BIRS Conceptual Models and Concepts for Capacity Building in Vaccine Manufacture

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The BIRS (Biotechnology Innovation and Regulatory Science) Sustainable Medicines in Africa program began in 2014 and was preceded by the Industrial Pharmacy Teaching Unit program beginning in 2008 (Ekeigwe, 2019; Fourman, 2018; Springer et al., 2016, 2017).

Our vision is to provide needed capacity building in order to improve quality of life and promote public health in African sub-regions. Our mission is to ensure access and affordability of quality essential medicines through capacity building with innovative educational programs, research, and pharmaceutical manufacturing in African sub-regions. We are working to ensure continuous availability to patients of quality medicines by:

- enabling pharmaceutical manufacturing in Africa by Africans;
- developing new knowledge that improves human health care in African sub-regions;
- establishing global and local/regional partnerships to build sustainable solutions to provide access to quality medicine.

We are building capability for sustainable medicines in Africa through our educational programs.

Our program began as a four-course certificate consisting of courses in:

- Drug Development
- Good Regulatory Practices
- Quality Management, Audits, and Inspections
- Molecular Basis of Manufacturing

These courses were originally developed at Purdue University by Dr. Michael Schmidt in the 2004 to 2006 timeframe. They were then taught in Africa starting in 2008. During one of the first courses, Dr. John Chilunda remarked in 2008, "*These words have never been spoken on African soil*." These words capture the appreciation of the early students of this program in both the US and Africa. The material presented was well received and assisted the career development of many students.

As the program grew, requests for an MS degree began in both the US and Africa. In the US it was relatively easy to set up the MS because of the numerous professional MS degrees offered at Purdue University. In 2014, the Merck Foundation provided scholarships to students in Africa to begin their MS degree. This highly successful program graduated 21 students in 2016 and an additional 19 students in 2017. The demographics of these two classes are illustrated in Figures 1 and 2.

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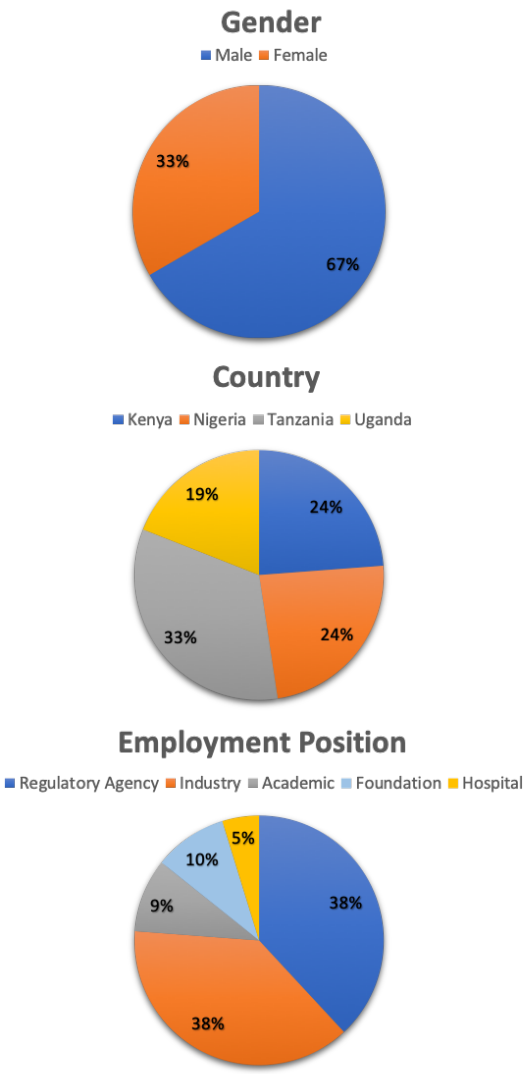

Figure 1. Demographics of 2016 BIRS MS class in Africa.

