improvements to processes by changing approaches and working practices, typically using recognized models Identifies and plans systematic corrective action to reduce errors and improve the quality of the systems and services provided by quality control laboratories Develops innovative approaches to managing significant organization-wide risks effectively and efficiently Develops and implements appropriate risk mitigation for significant and unusual risks to which the organization is exposed

L-B1. Establishes and implements policies, guidelines, and procedures to ensure quality control laboratory operates in a safe environment and prevent health hazards to the personnel

Early Level Professional	Develops and implements policies, guidelines, and procedures on laboratory safety, and handling of biohazardous materials Develops and implements standard operating procedures for handling biohazardous materials and usage of personal protective equipment (PPE), including labeling and equipment used Implements Laboratory Safety Programs for the quality control laboratories personnel Documents all safety related incidents and reports to appropriate authorities Participates in safety trainings and drills as required Ensures implementation of relevant safety policies, guidelines, and regulations related to laboratory safety within the quality control labs Ensures that appropriate safety information and documents, such as safety data sheets, are available on all chemicals, reagents, drugs, vaccines, biologics, and other applicable materials that are utilized in the quality control laboratories Ensures use of relevant PPE whilst working in the quality control labs Promotes health and safety by encouraging adherence to quality control policies and procedures within the organisations quality control labs
Mid Level Professional	Evaluates implementation of policies, guidelines, and procedures on laboratory safety and handling of biohazardous materials and sterile materials to ensure their effectiveness Evaluates implementation of SOPs for handling biohazardous materials and usage of PPE as well as flow of all equipment and materials Develops and implements in-house training programs on handling, labeling, and disposal of biohazardous materials Designs and maintains the safety program for quality control laboratories Develops relevant safety procedures, policies, guidelines, and regulations Maintains and implements the established waste management program with respect to disposal of all hazardous, biological, pharmaceutical, and chemical waste Reviews all safety-related documents
Senior Level Professional	Provides technical guidance and advice on newly emerging policies and procedures that impact laboratory, safety, and handling of biohazardous materials

	Evaluates implementation of policies, guidelines, and procedures on laboratory safety and handling of biohazardous materials Works to address any gaps in safety policies and procedures Develops and supervises the implementation of safety procedures required within the laboratory Ensures availability of relevant PPE for all laboratory personnel

L-C1: Establishes and sustains a maintenance program for laboratory systems and equipment to ensure a high standard of performance as well as to generate results/data which are accurate and precise (with minimal variations/errors)

Early Level Professional	Develops written policies and procedures for maintenance of laboratory systems, equipment, and all other items utilized in a laboratory Follows United States Pharmacopeia (USP) or International Organization for Standardization (ISO) procedures for all measurements and repair of equipment, including HVAC equipment, including Design Qualification (DQ), Installation Qualification (IQ), Operational Qualification (OQ), Performance Qualification (PQ) Implements the Laboratory Quality Management System that supports the analytical lifecycle Creates and adheres to Standard Operating Procedures for the quality control laboratories
Mid Level Professional	Reviews and approves written policies and procedures for maintenance of laboratory systems and equipment Monitors and trends performance of key quality control laboratory equipment
Senior Level Professional	Evaluates implementation of policies and procedures for maintenance of laboratory systems and equipment including DQ, IQ, OQ, PQ Advises the management on the need to commission and/or decommission laboratory equipment Establishes a Laboratory Quality Management System Works collaboratively with procurement department to ensure timely purchase and replacement of laboratory equipment and parts Audits and reviews all laboratory measurements by contract laboratories

L-D1: Participates in the design and development of analytical and verification methods and procedures for various vaccines and biologics. Works to facilitates method transfer of analytical and verification methods and procedures for various vaccines and biologics

Early Level Professional	Understands national, regional, and international guidelines for

