



UNIVERSITÀ
DI SIENA 1240

Master in Vaccinology and Pharmaceutical Clinical Development

2017 - 2018

5th Edition



Piazza del Campo, Shutterstock, Early Morning View of Beautiful Campo Square 41365712, author CHEN MIN CHUN

Sponsored by **BILL & MELINDA GATES foundation**



SANOFI PASTEUR



valneva

GlaxoSmithKline



Official Program of the University of Siena in collaboration with **FONDAZIONE SCLAVO**

master.vaccines@unisi.it

Organization

University of Siena in collaboration
with Fondazione Achille Sclavo
ONLUS

Venue

University of Siena – Santa Chiara
College – Refugio building, Siena -
Italy

Duration

June 2017 – December 2018

Sponsors

BILL & MELINDA
GATES foundation



SANOPI PASTEUR 



 valneva

GlaxoSmithKline



Letter from the directors



Prof. Sue Ann Costa Clemens

*Prof. of Pediatric Infectious Diseases
Head of Institute for Global Health
Director Master Program in Vaccinology, Dept. of
Molecular and Developmental Medicine, University of
Siena*



Prof. Emanuele Montomoli

*Prof. Public Health, Dept. of Molecular and Developmental
Medicine – University of Siena, Italy*

To this date much of the developing world poses many challenges to enjoying life free of vaccine preventable diseases; despite most government's good-will and the desire to ease the burden of these diseases. To achieve this goal, developing countries need to have native, well-rounded professionals in the fields of immunization, public health and infectious diseases. Professionals who can appreciate the impact of vaccine preventable diseases from different angles: value of vaccines, vaccine research and development, vaccine safety, vaccine procurement and vaccine delivery. Likewise, health care professionals from developed countries would benefit for themselves and would contribute to global health by more in-depth understanding of the contribution of immunization and vaccines to global development.

The Master Program in Vaccinology and Pharmaceutical Development provides high quality education involving key opinion leaders from around the world. This program, which started in 2008, has graduated more than 30 students from the developing world who are now making a difference in their countries. This year, 15 new Vaccinology professionals from Africa, Asia and Latin America will go back to their countries to start new careers. We are confident that very soon we will see the impact that they will have through their contributions.

This program demands excellence in every aspect, from the worldwide expertise of the teaching staff to the student's level of commitment and dedication. We are particularly impressed with their true desire to learn, improve and make a difference in their countries.

The success of this program is a collaborative effort and a unique partnership between industry and academia to help developing countries to overcome some of the gaps in vaccinology, via a very solid tool - Education. This program helps the countries to build their own resources, to disseminate knowledge, to develop new professionals and especially helps the developing countries to be independent on key aspects such as pharmacovigilance, regulatory and epidemiology.

Sincerely,

Prof. Dr. Sue Ann Costa Clemens

Prof. Emanuele Montomoli



The Master Program Our Vision

People in developing countries need life-saving vaccines – and they need them now.

But making this happen is not simple. It requires trained professionals to rollout effective national immunization plans, to generate local clinical data on vaccine safety and efficacy, and to share their public health expertise with others.

This means equipping local experts with internationally recognized skills.

Through our Master Program in Vaccinology and Pharmaceutical Clinical Development, young doctors develop the valuable scientific and practical knowhow they need to join the new generation of public health leaders in developing countries.

Every two years, we select and train the best medical graduates from developing countries across the globe – countries that are most in need of having access to vaccines at low costs.

Graduates of our program return home with a better understanding of their countries' epidemiology and public health needs. And with their top-class knowledge and skills, they bring hope where it is needed most.

The Master Program of the University of Siena offers a **hope for development**.

| | |
|--|----|
| The Master Course | 4 |
| Program overview | 5 |
| Module I: Public health, immunization and vaccine development process | 6 |
| Module II: Vaccine immunology and preclinical research | 7 |
| Module III: Vaccine manufacturing and quality control processes | 8 |
| Module IV: Infectious diseases and vaccine prevention | 9 |
| Module V: Clinical Development Methodology, Biostatistics and Clinical Data Management | 10 |
| Module VI: Pharmacovigilance | 12 |
| Module VII: Epidemiology | 13 |
| Module VIII: Clinical Quality Assurance and Clinical Trial Operations | 14 |
| Module IX: Regulatory Affairs | 15 |
| Module X: Policies and recommendations for vaccines in the world | 17 |
| Seminars | 18 |
| How to proceed..... | 19 |



A HOPE FOR DEVELOPMENT

The Master Course

Goals

- Capacity building in vaccinology and vaccine development;
- To prepare students for a career in academia, public health and research and development in public and private vaccine institutes.

