Siena, Italy

June 2011 – December 2012

MASTERS PROGRAMME IN VACCINOLOGY AND PHARMACEUTICAL CLINICAL DEVELOPMENT

Programme Organized by:

– University of Siena, Medical School
– Novartis Vaccines
– Novartis Vaccines Institute for Global Health

Siena - Italy

SENTRUM·S·UNIVERSITATIS·

NOVARTIS
VACCINES INSTITUTE
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Organisation

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Location & Duration

Novartis Vaccines, Siena, Italy
June 2011 – December 2012

Organized by

Preface

Vaccination has improved health in the world in an unparalleled way and has saved over 20 million lives in the last 2 decades. And yet, every year more than 3 million people, mostly children, die from vaccine preventable diseases. Preventable infectious diseases present a daily risk especially in countries where poverty and economic issues are the root cause for poor health care.

Immunization has proven to be one of the most cost effective interventions in health care systems. But it must be well planned, implementation must ensure high coverage, must be sustainable, and must have a reliable surveillance system. Just few years ago immunization programmes used few vaccines that had been developed decades ago. Major advances in immunology and biotechnology over the last decade have brought several new vaccines to reality.

This Masters Programme aims to provide to physicians with interest in public health and infectious diseases the opportunity to learn about vaccine preventable diseases, immunization impact, vaccine development and the roles of various stakeholders such as academia and governing authorities in vaccine policy setting and immunization programmes, focusing is developing countries.

Sue Ann Costa Clemens

Director Novartis Vaccines Academy

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First references to the university of Siena date back to 1240, making it one of the most ancient academic institutions in Europe. In 1357 Emperor Charles IV included Siena among the official universities of the Holly Roman Empire. Today, the University of Siena runs a wide selection of graduate and postgraduate courses, including doctoral degree programmes, specialization schools and masters programmes.

In 2009 the University of Siena and Novartis Vaccines have established a novel specialization programme for medical graduates, "The Masters Programme in Vaccinology and Pharmaceutical Clinical Development".

" Knowing is not enough; we must apply.
Willing is not enough,we must do."

Goethe

Goals

- Capacity building in vaccinology and vaccine development in developing countries.
- Prepare students for a career in academia, public health and Research & Development (R&D) in public and private vaccine institutes in developing countries.

Concept

- Provides Graduates in Medicine with training in epidemiology and disease burden of vaccine preventable infectious diseases, vaccine development from research to licensure and vaccine policy and funding.
- Is a collaborative effort between academia and vaccine industry.
- Combines classroom sessions by external and internal scientists with practical involvement in vaccine development and academia.
- The Masters course is conduced in English and is composed by:
    1. A complete one year course which includes lectures on all relevant disciplines of vaccinology and clinical development and a practical training at the University Hospital of Siena;
    2. A 6 month internship within different departments of the Novartis Vaccines development and divisions field trainings at various investigational sits involved with vaccine trials.

At the end of the Masters, following submission and discussion of a thesis, the students will receive a M. Sc. degree from the University of Siena.

Application and Selection Process

Entry requirements:

- University degree in Medicine.
- Minimum 2 years post-graduation or residency in clinical medicine.
- Excellent command of English, written and spoken.

To apply for the Masters in Vaccinology please send, before 15 December:

- Curriculum vitae and a letter of motivation in English to: vaccines_master.nvdit@novartis.com
- CV: must specify medical school, courses attended, specialization and or post graduation/ residency courses and employment career.
- Documents will be evaluated and candidates will be contacted for further interviews.

For information please contact:

- Masters Programme in Vaccinology and Pharmaceutical Clinical Development
  Novartis Vaccines S.r.l.
  Via Fiorentina 1, Siena, Italy – 53100
  E-mail: vaccines_master.nvdit@novartis.com

Funding:

- A 18 months grant will be provided to students who are accepted.