	analytical procedures and methods validation for vaccines and biologics Understands quality attributes of mRNA, DNA, Inactivated Viral Vector, Protein Subunit, virus-like particle, and attenuated vaccines Provides guidance to pharmaceutical industry on analytical methods development for vaccines and biologics including critical parameters such specificity, linearity, limits of detection (LOD), limits of quantitation (LOQ), range, accuracy, and precision Understands various bioassays applicable to vaccines (animal-based biological assays, cell culture based biological assays, and biochemical assays) Develops verification protocol for analytical procedures Participates in analytical method validation Participates in developing analytical method verification, validation, and method transfer protocol Develops tools and checklist to guide inspection of pharmaceutical industries on analytical methods used for various vaccines and biologics Prepares verification report for analytical methods for vaccines and biologics
Mid Level Professional	Participates in developing national and regional guidelines for analytical procedures and method validation for vaccines and biologics Develops toolkits for assessing quality attributes of various vaccines and biologics Performs the transfer/validation of new methods of analysis or manufacturers in-house test methods in accordance to a predefined protocol Evaluates robustness of analytical method for vaccines and biologics (scope, apparatus/equipment, operating procedures, reagents/standards, sample preparation, standards control solution preparation, procedure, system suitability, calculations, data reporting) and advises on any variations in method parameters that may occur Conducts revalidation (verification) of the performance of the method in case of a change in materials Conducts inspection of vaccines and biologics manufacturing facilities and evaluates analytical methods and documentation Provides training to NRA staff on how to conduct analytical methods

	for vaccines and biologics Verifies and validates analytical methods
Senior Level Professional	Reviews and approves implementation of testing and re-testing policies Reviews and approves implementation of all validation procedures Reviews, and approves of, revising validation procedures and protocols, including method transfer Provides technical guidance on advancement in technology for vaccines/biologics manufacturing Updates existing analytical methods as well as specifications to align with current science and knowledge Reviews technical reports and documentation such as deviation reports, testing protocols, and trend analyses, identifying root causes and advises on corrective actions Leads a team of inspectors to conduct evaluation of robustness of analytical methods for vaccines/biologics Leads a team of inspectors to review the robustness of specifications and monographs for vaccines Reviews the validation of analytical methods Reviews and approves verification protocols for analytical procedures for vaccines and biologics Reviews and approves implementation of a system for analytical method lifecycle management Interprets analytical method verification and validation results Collates and interprets validation and verification test results and reports in line with defined acceptance criteria Supervises the qualification, validation, and calibration program of analytical equipment

L-E1: Ensures establishment of scientifically sound and appropriate specifications, standards, and test procedures. Specifications, standards and test procedures are designed to ensure components, containers and closures, in-process materials, and finished vaccines and biologics, conform to the established standards

Early Level Professional	Understands national, regional, and international regulations and guidelines on investigation of out-of-specification (OOS) results Plans and participates in out-of-specification and failure investigations

	Addresses and resolves issues arising from the investigation of OOS results as well as failure investigations Plans and participates in CAPAs with the goal of eliminating recurrences
Mid Level Professional	Oversees creating and implementing procedures related to investigations due to OOS results as well as nonconformances Participates in investigations of OOS results Performs root cause analysis using Root Cause Analysis (RCA) tools (e.g., FEMA, 5-Whys, Fishbone, Fault tree analysis) Identifies CAPAs and performs effectiveness review of CAPAs for OOS and trend analysis
Senior Level Professional	Evaluates effectiveness of the implementation of procedures on investigation of OOS results Reviews effectiveness of deviation investigations and drives improvement in the system, if warranted Uses lab expertise and knowledge to follow up on the effectiveness of CAPAs Performs CAPA and OOS investigations trending to identify potential repeat occurrences Identifies and coaches teams on continuous improvement opportunities

L-F1: Establishes and implements guidelines, procedures, and programs for qualification of laboratory equipment to ensure accuracy and integrity of equipment to generate reliable and accurate data

Early Level Professional	Understands national, regional, and international guidelines and procedures for qualification of laboratory equipment Develops policies, procedures, and guidelines for equipment qualification on non-sophisticated laboratory instruments, e.g., weighing balance, conductivity meter, and pH meter Performs calibration and verification of laboratory equipment Documents and maintains records of equipment qualification activities in approved report Troubleshoots non-sophisticated equipment as a facilitation to their qualification process Guides pharmaceutical manufacturing on development of plans and protocols for laboratory equipment calibration taking into account design qualifications (DQ), installation qualifications (IQ), operational