Concept

- Provide graduates in medicine a Master degree in vaccinology via a tailor-made training in immunization, public health and vaccine development. The program is very extensive and complete, covering subjects from epidemiology, health economics, disease burden of vaccine preventable infectious diseases, vaccine development from research to licensure and vaccine policy and funding;
- Collaborative effort between academia and vaccine industry;
- 18-month program, combining theoretical and practical training. The faculty members are worldwide experts from academia, well known international universities, supranational organizations and industry:
 - WHO, PATH, EMA, BMGF, GAVI, PEI, IVI, CDC, ECDC, EU Commission, DCVMN, ADITEC, Achille Sclavo Foundation; Sabin Institute, Bio-Manguinhos / Fiocruz, DoH UK and Italy, FAMHP Belgium, Wellcome Trust, CHERMID, MRC Gambia, Brighton Collaboration;
 - Johns Hopkins Institute, Baltimore, US; Institute Pasteur, Paris, France; Erasmus Medical Center, Rotterdam, Netherlands; Imperial College, London, UK; Karolinska Institute, Stockholm, Sweden; Swiss Tropical Institute, Basel, Switzerland; Carlos Chagas Institute, Rio de Janeiro, Brazil; and other prominent universities and academic institutions from Austria, Belgium, Canada, Germany, Ghana, Greece, Finland, Italy, Mali, Spain, South Africa, UK, US;
 - GSK, Novartis, Takeda Vaccines, Sanofi-Pasteur, Pfizer, Roche, GRID Europe & Asia, FIDEC, VisMederi; G-Con, BLF councils, 4Clinics.

Program overview

Program agenda (11 months)

- Module I: Public Health and Vaccine Development Process;
- Module II: Vaccine Immunology and Preclinical Research;
- Module III: Vaccine Manufacturing and Quality Control Processes;
- Module IV: Infectious Diseases and Vaccine Prevention;
- Module V: Clinical Development Methodology, Biostatistics and Clinical Data management;
- Module VI: Pharmacovigilance;
- Module VII: Epidemiology, Health Systems and Economics;
- Module VIII: Good Clinical Practices, Clinical Quality Assurance and Clinical Trial Operations;
- Module IX: Regulatory Affairs;
- Module X: Policies and Recommendations for Vaccines in the World;
- Extra Curriculum: parallel educational seminars for personal and professional development.

Internships (7 months)

Students will spend:

- 1 month at the University of Siena within its different departments at the university hospital and public health centers;
- 6 months within different departments of the sponsors and collaborative institutions, followed by investigational site training.

Thesis

- Each student selects a subject for a written thesis;
- The thesis will be submitted to the University of Siena Medical School and evaluated by a panel of experts (written and oral presentation) during the public thesis defense at the end of the 18-month program

Graduation

- In order to graduate and receive the official University Master Degree, the students shall pass the following steps:
 - First step: students have to pass the written exams in each of the 10 modules, achieving the official minimum grade to proceed to the thesis defense;
 - Second step: students have to achieve the minimum thesis grade.

Module I: Public health, immunization and vaccine development process

Directors

Prof. Dr. Emanuele Montomoli

Prof. Public Health, Dept. of Molecular and Developmental Medicine, University of Siena, Italy

Prof. Dr. Sue Ann Costa Clemens

Prof. of Pediatric Infectious Diseases

Head of Institute for Global Health

Director Master Program in Vaccinology, Dept. of Molecular and Developmental Medicine, University of Siena

Aim

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

Contents

- Public Health basic concepts;
- The role of vaccines in public health;
- Role of stakeholders;
- 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 preclinical research

Directors

Prof. Dr. Emanuele Montomoli

Prof. Public Health, Dept. of Molecular and Developmental Medicine, University of Siena, Italy

Prof Jean Paul Prieels

CEO, JPP Consulting, Brussels, Belgium

Aim

To understand the basic concepts of immunology and immune response to vaccines.

Contents

- Historical background to vaccination:
 - 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;
 - Functional assays versus quantitative assays.

Module III: Vaccine manufacturing and quality control processes

Directors

Prof. Dr. Emanuele Montomoli

Prof. Public Health, Dept. of Molecular and Developmental Medicine, University of Siena, Italy

Dr. Rahul Singhvi

Chief Operating Officer, Takeda Vaccines Inc, Deerfield, USA

Aim

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

Contents

- Short history of Vaccines Manufacturing
- Differences between Pharma and Vaccines
- Objectives of production
 - Clinical lots
 - Market supply
- Regulatory Compliance
- Fundamental Pillars of Manufacturing
- Concepts in vaccines manufacturing present and future
- Process Development
- Technical transfer, scale up, cost of goods, supply chain, engineering
- Quality Control
- Analytical Characterization and lot potency
- Viral production
- Quality Assurance / inspections

Module IV: Infectious diseases and vaccine prevention

Director

Prof. Giuseppe Buonocore

Principal of Pediatrics and Neonatology, Siena Hospital, University of Siena, Italy

Prof. Dr. Sue Ann Costa Clemens

Prof. of Pediatric Infectious Diseases
Head of Institute for Global Health
Director Master Program in Vaccinology, Dept. of Molecular and Developmental Medicine, University of Siena

Prof. Steve Black

Professor of Pediatrics, Center for Global Health, University of Cincinnati Children's Hospital, Cincinnati, USA

Aim

To get familiar with the most important vaccine preventable infectious diseases from a clinical and from a global epidemiological perspective.