Overview of Modules

First Year

– Module I: Public Health, Immunization and Vaccine Development Process
– Module II: Vaccine Immunology and Preclinical Research
– Module III: Infectious Diseases and Vaccine Prevention
– Module IV: Vaccine Manufacturing and Quality Control Processes
– Module V: Clinical Development Methodology and Pharmacovigilance
– Module VI: Biostatistics and Clinical Data Management
– Module VII: Good Clinical Practices and Clinical Quality Assurance
– Module VIII: Clinical Trials Operations
– Module IX: Regulatory Affairs
– Module X: Policies and Recommendations for Vaccines in the World
– Extra Curriculum Modules: Special Topics

Second Year

– Internships
– Thesis

Students Evaluation

Students will be evaluated during and after each module:

First Year

- Written assignments
- Written tests
- Oral tests
- Oral presentations

Second Year

- Each student will have a supervisor during the internship programme.
- Students will have objectives for the departments they are assigned.
- Supervisors will evaluate students via seminars, performance appraisals.

Thesis

- Each student will select a subject for a written thesis.
- The thesis will be submitted to University of Siena for oral and written evaluation at the end the second year.

MODULE I

Public Health, Immunization and Vaccine Development Process

Duration: *70 h* Semester: *1*

Module Directors:

- *Prof. Emanuele Montomoli - Dept of Physiopathology Experimental Medicine, Public Health, University of Siena*
- *Prof. Sue Ann Costa Clemens - Director Novartis Vaccines Academy*

Aim: *To get a general overview on immunization and public health in the world and to understand the overall principles of pharmaceutical clinical development process from research to the market.*

Content

– The role of vaccine in public health.

– Role of steakholders
- Governments, NGO's, Supranational Organizations
- Academia
- Vaccine industry

– Vaccine development process
- From research to licensure and recommendations.
- How vaccine companies function.
- How to manage projects in vaccine companies.

MODULE II

Vaccine Immunology and Pre Clinical Research

Duration: *100 h* Semester: *1*

Module Directors:

- *Prof. Gian Maria Rossolini - Dean Medical School, University of Siena, Italy*
- *Dr. Giuseppe Del Giudice - Global Head Translational Medicine, Novartis Vaccines*
- *Dr. Emanuela Palla - Head Early Development Projects, Novartis Vaccines*

Aim: *To understand the basic concepts of immunology, immune response to vaccines and how to translate this into vaccine production and licensing.*

Content

– Human Immune response
- Innate immunity
- B- cell and T- cell responses
- How to measure B and T cell function

– Identification of vaccine targets
- Antigen structures as potential vaccine candidates
- Conventional and novel approaches to vaccine development

– Type of vaccines

– The role of adjuvants

– Pre clinical evaluation of vaccine immunology and safety

– Analysis of immune response to vaccines in humans
- Antibody response and correlate of protection
- Functional assays versus quantitative assays
- Scientific and regulatory constrains of serological endpoints

MODULE III

Infectious Diseases and Vaccine Prevention

Duration: *150 h* Semester: *1*

Module Directors:

- *Prof. Roberto Gasparini - Director Public Health Department, University of Genoa, Italy*
- *Dr. Audino Podda - Head Clinical Development & Regulatory Affairs, Novartis Vaccines Institute for Global Health*

Aim: *To have an understanding of vaccine preventable diseases, epidemiology and vaccine clinical development.*

Content

– Vaccine preventable diseases
– Epidemiology and disease burden
– Historical background to vaccination
– Licensed vaccines
– New vaccines under development

MODULE IV

Vaccine Manufacturing and Quality Control Processes

Duration: *70 h* Semester: *1*

Module Directors:

- *Prof. Emanuele Montomoli - Dept of Physiopathology Experimental Medicine, Public Health, University of Siena*
- *Dr. Massimo Bugnoli - Technical Operations, Novartis Vaccines, Siena*

Aim: *To get an understanding of concepts , methods and challenges of technical operations and quality of vaccine manufacturing.*