	qualification (OQ) and performance qualification (PQ)
Mid Level Professional	Reviews guidelines and procedures for qualification of laboratory equipment Reviews procedures for equipment qualification and validation Reviews and oversees implementation of policy, guidelines, and procedures, as well as documentation for equipment qualifications management Develops and monitors equipment qualification/requalification schedule/plan Participates in design qualification activities of new equipment Participates in trainings and capacity building programs on equipment qualification Identifies safety requirements and drafts procedure on safety rules followed during equipment handling and qualification exercise Identifies inputs and utilities to equipment installation and qualification and ensures they are procured in a timely manner
Senior Level Professional	Approves and oversees implementation of policy, guidelines, and procedures for qualification of laboratory equipment Oversees set-up and maintenance of equipment: (a) evaluating equipment needs; (b) developing user requirements specifications; (c) preparing and executing protocols; (d) preparing equipment qualification reports; (e) managing equipment calibration, maintenance, and requalification Identifies training needs and provides mentorship to subordinate laboratory personnel on elements of equipment qualification Reviews and verifies computer systems validation data, ensures qualified equipment are run with appropriate computer systems Identifies competent contract agents for equipment qualification and maintains a shortlist of contract parties for the entire scope of equipment qualification Troubleshoots sophisticated equipment and devises solutions to complex problems encountered during the equipment qualification process Performs factory acceptance and site acceptance inspections to ensure the requisitioned equipment is supplied

L-G1: Quality system for Analysis Laboratory

Early Level Professional	Establishes quality system for Analytical Laboratory

	Utilizes ISO Documents to set up quality laboratory Adheres to ISO documents and quality manual Performs analysis of samples
Mid Level Professional	Reviews analytical test reports Ensures that laboratory analytical data is linked to the reviewer's findings
Senior Level Professional	Utilizes modern project management approaches to handle laboratory projects Performs statistical analysis and other data analysis as needed

L-H1: **Establishes accuracy of analytical reports and data management**

Early Level Professional	Confirms that all required data and reports are submitted for review Devises and implements master data management processes for specific subsets of data Maintains and implements information handling procedures for analytical data Enables the availability, integrity, and searchability of information through the application of formal data and metadata structures as well as protection measures
Mid Level Professional	Devises and implements master data management processes for all analytical reports Derives data management structures and metadata to support consistency of information retrieval, combination, analysis, pattern recognition and interpretation, throughout the organization and ensures all studies are performed according to quality manual Plans effective data storage, sharing, and publishing within the organization Independently validates external information from multiple sources Assesses issues that might prevent the organization from making maximum use of its information assets Provides expert advice and guidance to enable the organization to obtain maximum value from its data assets
Senior Level Professional	Derives an overall strategy of master data management that supports the development and secure operation of information and digital services Utilizes the master data management strategy to approve all reports Develops organizational policies, standards, and guidelines for data

	management, and data collection, aligned with ethical principles Plans, establishes, and manages processes for regular and consistent access to external information from multiple sources Ensures there is a process for independent validation of external information

L-I: Participation in Research

Early Level Professional	Understands the research and development of vaccines as well as biological products Demonstrates a thorough understanding of the regulations that govern the development of drugs, vaccines, and biological products Demonstrates basic understanding of scientific research methods, study designs, and the different sources of data utilized in the development of drugs, vaccines, as well as biological products Understands the purpose, concept, and topic of a scientific study Possesses ability to pose relevant research questions
Mid Level Professional	Identifies questions that need to be answered in the drug, vaccine, and biological product development process Designs research protocols for use in the development of drugs, vaccines, and biological products Conducts/implements research as part of an overall development process Uses appropriate tools and techniques for collecting, analyzing and interpreting data Implements and utilizes peer review principles for studies conducted during the development of drugs, vaccines, and biological products Identifies and explains the elements that support the principles and processes of designing a research study Analyzes quantitative and qualitative data related to a research question Evaluates the design, conduct, and documentation of clinical studies as required for compliance with best practices and scientific/research guidelines such as cGCPs Evaluates preclinical and clinical research methods, study designs, and the different sources of data (primary and/or secondary) Provides support to organizations developing new drugs, vaccines, and

	biological products in order to ensure the correct scientific information is being collected during the development process
Senior Level Professional	Approves research protocols to be utilized in the development of new drugs, vaccines, and biological products Evaluates the conduct of the research Develops descriptions, explanations, predictions, and models based on evidence Applies research results to inform regulatory decision Possesses advanced knowledge of scientific evidence by publications and/or presentations on methods to generate and/or evaluate scientific evidence Identifies trends and anomalies within the pharmaceutical development program Identifies issues early in the development or research phase that could impact regulatory strategy