To learn which vaccines are already available against these infectious diseases and which new vaccines are being developed.

Contents

- Bacterial diseases: clinical profile, epidemiology, and vaccines:
 - Diphtheria, Tetanus, Pertussis, Haemophilus influenza type b disease, Meningococcal disease, Pneumococcal disease, Lyme disease, Borreliosis, Group A Streptococcal disease, Group B Streptococcal disease, Staphylococcal disease, Tuberculosis, Helicobacter pylori infection, Cholera, Enterotoxigenic Escherichia coli, Salmonellosis, Shigellosis, Others
- Viral diseases: clinical profile, epidemiology, and vaccines:
 - Hepatitis A, B, C and E, Measles, Mumps, Rubella, Varicella & Zoster, Influenza & Pandemic Influenza, Respiratory syncytial virus, Cytomegalovirus, HIV/AIDS, Tick Borne encephalitis, Japanese encephalitis, Yellow Fever, Dengue Fever, Rabies, Human papillomavirus, Herpes Simplex virus, Rotavirus, Ebola, Malaria, Noroviruses

Module V: Clinical Development Methodology, Biostatistics and Clinical Data Management

Director

Prof. Salvatore Grosso

Prof. of Pediatrics, Siena Hospital, University of Siena, Italy

Dr. Astrid Borkowsky

Head of Clinical Development, Vaccines, Takeda Pharmaceuticals, Berlin, Germany

Aim

To understand the basic principles of clinical trial methodology, especially in vaccine development. To understand basic concepts of statistics and data management for clinical trials.

Contents

- 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;
 - Life-cycle of a product;
 - Geographical, logistical & economic considerations.
 - Clinical trial methodology and protocol development:
 - Why clinical trials? Variability of biological phenomena and measurement errors;
 - Defining the treatment effect: from measurements to end-points;
 - 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.
- Vaccine trial methodology:
 - Safety, immunogenicity, efficacy and effectiveness;
 - Surrogate end-points, correlates of protection and constraints of serological end-points;
 - Ethical considerations in clinical development.

- Statistical methodology for clinical trials:
 - Basics, International Conference on Harmonization (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 (Medical Dictionary for Regulatory Activities [MedDRA], WHO-drug).

Module VI: Pharmacovigilance

Directors

Prof. Dr. Emanuele Montomoli

Prof. Public Health, Dept. of Molecular and Developmental Medicine, University of Siena, Italy

Dr. Bernadette Hendrickx

CEO and Founder of SAHB Consulting, Wavre, Belgium

Dr. Corinne Jouquelet-Royer

VP, Head Global Pharmacovigilance - Sanofi Pasteur, Lyon, France

Aim

To understand main rational, best practice and present overview on Pharmacovigilance systems in the world. The learning is focused on: how to write an individual case narrative, how to assess causality and expectedness of cases, how to determine certainty of diagnosis according to Brighton collaboration guidelines.

Contents

- Introduction to clinical safety, Pharmacovigilance and benefit-risk management;
- Clinical safety in the Developing World;
- Statutory basis for safety in humans:
 - Historical basis; Governing bodies and Health Authorities: ICH, Council for International Organizations of Medical Sciences (CIOMS), WHO; Safety data collection in clinical trials; Spontaneous adverse events;
- Adverse Events:
 - Definitions and classification; Processing, archiving and retrieval; Assessment: expectedness, listedness, causality and reference documents; Analysis and decision-making; Regulatory Reporting;
- Life-Cycle Clinical Product Safety:
 - Discovery and pre-clinical science; Pre and post authorization clinical safety; Structured benefit-risk assessment and management; Safety strategy, issue management and crisis prevention; Communication in Pharmacovigilance

Module VII: Epidemiology

Directors

Prof. Felice Petraglia

Prof. Gynaecology - Dept. of Molecular and Developmental Medicine, University of Siena, Italy

Dr. John Weil

Lead epidemiologist for dengue and norovirus at Takeda Vaccines Business Unit, Takeda Vaccines, Zurich, Switzerland

Michael Greenberg

VP Head Global Medical Franchise Strategy, Sanofi Pasteur, Lyon, France

Aim

To understand basic principles of Epidemiology and Health Economics and the relevance for vaccine development.

