2nd Human Challenge Trials in Vaccine Development

September 28-30, 2017

Hilton Washington DC / Rockville Hotel
Rockville, Maryland

Our world needs safer, more effective vaccines and drugs to prevent and treat infectious diseases. Controlled human infection models (CHIMs) have served as an effective tool to promote this objective. For example, CHIMs have led to progress in developing interventions against respiratory pathogens, enteric pathogens, and parasites. The most frequent application is the conduct of human challenge trials (HCTs), which can safely assess the value of novel or improved drugs and vaccines much more rapidly and efficiently than field trials, particularly if efficacy against controlled human infection (CHI) bridges to the field. Progress against an infectious threat is greatly hampered when the field lacks a supporting CHIM, such as is the case for human immunodeficiency virus (HIV) or *Mycobacterium tuberculosis*.

Based on the premise that optimal use of CHIMs is one of the best, most efficient ways to achieve rapid progress against infectious diseases, IABS is hosting a conference to review their use to promote the development of new vaccines, the benefits and risks of this approach, the regulatory framework within which HCTs are conducted, and novel CHIM applications that could open new translational pathways. This conference follows two and a half years after the first such meeting hosted by IABS in Strasbourg, France, September 2014.

Scientific Committee

Thomas L. Richie	Co-Chair; The Sanaria Institute for Global Health & Tropical Medicine (SIGHTM)
Pieter Neels	Co-Chair; Chair, IABS Human Vaccine Committee
Anastazia Older Aguilar	Bill & Melinda Gates Foundation
Cristina Cassetti	National Institutes of Health
Beth D. Kirkpatrick	University of Vermont
Ivana Knezevic	World Health Organization
Matthew Laurens	University of Maryland School of Medicine
Mark S. Riddle	Uniformed Services University of the Health Sciences, F. Edward Hebert School of Medicine
Meta Roestenberg	Leiden University Medical Center
Taryn Rogalski-Salter	Takeda Vaccines, Inc.
Zoe Seager	Wellcome Trust
Rebecca Sheets	Grimalkin Partners
Charlie Weller	Wellcome Trust
Adrian Wildfire	SGS - Life Sciences, United Kingdom

Day 1 – Thursday, September 28, 2017

8:00 am **Registration & Welcome Coffee**

Introduction

8:20 am **Welcome**
Pieter Neels, Chair, IABS Human Vaccine Committee

8:30 am **Meeting objectives**
Thomas L. Richie, The Sanaria Institute for Global Health & Tropical Medicine (SIGHTM), Rockville, Maryland

8:40 am **Keynote** – Introduced by **Matthew Laurens,** University of Maryland School of Medicine, Baltimore, Maryland
Historical perspective on Human Challenge Trials
Myron Levine, University of Maryland School of Medicine, Baltimore, Maryland

Session 1 – Human Challenge Trials to Support Licensure

Chairs:
Marco Cavaleri, European Medicines Agency; London, United Kingdom
Ivana Knezevic, World Health Organization, Geneva, Switzerland

9:10 am Cholera Human Challenge as pivotal efficacy study
Marc Gurwith, PaxVax, Redwood City, California

9:30 am Use of Human Challenge Trials to support vaccine development: regulatory considerations
Roshan Ramanathan, CBER / FDA, Silver Spring, Maryland

9:50 am Whole sporozoite (PfSPZ) malaria vaccines – proposed pivotal role for controlled human malaria infection (CHMI) in development and licensure)
Thomas L. Richie, The Sanaria Institute for Global Health & Tropical Medicine (SIGHTM), Rockville, Maryland

10:10 am Discussion

10:30 am Coffee break

10:50 am Pivotal role for Human Challenge Trials (HCT) in the development of a candidate norovirus vaccine
Paul Mendelman, Takeda Bozeman, Montana

11:10 am Bioconjugate vaccine preventing shigellosis: bridge from HCT to field studies
Mark S. Riddle, Uniformed Services University of the Health Sciences, Bethesda, Maryland

11:30 am Controlled human malaria infection (CHMI) in malaria vaccine development: a US regulatory perspective
Rana Chattopadhyay; **Douglas Pratt**, CBER / FDA, Silver Spring, Maryland

11:50 am **Panel discussion**
Chair: Marco Cavaleri, European Medicines Agency, London, United Kingdom

Rana Chattopadhyay, CBER / FDA; **Michael Pfleiderer**, Biopharma Excellence; **Stephen Hoffman**, Sanaria Inc.; **Marc Gurwith**, PaxVax; **Taryn Rogalski-Salter**, Takeda; **Patricia Martin**, LimmaTech Biologics AG