VII. Vigilance Professionals

a. **Pharmacovigilance (PV) assessment for marketing drugs and vaccines**

VA-1 Robust assessment of safety signals	
Collection and evaluation of adverse events from numerous sources	
Early Level Professional	Categorization of ADRs/AEFIs from reports Extract authentic vaccine or biologics effects from medical and patient Identify and report idiosyncrasies and new reactions associated with vaccines and biologics Maintain list of AEFIs and sources
Mid Level Professional	Appraises observational studies, strengths, and weaknesses Selects relevant data collectable for vaccines and biologics Defines idiosyncrasies and rare reactions in vaccines and biologics Appraises, confirms, and updates new AEFIs and ADRs
Senior Level Professional	Ensures that robust data has been collected around the reporting of any adverse events Ensures that a thorough scientific and medical review is conducted for any adverse event prior to changing risk benefit, profiles Ensures that an extensive scientific medical review has been conducted prior to communicating changes in risk profile to medical professionals and patient populations

VA-2 Individual case safety reporting for vaccines and pharmaceutical products	
Reporting of individual case, safety data to the appropriate regulatory authorities for both drugs and vaccines/biologics	
Early Level Professional	Conducts trend analysis of locally received ADRs/AEFIs for identification of probable/possible safety concerns and signal and reports/shares data within and outside the NRA for further investigations Understands the difference between individual case study reports for drugs versus that for vaccines/biologics Understands how to submit data to VAERS and FAERS
Mid Level Professional	Ensures that ongoing safety of vaccines and drug products are monitored Ensures that individual case safety reports are submitted in a timely fashion
Senior Level Professional	Ensures that all of the necessary information on the patient, reporter, event, and suspected drug are included Ensures the case narrative includes information on the clinical course, therapeutic measures outcomes, and all additional relevant information Works with appropriate experts to ensure the timely, accurate, and complete reporting of safety issues
VA-3 Utilization of PV centers to detect medication errors, substandard, and counterfeit drugs, vaccines, and biologics	
Detection of medical errors, substandard and counterfeit drugs, vaccines, and biologics through the establishment of robust PV systems and processes	
Early Level Professional	A thorough understanding of PV systems and processes, and a thorough understanding on how to detect medical errors for substandard and counterfeit drugs, vaccines, and biologics
Mid Level Professional	Ensures that PV centers are established to identify, detect, and analyze medical errors Ensures that PV centers have the analytical capability to discern medical errors, substandard, and counterfeit drugs Ensures that efforts are in place to decrease medical errors Ensures robust communication plan to communicate with medical professionals regarding medication errors Works with PV centers to prevent medication errors by informing healthcare professionals about the importance of reporting medical errors and creating a culture of patient safety Ensures collaboration between PV centers and poison control centers as well as organizations dedicated to patient safety

	Ensure robust review of all adverse events to determine root cause, especially focusing on medication errors
Senior Level Professional	Ensures that robust processes and mechanisms are in place to gather adverse event data from a variety of different sources, including the medical and scientific literature
VA-4 Ongoing risk assessment	
Assessment and communication of risk utilizing a PV system	
Early Level Professional	Ensures that risk management, tools, and techniques are in place to monitor safety and evaluate risk benefit ratios on an ongoing basis Ensures that all of the risk management policies and procedures are codified in SOPs Conducts initial reviews of risk management plans and summarizes key components for further decision-making Monitors all products and conducts post-market evaluations to ensure drug safety Applies professional knowledge on risk associated with continuous exposure Ensures that the good pharmacovigilance practices (GVP) are followed Ensures that staff are trained on PV regulatory requirements Ensures that the sponsor submits a risk management plan at the time of applying for market authorization Ensures risk management plans distill technical detail into information that the general public can understand Ensures that the risk management plan is modified and updated on an ongoing basis as new risk information becomes available Ensures that the risk benefit ratio is modified and updated as new information on risk becomes available, as the updated risk benefit ratio should reflect either increases or decreases in risk as new data becomes available
Mid Level Professional	Implements, monitors, and assesses effectiveness of risk mitigation measures for specific products Implements and maintains Quality Management Systems for management of risks/harms from biological products and vaccines Participates in risk communication specifically drafting narratives, dear doctor/patient letters, and briefs to decision makers regarding management of identified and potential risks
Senior Level Professional	Establishes quality system to manage risks and evaluates the overall