Content

– History of vaccine production, challenges and advances

– Production processes in bacterial and viral vaccines
- Working seed, bulk formulation, filling and packaging
- Products in development
- Industrialization (scale-up)
- From idea to product

– Organization
- Procedures and flows in manufacturing and control vaccines
- Plant structure and layout, shifts

– Quality and the importance of Good Manufacturing Practices (GMP) to guarantee an immunogenic and safe product
- Selection of raw materials
- Systems as tools to monitor and control quality

– Labeling and packaging

– Differences between vaccine and pharmaceutical production

MODULE V

Clinical Development Methodology and Pharmacovigilance

Duration: *175 h* Semester: *1*

Module Directors:

- *Prof. Franco Laghi Pasini - Department of Medicine and Immunological Sciences, University of Siena*
- *Dr. Giovanni Della Cioppa - Head Clinical Development, Novartis Vaccines*

Aim: *To understand the basic principles of clinical development in pharmaceutical industry and of clinical trial methodology, specially in vaccine development.*

Content

– Overview of the clinical development
- Clinical development plans
- Phases of the clinical development process: Phase I - II - III - IV trials
- Experimental studies (clinical trials) vs. epidemiological (observational) studies
- Safety, immunogenicity, efficacy
- Life-cycle management of a product
- Geographical, logistical & economical considerations

– Clinical trial methodology and protocol development
- Why clinical trials? Variability of biological phenomena and measurement errors
- Defining the treatment effect
- The choice of the sample: which subjects, how many subjects
- The choice of treatments: study treatments, concomitant treatments
- Experimental designs
- The protocol approval processes: internal, external, amendments

– Ethical considerations in clinical development

– Health economics considerations in clinical development

– Clinical study reports
- Content
- Report writing principles
- Quality control and approval processes: internal, external

– Safety reporting and pharmacovigilance
- Benefit-risk assessment and Management
- Adverse Events (AEs), Serious Adverse Events (SAEs), Suspected Unexpected Serious Adverse Reactions (SUSARs)
- Expedited reporting, annual safety reports to regulatory authorities
- Psurs

– Pitfalls & challenges in clinical development
- Cost-benefit, logistical issues, patents, competition, supply problems, seasonal vaccines

MODULE VI

Biostatistics and Clinical Data Management

Duration: *80 h* Semester: *2*

Module Directors:

- *Prof. Stefania Rossi – Department of Physiopathology Experimental Medicine & Public Health, University of Siena*
- *Dr. Uwe Nicolay - Head Biostatistics, Novartis Vaccines*

Aim: *To understand basic concepts of statistics and data management for clinical trials testing vaccines.*

Content

– Statistical methodology for clinical trials

- Basics, ICH guidelines (E8, E9, E10), EMEA/FDA guidelines
- Descriptive vs. inferential statistics
- Importance of randomization to avoid bias
- Power & sample size calculations for hypothesis testing
- Superiority, equivalence, non-inferiority
- Designs & analytical approaches
- Endpoints (measures and variables), surrogate, markers
- P-values: statistical and clinical significance
- Statistical analysis plan
- Interim analyses, meta analyses
- Alignment of protocol, data collection and reports

– Clinical Data Management

- Case Report Form (CRF) design
- Electronic Data Capture and paper CRF processes and systems
- Database design and setup with edit checks, rules and derivations
- Validation of computerized systems for data management
- Data collection and data cleaning
- Data integration (e.g. lab data transfers)
- Data quality, database lock, post database lock changes
- Adverse Event reporting
- Coding dictionaries (MedDRA, WHO-drug)

MODULE VII

Good Clinical Practice and Clinical Quality Assurance

Duration: *50 h* Semester: *2*

Module Directors:

- *Prof. Stefano Gonelli - Department of Internal Medicine, University of Siena*
- *Dr. Elisabetta di Martino - Senior Manager Global Clinical Quality Assurance, Novartis Vaccines*

