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). This program taught a four-course curriculum consisting of courses in:

- Drug Development
- Good Regulatory Practices
- Quality 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 Africa, the Merck Foundation provided 50 MS degree scholarships to students in Africa. This highly successful program graduated 21 students in 2016 and another 19 students in 2017. The demographics of these two classes are illustrated in Figures 1 and 2.

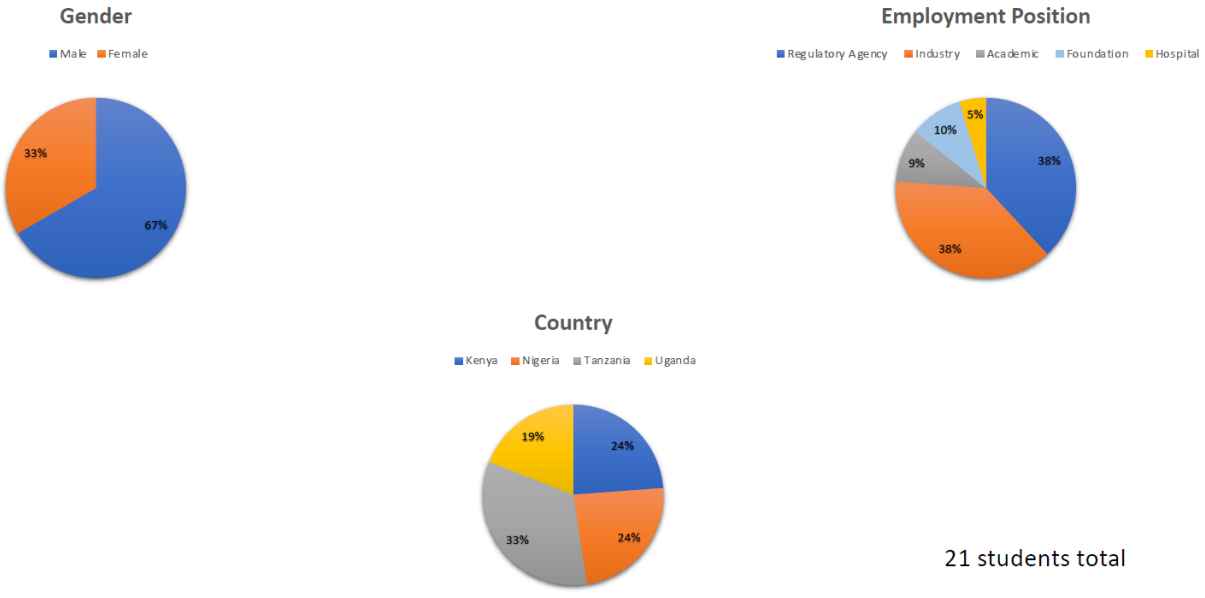

Figure 1. Demographics of 2016 BIRS MS class in Africa.

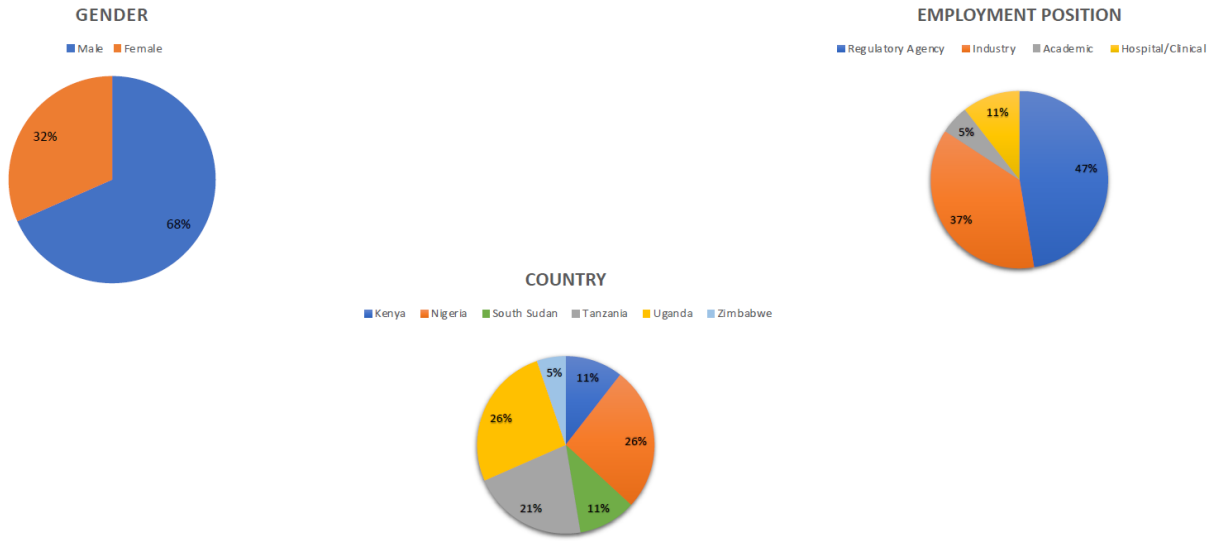

Figure 2. Demographics of BIRS 2017 MS class.

In 2018, the Bill and Melinda Gates Foundation provided scholarships for the next MS class, and about 50 students graduated with an MS degree in 2020. Figure 3 shows the demographics of this class.