	approach to how quality risk management is used in the organization Supports external monitoring, as a part of the PV system, for adverse events from vaccine, drugs, and biological products Participates at all levels (internally and externally) in the formulation and preparation of regulatory policies and opinions or briefs
VA-5 Detection of safety signals	
Early Level Professional	Collates and upload causality reports on database Participates in analyzing an ICSR
Mid Level Professional	Ensures that there is a robust system in place for signal detection, validation, confirmation, analysis, and assessment Ensures the signal management process result in a recommendation of action is warranted by the data Ensures that signal detection activities for medication errors focus on the verification of harm Engages in the determination of which signals represent a risk and which signals do not represent a risk Understands that the system obtains input from events reported in multiple areas (e.g., clinical trials, spontaneous reports, commercial complaints, pre-clinical studies, social media, medical literature, and literature searches)
Senior Level Professional	Ensures that the system obtains input from events reported in clinical trials, spontaneous reports, commercial complaints, pre-clinical studies, social media, medical literature, and literature searches Ensures that PV staff employ some combination of statistical and clinical methodology for the evaluation of a potential signal
VA-6 Separation of signal versus noise	
Differentiation of safety signals from background noise	
Early Level Professional	Ensures that the organization monitors ADR and AEFI for vaccines and biological products Ensures that after appropriate medical and scientific evaluation of the ARD and /or AEFI the appropriate communication ensues to healthcare professionals, patients, as well as regulators
Mid Level Professional	Ensures that PV scientists engage in a systematic process for signal validation Ensures that clinical relevance, as well as previous awareness are taken into consideration in validating the potential signal Ensures that the data collected demonstrates sufficient evidence of the existence of a new safety signal Ensures that the signal is validated/accepted, or not validated/ rejected,

	or pending/requiring further monitoring Ensures that the appropriate documentation is put in place after the investigation of each signal
Senior Level Professional	Facilitates the signal management by: Proposing actions and other risk minimization measures Enables decision making regarding potential risks and the communication of signals
VA-7 Periodic Safety Update Reports (PSURs) or Periodic Benefit-Risk Evaluation Report (PBRERs). Both of these reports are authored to provide a periodic evaluation of risk to benefit ratio	
Early Level Professional	Reviews and analyzes the appropriateness/completeness of PSURs and PBRERs as per national regulations and international set standards (i.e., the International Conference on Harmonization [ICH]) Reviews and analyzes ICSRs, to ensure that they include signal detection, signal validation, and signal management, and risk minimization as described in VA-5 (Detection of safety signals) Is proficient in the uses of search engines, medical databases, and study registers so as to assist in the identification and processing of ADR's or AEFI
Mid Level Professional	Understands and interprets the regulatory/legal requirements of the NRA in relation to safety, quality, efficacy, and effectiveness to intending market authorization holders Is knowledgeable of medication errors, drug misuse, and drug abuse Critically appraises randomized clinical trials, case control, and cohort study reports/summaries, and other published literatures on the benefit/risk balance of biological products and vaccines Conducts quality assurance reviews on risk management data to ensure that PSURs contain the most recent risk evaluations Synthesizes and summarizes safety data presented in PBRERs/PSURs Drafts regulatory responses to submitted PBRERs Identifies potential risks and evaluates them with the appropriate scientific and medical personnel following internal policies and procedures Identifies safety signals
Senior Level Professional	Reviews, formulates, and oversees the implementation of risk minimization/mitigation plans in relation to reported identified and potential risks Communicates risk/benefit evaluations to the public and advises on the right course of action

	Updates the Product/Patient Information Leaflets with the necessary risk/benefit information to inform the medicines users Establishes competencies for signal detection following the appropriate policies and procedures Updates PSUR's to provide the most current evaluation of risk benefit ratios for a medical product, such as a vaccine or biologic
VA-8 Advertisement/medical products promotion	
Knowledge, skills to enable one to judge if advertisement/promotional information is fit for consumption by either public or health care professionals	
Early Level Professional	Reviews promotional material related to vaccines and biological products Reviews potential adverse reactions for drugs, vaccines, as well as biological products from a variety of different sources, including publications, social media reports, healthcare professionals, and ongoing clinical research Retrieves all relevant data on potential adverse reactions related to drugs, vaccines, as well as biological products Ensures that the relevant data is appropriately reviewed by medical and scientific staff Ensures that data relevant to adverse reactions is subject to statistical analysis where appropriate Critically appraises clinical trials publications and other studies/literature published to justify claims made on promotional materials/advertisement and explore the limitations of such studies to authenticity and generalizability of generated evidence Assesses appropriateness of advertisements/promotional material to the targeted audience considering rational use of the vaccine/biological product
Mid Level Professional	Develops guidelines and SOPs on how to review advertisements and promotional material Evaluates the balance of information proposed to be included in direct-to-prescriber drug promotional materials/advertisements and direct-to-consumer drug promotional materials/advertisements
Senior Level Professional	Formulates policies, laws, regulations, and guidelines that guide advertisement and promotional/ product labeling activities Designs studies and tools to evaluate/analyze how drug advertisement impacts/influences prescribing patterns of prescription drugs and its