Contents

- Epidemiology;
- Principles of infectious diseases epidemiology;
- Measures of disease occurrence;
- Measures of impact;
- Sensitivity - specificity;
- Observational studies: cohort and case-control, alternative designs, how to write a study protocol, choice of a reference group, synthesis causal inference, sampling;
- Methodology: matching, bias, confounding, third factor, disentangling;
- Calculations - analysis: sample size calculation, significance, logistic regression;
- Surveillance: principles of surveillance, event based surveillance, analytical tools in surveillance, lab-based surveillance, evaluation of surveillance.

Module VIII: Clinical Quality Assurance and Clinical Trial Operations

Director

Prof. Franco Laghi Pasini

Principal of Internal Medicine, Siena Hospital, University of Siena, Siena Italy

Dr. Luis Rios Nogalis

VP and Head, Global Development Delivery and Operations, Takeda Vaccines Inc. Deerfield, USA

Aim

To understand the requirements and to ensure quality in clinical trials execution and the operational requirements for planning and executing vaccines clinical trials.

Contents

- 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.
- Introduction to Clinical Trial Operations (CTO):
 - 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; Database lock and close-out data management activities;
- Operational systems and processes:
 - Trial management systems; Efficiencies and quality control in process; Clinical Study Report.

Module IX: Regulatory Affairs

Directors

Prof. Franco Laghi Pasini

Principal of Internal Medicine, Siena Hospital, University of Siena, Siena Italy

Dr. Anne-Marie Georges

Independent Consultant, Regulatory Affairs - Cahors, France

Dr. Bernadette Hendrickx

CEO and Founder of SAHB Consulting, Wavre, Belgium

Aim

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

Contents

- Introduction:
 - General overview of main competent authorities (FDA, EMA, MHLW); International Conference on Harmonization (ICH).
- Drug development and life cycle from a regulatory perspective:
 - Preclinical; Phase I – initial safety; Phase II – proof of concept, dose ranging; Phase III – efficacy, large scale safety;
 - Regulatory constraints of serological endpoints;
 - 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:
 - US Package Insert;
 - EU Summary of Product Characteristics;
 - Package inserts and labels, what needs to be included?

- Regulatory differences between drugs and biologics;
- Promotional compliance;
- Regulatory Inspections

Module X: Policies and recommendations for vaccines in the world

Directors

Prof. Paolo Bonanni

Dept. Public Health, University of Florence, Italy

Prof. Dr. Sue Ann Costa Clemens

Prof. of Pediatric Infectious Diseases

Head of Institute for Global Health

Director Master Program in Vaccinology, Dept. of Molecular and Developmental Medicine, University of Siena

Dr. Stefano Malvoti

Managing Director MMGH Consulting for Global Health, Zurich, Switzerland

Aim

To understand that the introduction of new vaccines into the immunization calendars of different countries is dependent on a number of local and international factors.

Contents

- The role of Public Health
- The role of the European Community to promote vaccination policies
- Vaccination systems and policies in developing Countries
- Health Technology Assessment as a tool for prioritization
- Economic analysis applied to vaccination programs
- Vaccination in the Developing World: the role of the GAVI Alliance
- Investment case for vaccine preventable diseases
- Vaccination systems and policies in the USA
- Public acceptance of new vaccines

Seminars

Aim

To provide tools for the students' personal and professional growth.

First and second semester

- Critical and scientific thinking;
- How to write a clinical trial protocol;
- Health Systems and Economics;
- How to write an epidemiologic protocol;
- Good Clinical Practices
- How to write grant applications and where to apply;
- How to write a thesis;
- How to write a paper to be published;
- Presentation skills;
- Communication and crisis management.

How to proceed

Entry Requirements

- University degree in Medicine;
- Excellent command of English, written and spoken. The full Master Program is conducted in English;
- Minimum 1-year clinical experience post-graduation.

The technical-Scientific Committee may evaluate for admission applications from candidates with other degrees, provided they have proof of specific activities or degrees in the field of the Master course.

Funding

- An 18-month grant will be provided to students who are accepted.

Application & Information

Application to the University of Siena

The 5th Edition of the Master Program in Vaccinology will start on June 2017.

The application process is already open, please check the official link:

http://bandi.unisi.it/simaco/modulistica/tutorial%20ammi-iscr%20online%202014__eng.pdf

Candidates must send the official application form to the University of Siena by **January 30, 2017**.

Assistance or further information to the candidates will be provided by Master Program Coordination. Please send an e-mail to master.vaccines@unisi.it preferably **January 10, 2017**.

Contact information

Master Coordination:

Web: <http://www.fondazioneclavo.org/en/master-in-vaccinology>

E-mail: master.vaccines@unisi.it

Keep the hope alive.

To continue building capacity, sharing knowledge, and developing expertise in developing countries, we need continued support.

Get in touch to be a sponsor

master.vaccines@unisi.it