Aim: *To understand the requirements and to ensures quality in clinical trials execution.*

Content

– Introduction to Good Clinical Practice (GCP)

- Regulatory requirements, ICH and GCP and regional differences
- Roles and responsibilities of sponsors, investigators and monitors
- The importance of the Informed Consent
- Essential documents

– Elements of the Clinical Quality System

- Quality Policies and Quality Manual
- Standard Operating Procedures (SOPs)
- Qualification and training of staff
- Qualification of third parties (Contract Research Organizations (CROs)
- Trial Master File
- Auditing: Internal and external auditing, system audits

– Regulatory inspections

- Preparation of an inspection (sponsor and site)
- Types, procedure, reports
- Frequent findings

MODULE VIII

Clinical Trials Operations

Duration: *100 h* Semester: *2*

Module Directors:

- *Prof. Emanuele Montomoli - Dept. of Physiopathology Experimental Medicine, Public Health, University of Siena*
- *Elisa Marchetti - Head Clinical Operations and Training, Novartis Vaccines Institute for Global Health*

Aim: *To understand the operational requirements for planning and executing vaccines clinical trails.*

Content

– Introduction
- From protocol to clinical study report
- Clinical project management & planning

– Clinical trials preparation
- Protocol, Informed Consent Form and related documents
- Labeling & packaging of vaccines
- Site qualification
- Clinical research organizations (CRO)
- Documentation

– Clinical trial execution
- Initiation visit
- Monitoring
- Safety
- Study closure

– Operational systems and processes
- Trial management systems
- Efficiencies and quality control in process

MODULE IX

Regulatory Affairs

Duration: *70 h* Semester: *2*

Module Directors:

- *Prof. Antonio Nicita - Department of Economics, University of Siena*
- *Edward Thomas Reilly - Head Regulatory Affairs for Europe and International, Novartis Vaccines*

Aim: *To understand international regulatory environment and requirements related to obtaining approval for marketing vaccines and the maintenance of these licenses.*

Content

– Introduction
- General overview of main Competent authorities (FDA,EMA,MHLW)
- International Conference on Harmonization (ICH)

– Drug development life cycle from a regulatory perspective
- Preclinical
- Phase I – initial safety
- Phase II – proof of concept, dose ranging
- Phase III – efficacy, large scale safety
- Post Approval Commitments – studies to detect rare vaccine Adverse Events, impact studies; epidemiology
- Health Authority review and approval procedures

– Regulatory systems
- US regulatory system
- EU regulatory system
- WHO prequalification process
- Other selected regulatory systems

– Product labeling
- U S Package Insert
- EU Summary of Product Characteristics
- Package Inserts and labels, what needs to be included

– Regulatory differences between classical drugs and biologics

– Promotional compliance

– Regulatory Inspections

MODULE X

Policies and Recommendations for Vaccines in the World

Duration: *50 h* Semester: *2*

Module Directors:

- *Prof. Paolo Bonanni - Department of Public Health, University of Florence*
- *Dr. Joe Schmitt - Head Medical Affairs Europe, Novartis Vaccines*

Aim: *To understand the introduction of new vaccines into the immunisation calendars of different countries is dependent on a number of local and international factors.*

Content

– Factors influencing introduction of new vaccines in different countries

- Epidemiology
- Health economics
- Priority settings
- National Immunization Committees
- Vaccine schedules
- National budgets

– Financing mechanisms

- GAVI, AMCs, Revolving Fund – PAHO, others

– Policies and recommending authorities

- WHO, UNICEF, PAHO, local and Regional Technical Advisory Groups

Specials Topics

– How to read and interpret scientific papers
– How to search scientific databases and websites
– How to write a clinical trial protocol and protocol synopsis
– How to write grants and where to apply
– How to write a thesis
– Presentation skills
– Communication
    • Crisis management (clinical studies, SAEs, marketed products)
– Marketing overview of private and public markets