	influence on the use of prescription drugs

b. BV-1 PV during the drug development process

Early Level Professional	Ensures that appropriate criteria such as the Bradford Hill criteria or adverse drug reaction probability scale are used in the analysis of adverse event reports on drugs, vaccines, as well as biological products to determine causation
Mid Level Professional	Establishes procedures for the investigation process for examination and substantiation of individual case reports and aggregates data Reviews risk minimization and mitigation plans Ensures appropriate reporting of adverse events occurring during drug development studies Ensures appropriate amounts of data are collected on adverse events when reported Distinguishes true safety signals versus noise in ongoing event reporting Identifies risk factors and possible mechanisms for adverse events Evaluates risk benefit ratio on an ongoing basis Communicates any changes in the risk benefit calculation to clinical investigators, IRB, and regulatory authorities
Senior Level Professional	Participates in development and enforcement of compliance to rules and regulations related to clinical trials, PV/Regulatory requirements (WHO, EU, US, PMDA, and ICH guidelines) Formulates and reviews clinical trial risk minimization and mitigation plans (clinical trial risk management)

c. **PV system strengthening**

VC-1 Capacity Building	
Knowledge and skills that enable horizontal cooperation	
Early Level Professional	Adapts/develops PV training materials for various audiences Facilitates/conducts PV training for healthcare professionals Conducts PV awareness/sensitization campaigns for the general public
Mid Level Professional	Works with PV centers in preventing medication errors and identifying substandard and falsified vaccines, as well as biological products Ensures that PV centers are appropriately staffed with experts in medicine, PV, toxicology, and communications Ensures the PV staff clearly understands their roles and responsibilities

	Ensures that job descriptions are in place for all PV staff Ensures that PV centers have policies and procedures in place for staff to follow and execute Ensures the staff of PV centers are appropriately trained on policies and procedures Monitors staff workload to ensure adequate staff to manage the PV system
Senior Level Professional	Works with organizational management to address shortages when workload of existing staff is not able to handle the volume of issues Ensures the hiring of staff members with the needed training and expertise Rigorously trains incoming staff members in all organizational policies and procedures Ensures that the training of new staff members is documented and retained Ensures that new staff members are mentored in their roles and responsibilities by experts in the field
VC-2 Maintaining public health through the use of a PV system	
Utilizes the data from PV to maintain and approve public health	
Early Level Professional	Ensures that there is a robust PV system in place to detect adverse events for marketed drugs/vaccines/biological products
Mid Level Professional	Designs procedures and tools for detection and reporting of ADRs/AEFIs by the public Communicates risk from vaccines and biological products to the public and highlights products of public health concern, like those with potential for abuse
Senior Level Professional	Builds scientific evidence based on safety by identifying trends and anomalies based on the presented scientific problems to reduce the risk or anticipate problems Develops and incorporates risk communication in public health campaigns for vaccines
VC-3 PV System Development	
Early Level Professional	Understands the principles of GVP and the importance of an organization being in compliance with GVP Has a foundation in systems' thinking and approaches as well as understands how this system impacts safety monitoring and vice versa Understands risk management including risk identification, risk assessment, risk mitigation, and tools associated with the risk system Understands the quality system that resides within the PV system

	Understands the importance of policies and procedures in place and in use
Mid Level Professional	Ensures that there is a systematic approach in place to monitor safety of products which is designed to detect any change in risk to benefit ratio Ensures that the organization is in compliance with the principles of GVP Ensures that the PV system captures quality planning, quality adherence, quality control, quality assurance, and quality improvement Ensures that the training for members of the organization is documented and retained Ensures that the PV system is proactive, and that evidence of the risk to benefit ratio for the drug product or vaccine is current and up-to-date Ensures that an organization has the policies and procedures in place to document the key elements of the PV system Ensures that the organization is in compliance with the principles of GVP Ensures the continuous monitoring of PV data for marketed products Ensures that there is a rigorous and robust scientific and medical evaluation of all information related to the risks of medical products that the organization is accountable for Ensures that the data on adverse events is complete and of high quality so that it can be evaluated rigorously by scientific and medical experts Ensures there is a record management system in place in order to retain all information related to the operation of the PV Ensures that the PV system in monitored for compliance on an ongoing basis, through the use of audits and inspections
Senior Level Professional	Responsible for ensuring training on system changes and improvement Ensures appropriate resources to meet system requirements and ensures patient safety are identified, approved and in place Ensures clear roles and responsibilities within the organization, which are codified in job descriptions, to maintain the PV system, Ensures that the overall objectives for a PV system are achieved, including complying with all legal requirements, preventing patients from being harmed by adverse reactions, and contributing to the overall protection of patients, as well as public health Ensures that there is organization-wide training on the principles of GVP
VC-4 PV regulations and guidelines	