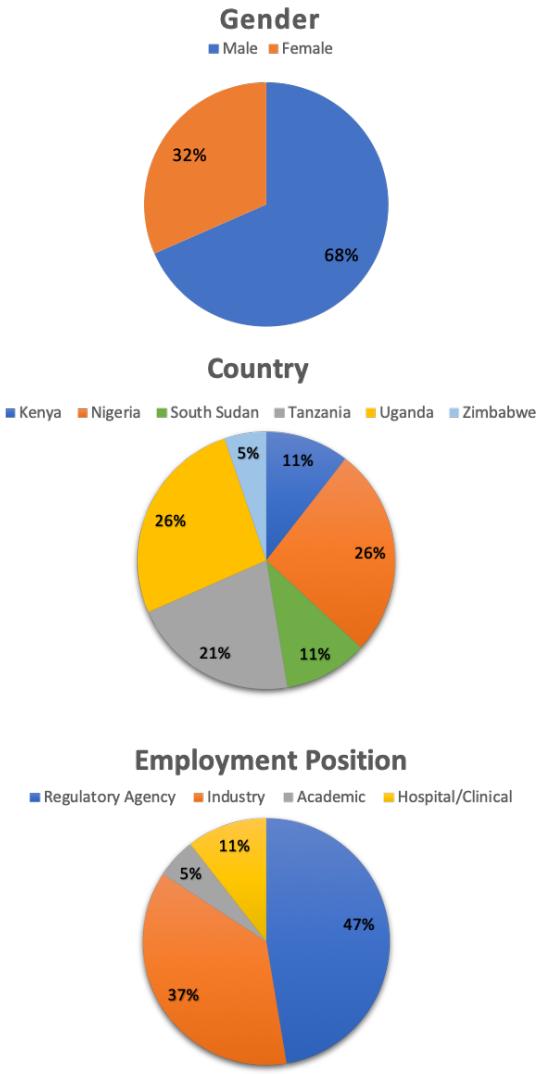

Figure 2. Demographics of BIRS 2017 MS class.

In 2018, the Bill and Melinda Gates Foundation (BMGF) provided funding towards capacity building for the Sustainable Medicines in Africa program. This support enabled scaling the initial efforts from the first two MS cohorts to a third MS cohort. In 2020, an additional 51 students graduated with an MS degree from Purdue University with a concentration in Biotechnology Innovation and Regulatory Science (BIRS). Figure 3 shows the demographics of this class.

The support from the Bill and Melinda Gates Foundation also enabled the transformation of the Industrial Pharmacy Advanced Training Certificate to the Biotechnology Innovation and Regulatory Science (BIRS) certificate program. In August 2020, a new cohort of post-baccalaureate students enrolled in the certificate program. The following year, in 2021, approximately 100 students successfully completed the BIRS post-baccalaureate certificate. This cohort is currently enrolled in the Purdue MS degree program with a concentration in BIRS and projected to graduate during the academic year in 2023-2024.

It is noteworthy that the number of students employed by national regulatory authorities has increased in the last two cohorts (Figure 2, 3). Additionally, the number of women in the last two cohorts has also increased—42% of the most recent class are female (Figure 3). The flexible nature of this program may contribute towards an increase in student diversity since active students do not need to leave their current place of employment. Course activities and content are shared and assessed through synchronous and asynchronous learning sessions delivered both virtually and face-to-face. Working professionals currently employed in both industry and regulatory organizations can participate and persist to graduation---even as they continue to meet both work and family responsibilities.