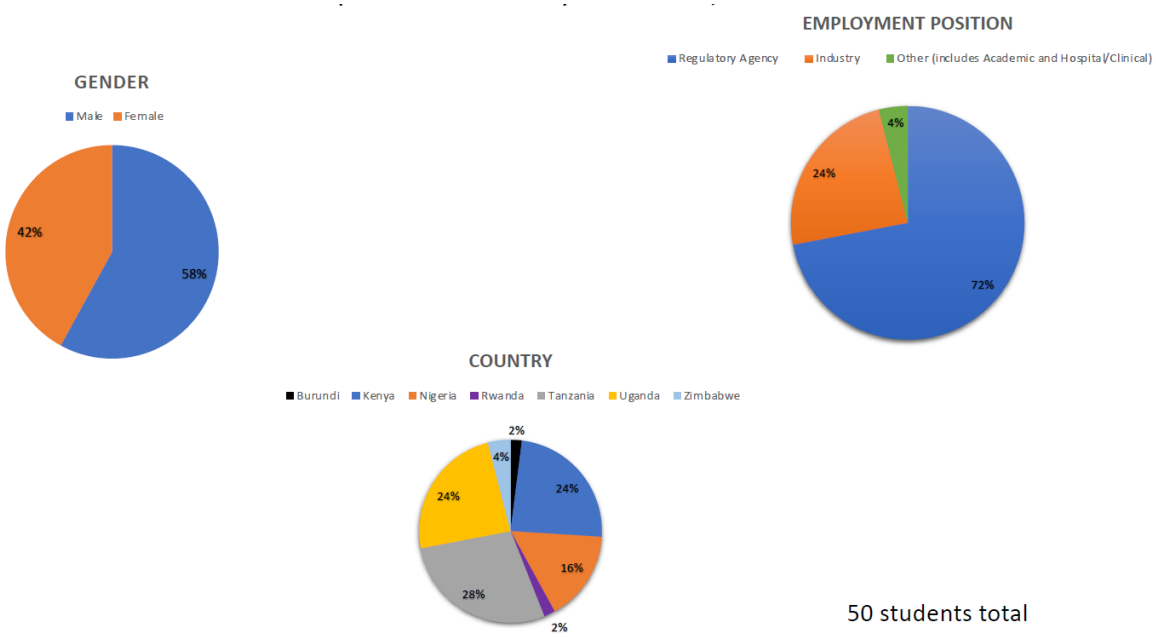

Figure 3. Demographics of BIRS 2020 MS class.

The Bill and Melinda Gates Foundation provided funding to scale capacity-building efforts, and a new cohort of students graduated with a BIRS post-baccalaureate certificate in 2021. Approximately 100

African students are currently enrolled in the Purdue BIRS MS degree program with a concentration in BIRS and projected graduation in 2023.

It is noteworthy that the number of students from regulatory authorities has increased in the last two cohorts. Additionally, the number of women in the last two cohorts has increased with 46% of the most recent class being females. The HyFlex nature of this program, with a significant on-line component, helps students make steady progress towards their degree without leaving their current place of employment and could be a contributing factor for the increase in the number of women. Working professionals currently employed in both industry and regulatory organizations can successfully participate and persist to graduation in the flexible Purdue ABE BIRS graduate program ---even as they continue to meet both work and family responsibilities, including many women with young families.

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.

The BIRS master's degree requires a student project and paper following current, academic formatting guidelines and best practices for scholarly work. Students are encouraged to disseminate their papers and 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 student activities in the BIRS program. The current cohort of about 100 BIRS students are completing their papers now, and these additional papers will be published in the same technical series.

Innovative BIRS Programs

Approximately 50 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 organizations. The PhD students serve as peer leaders within the program to build technological, pedagogical, and content knowledge, (TPACK) skills and capabilities, aligning with the development of their independent proposal for PhD dissertation research focused in capacity building for lower resource settings. 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.

BIRS established a non-credit to-credit model for the post-baccalaureate BIRS certificate with previous support from Merck Foundation and the Bill and Melinda Gates foundation. The certificate program included the four courses listed above. A critical component of our model for scale and sustainability includes the application of the non-credit post-baccalaureate BIRS certificate to the MS plan of study in later semesters. BIRS has successfully scaled this model to the current MS student cohort. Approximately 100 students from the current cohort have completed a 4-course certificate (received in Summer 2021), along with enrollment in four graduate courses towards completion of their MS plan of study (two courses in Fall 2021 and two courses in Spring 2022).

BIRS is also making significant progress in their scaffolded Professional Apprenticeship, a significant component of the program for both previous and current student cohorts. The scaffolded project 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 in work environment 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 project provide value to the organization and help the student practice and build their research capabilities and technical expertise throughout the duration of the program, which results in a distribution of focused MS project time and course time throughout the duration of the program. It is interesting to note that the BIRS program is related to the Work Integrated Learning concept recently described (Dean et al., 2020).

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 a 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 HyFlex format as a mixture of 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

Acknowledgement

The BIRS program would like to gratefully acknowledge the support of UNIDO, the Merck Foundation, and the Bill and Melinda Gates Foundation who made these programs possible. We would like to thank all of the BIRS guest faculty from global industry and regulatory organizations for generously sharing their professional expertise and providing donated, in-kind time towards building the professional skills and technical capabilities of the students within the BIRS program. We are grateful for all of the critical members of the BIRS community—current students, alumni, and leaders throughout regulatory and manufacturing organizations world-wide. Thank you for your tireless contributions and efforts as we continue to learn and grow together to achieve the vision of sustainable medicines for Africa. The international component of the Purdue BIRS program was initiated through educational support provided by the Merck Foundation and most recently through a capacity building effort funded by the Bill and Melinda Gates foundation, grant # 41000460.

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