Compliance with GVP	
Early Level Professional	Knowledgeable of local/regional regulatory requirements governing PV activities Understands and applies GVP Understands and complies with policies and procedures to comply with PV regulatory guidance Participates in audits and inspection activities and has a strong understanding of these areas Articulates why record management is important in PV and follows record management procedures and best practices
Mid Level Professional	Ensures that the organization has detailed policies and procedures in place to comply with regulatory guidance on PV, including application of knowledge from local, national, and global regulatory requirement governing PV activities Ensures compliance through inspection and audit activities Ensures a robust record management process to store and retain all relevant information regarding PV
Senior Level Professional	Responsible for ensuring the organization follows GVP Provides appropriate resources to ensure GVP practices is achieved and sustained Ensures the organization has a robust system in place that complies with the requirements of all applicable rules and regulations for PV Provides regular updates and communicates issues to upper management in order to ensure the organization is able to meet and sustain good GVP

d. **Updating of market status**

VD-1 Responses to the PV signal	
Ensures that the organization has the appropriate policies and procedures in place to support any action required as a result of a PV review. The outcome of a PV review could include communication with the public, communication with healthcare providers, or recalling products	
Early Level Professional	Advises consumers on where they can find additional information (i.e. NRA's website, consulting with pharmacist) for vaccines or biologics on recall list Ensures proper documentation and accountability for recalled products Writes technical reports for simpler applications or cases

	Records observations and/or data obtained in the course of one's duties in a timely manner to prevent loss of relevant information Prepares general documentation in relation to the role Ensures proper application of laws, regulations, and guidelines for regulatory decisions Provides rationale for regulatory decisions Ensures adequate application of good regulatory practices in regulatory actions
Mid Level Professional	Ensures that validated risks are assigned the appropriate classification based upon their severity (i.e. the FDA classification of class I, II, and III may be appropriate for this purpose) Develops procedures for informing patients if their prescription medication, vaccines, or biological products are on a recall list Establishes and implements procedures for updating the community on the website or public notice boards on product recalls/market actions in progress Integrates information from multiple sources to inform recommendations and decision making Writes comprehensive, clear, and coherent technical reports Prepares reports to support evidence-based decision making based on different sources of information, including own analysis or observations, or reliance on decisions from other authorities Critiques written reports from others within one's discipline or specialty Prepares status reports on applications received, in-process, or completed within a specified period Ensures proper application of laws, regulations and guidelines on regulatory decision making Reviews recall reports and evaluates the proposed CAPA
Senior Level Professional	Ensures that the appropriate policies are in place in the event that a recall is necessary Ensures that there are policies and procedures in place to assess the adequacy of recalls of drugs, vaccines, or biological products Monitors and evaluates the effectiveness of overall mechanisms put in place for recalls and associated communication and feedback for the public

	Conducts secondary reviews (critiques) written reports from colleagues at all levels for all types (complexity) of applications within one's specialty or discipline Prepares/reviews technical guidelines Ensures that regulatory decisions are made in accordance with the appropriate laws, regulations, and guidelines Ensure sound regulatory processes are utilized in the decision to recall products based on defects or ADRs Facilitates the involvement of level I and II regulatory in assessing the effectiveness of the recall activity Notifies overseas clients and all other stakeholders on recalls that affect them Monitors and evaluates the effectiveness and completeness of the recall Reports the reason/cause to WHO Program for International Drug Monitoring
VD-2 Routine auditing of the quality system to ensure continued compliance with GVP	
Early Level Professional	Participates in internal and external audits of PV systems for the NRA, industry, and sponsors Assists in compiling of data for inspection reports Supports external compliance monitoring with PV obligations Drafts and writes inspection and audit reports
Mid Level Professional	Prepares, organizes, and conducts internal and external PV systems inspections and writes inspection report Identifies and records non compliances Evaluates and/or approves CAPA plans Provides training to sponsors and industry members on GVP Provides technical advice and guidance to NRA, industry, and sponsors on PV Participates in authoring audit reports of the PV system Ensures that the PV organization replies to any audit findings and institutes appropriate corrective action Ensures that the appropriate, corrective action steps are codified in updated policies and procedures