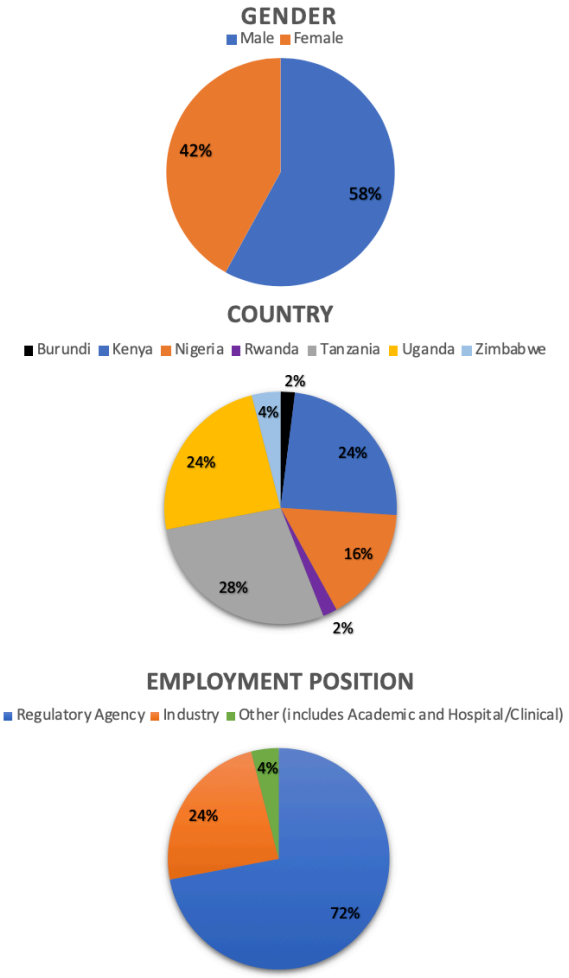

Figure 3. Demographics of BIRS 2020 MS class.

Over 20 employees of Tanzania Medicines and Medical Devices Authority (TMDA) received master's degrees from Purdue University. TMDA is the first regulatory body in sub-Saharan Africa to be recognized by the WHO as a well-functioning regulatory system (Khadem Broojerdi et al., 2020). Now, several other regulatory authorities in Africa have achieved this status.

Innovative Elements of the BIRS Model

There are several key innovations that have been critical to the success and scale of the program thus far.

Previous support from Merck Foundation and the Bill and Melinda Gates Foundation enabled implementation of a non-credit to-credit model for the post-baccalaureate BIRS certificate . A critical component of our model for scale and sustainability includes the option to apply the

four courses completed in the graduate BIRS certificate towards an MS plan of study, upon formal acceptance to the MS degree program. The non-credit to credit model was first implemented in 2020 and then successfully scaled as the current MS student cohort doubled in size.

Another key innovation for the BIRS program includes a Scaffolded Professional Apprenticeship. The Scaffolded Professional Apprenticeship includes individual guidance and mentoring on a project developed and implemented by the student with "just in time" feedback from the faculty. Critical components of the Scaffolded Professional Apprenticeship include:

- Dynamic, flexible, responsive, resilient support network of global experts and resources to equip students to lead projects that address challenges within their organizations and implement sustainable solutions;
- Guided mentorship and coaching from Purdue faculty, industry and regulatory experts, program alumni, to develop research and critical thinking skills and implement evidence-based solutions;
- Development of scientific professional identity as future change agents.

The outcomes for the Scaffolded Professional Apprenticeship provide value to the organization and are distributed to help the student practice and build their research capabilities and technical expertise throughout the duration of the program. It is interesting to note that the BIRS Scaffolded Professional Apprenticehip has similarities to the rWork Integrated Learning concept recently described (Dean et al., 2020).

The project outcomes from the Scaffolded Professional Apprenticeship are documented in a confidential paper following current, academic formatting guidelines and best practices for scholarly work. Students are encouraged to adapt their project papers and disseminate to share with the broader academic community as a part of the BIRS Africa Technical reports in the Purdue Libraries e-Pubs Open Access site (https://docs.lib.purdue.edu/birsafricatr/). A review of these papers shows the breadth and depth of the students' capacity building project efforts, a direct reflection of the broad outcomes from the BIRS Scaffolded Professional Apprenticeship. The technical series is dynamic and continues to grow and evolve as a reflection of the new knowledge and recommendations shared by new alumni from the global BIRS community each semester.

Approximately 40 Purdue BIRS MS alumni have continued their graduate studies into a PhD program. The Purdue Ph.D. students have developed manufacturing methods for essential medicines and are engaged in design-based research using learning sciences methodologies to design and implement professional development programs to meet training needs within their region. Students also collaborate with Purdue faculty and guest speakers in leadership positions from both regional professional quality medicine organizations as well as regulatory and industry leaders from global pharmaceutical and regulatory organizations to develop and implement various aspects of the program. Students serve as peer leaders within the program, building technological, pedagogical, and content knowledge (TPACK), skills, and capabilities, in alignment with their dissertation research focused in capacity building for lower resource settings.

BIRS Competency Concepts for Vaccine Manufacture

Vaccine manufacture is a complex, high-technology endeavor (Juvin, 2019; Plotkin et al., 2017). Vaccine manufacturing is typically built on 4 competencies (Gomez et al., 2013):

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 in 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 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 Courses and Concepts

- 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
  - Lyophilization
  - 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 system
  - 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

Acknowledgements

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