	Ensures that PV staff are trained on updated policies and procedures
Senior Level Professional	Plans and coordinates the conduct of internal audits of sponsors and regulatory authorities Communicates with senior management on audits and updates Develops and implements training on SOPs governing the PV center to all employees
VD-3 Dissemination of information related to the risk benefit ratio	
Communication with regulators, medical professionals, patients, journalists, and the general public regarding changing risk benefit ratios	
Early Level Professional	Ensures that safety communications deliver relevant, clear, and accurate information to the right audiences Ensures that safety communications are tailored to the appropriate audience, i.e. healthcare professional versus professionals Ensures coordination and cooperation among the different parties involved in issuing safety communications Ensures that information on risks be presented in the context of risk to benefit ratios Ensures that safety communications comply with all relevant regulations Coordinates with regulatory authorities regarding the need and content of any press releases Ensures that safety information disseminated online via social media is accurate Ensures that procedures are in place for the communication of safety information Ensures that safety communications are subject to quality control reviews to ensure their accuracy and clarity prior to release
Mid Level Professional	Reviews Direct Healthcare Professional/Provider Communication for a drug, vaccine or biological related issue Reviews manuscripts for publication of an ADRs/AEFIs or a series of events in a scientific journal Reviews patient information leaflets for distribution by health care professionals for drug, vaccine or biological related problems in appropriate language and format suitable for multi-lingual and diverse literacy levels Carries out and critique systematic literature reviews of the potential risk of drugs, vaccines, and biologics Participates in design and implementation of vaccine public campaigns
Senior Level Professional	Facilitates and coordinates the response to crisis in PV, e.g., a sudden

	batch of unexpected ADRs/AEFIs Designs and appraises risk communication plans for healthcare workers and the public
VD-4 Quality Management System (QMS)	
Early Level Professional	Strong understanding of, and commitment to, the QMS and the associated activities Participates in delegated QMS activities
Mid Level Professional	Conducts internal audits of the regulatory authority and sponsors Contributes to the development and update of guidelines on GVP Provides training to NRA, industry, and sponsors on good pharmacovigilance practices
Senior Level Professional	Manages the development and documentation of the regulatory authority's QMS (quality plans, quality manuals, and quality records) Develops and maintains risk-based PV audit plans Ensures that internal GVP policies and procedures are updated on a timely basis to reflect external regulatory changes Ensures that the PV system is assessed on a regular basis for effectiveness Ensures that the PV system is updated when improvements are necessary based on internal assessments and audits Ensures that PV staff is trained when improvements are implemented
VD-5 PV Intelligence	
Applies Pharmacovigilance Intelligence in regulatory strengthening	
Early Level Professional	Gathers information-related changes in regulatory landscape related to PV Applies the global safety regulations for vaccines and biologics
Mid Level Professional	Monitors and scans the regulatory environment for potential sources of PV information on vaccines and biologics Detects early warning signs that impact vaccines and biologics Identifies knowledge gaps in safety regulations for vaccines/biologics
Senior Level Professional	Develops strategies for collection of PV intelligence Implements changes in regulatory requirements that may impact vaccines and biologics Communicates changes in regulatory landscape to inform regulatory strengthening/policy change
VD-6 Use of Apps for PV	

Utilization of smart phone mobile applications for adverse drug reaction/reporting	
Early Level Professional	Reviews the utility of smart phone applications for adverse drug reporting with the staff of the PV center Evaluates the utility of smart phone applications for adverse drug reporting Creates awareness on availability of smart phone applications for adverse drug reporting Participates in the review of existing smart phone applications for adverse drug reporting and selects the best application for the PV center
Mid Level Professional	Oversees the implementation of a smart phone app system when viewed as advantageous for the reporting of adverse events Monitors the utility of the smart phone application, once implemented Seeks ongoing input from PV staff on the adequacy of adverse event reporting through smart phone applications Ensures that all existing PV staff members are trained on the smart phone application for adverse drug reporting
Senior Level Professional	Seeks approval for resources, including capital and expenses needed to implement a mobile application Ensures communication and training/education is available to PV staff and others involved in implementation

VIII. References

Numerous references contributed to the concepts and statements in the Competency Framework. It was not possible to link many of the references to a specific statement but instead to a concept included in the competency framework. The reader is directed to an review of all of these documents to provide a complete picture of the background.

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