12:30 pm Lunch

Session 2 – Development of Challenge Strains

Chairs:
Steve Hoffman, Sanaria Inc.
James Southern, Developing Country Vaccine Regulators' Network (DCVRN), West Cape Province, South Africa

1:40 pm Developing new *Plasmodium* strains as injectable products
Kim Lee Sim, Protein Potential, LLC, Rockville, Maryland

2:00 pm Genomic characterization of *Plasmodium falciparum* vaccine and challenge strains
Joana Carneiro da Silva, University of Maryland School of Medicine, Baltimore, Maryland

2:20 pm Developing wild type influenza strains for HCT
Matthew Memoli, NIAID / NIH, Bethesda, Maryland; **Adrian Wildfire**, SGS Belgium NV, Mechelen, Belgium

2:40 pm FDA perspective on CMC section for challenge strain
Scott Stibitz, FDA - OVRR / DBPAP / LESTD, Silver Spring, Maryland

3:00 pm Developing and using dengue virus strains for HCT
Stephen Whitehead, NIAID / NIH, Bethesda, Maryland

3:20 pm Discussion

3:40 pm Coffee Break

4:00 pm Fit-for-purpose chimeric parasites for use in challenge models
Fidel Zavala, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland

Session 3 – Quality Standards for Challenge Strains

Chairs:
Robert Johnson, NIH / DMID, Bethesda, Maryland
Adrian Wildfire, SGS Belgium NV, Mechelen, Belgium

4:20 pm The status of challenge material within the EU regulatory framework
Alan Fauconnier, Federal Agency for Medicines and Health Products (FAMHP), Brussels, Belgium

4:40 pm Requirements for challenge strains for clinical trial applications and marketing authorization applications
Michael Pfleiderer, Biopharma Excellence, Munich, Germany

5:00 pm A CHIM Site's Experience with an FDA Inspection
Caroline Lyon, University of Vermont School of Medicine, Burlington, Vermont

Session 4 – Regulatory framework for Human Challenge Trials

5:20 pm **Panel discussion**
Chairs:
Ivana Knezevic, World Health Organization, Geneva, Switzerland
Pieter Neels, Chair, IABS Human Vaccine Committee

Scott Stibitz, FDA - OVRR / DBPAP / LESTD: CBER perspective on HCT
Marco Cavaleri, European Medicines Agency (EMA) - EMA perspective on HCT
Alambo Mssusa, Tanzania Food and Drugs Authority (TFDA) - Challenges in control of HCT in Tanzania

6:00 pm Reception

7:00 pm **Point Counterpoint discussion** - What level of development and qualification should be required for the challenge strains?
Moderator: Jean-Hugues Trouvin, IABS Vice-president

7:05 pm Quality standards for challenge strains: the case for full GMP
Nele Berthels, Federal Agency for Medicines and Health Products, Belgium

7:20 pm Quality standards for challenge strains: the case for GMP light/partial compliance
Adrian Wildfire, SGS Belgium NV

7:35 pm Discussion

Day 2 – Friday, September 29, 2017

8:00 am **Registration & Coffee**

Introduction
8:20 am **Announcements**
Pieter Neels, Chair, IABS Human Vaccine Committee

8:25 am Objectives for Day 2
Thomas L. Richie, The Sanaria Institute for Global Health & Tropical Medicine (SIGHTM), Rockville, Maryland

8:30 am **Keynote** – Introduced by **Andrew J. Pollard,** Oxford University, United Kingdom
Advancing the frontiers of human challenge research: the typhoid example
Thomas Darton, Oxford University, United Kingdom

Session 5 – What can we learn about human immunity from Human Challenge Trials

Chairs:
Andrew J. Pollard, Oxford University, United Kingdom
Philip Bejon, KEMRI-Wellcome Trust Research Programme, Kenya

9:00 am Insights into human immunology from challenge models: examples from dengue and campylobacter
Beth D. Kirkpatrick, University of Vermont School of Medicine, Burlington, Vermont

9:20 am Dissecting immunity to RSV using Human Challenge Trials
Christopher Chiu, Imperial College London, United Kingdom

9:40 am Norovirus; It's no picnic!
Robert Frenck, Cincinnati Children's Hospital, Cincinnati, Ohio

10:00 am How to count pathogens and microbiota during controlled human infections
O. Colin Stine, University of Maryland School of Medicine, Baltimore, Maryland

10:20 am Discussion

10:30 am Coffee break

10:50 am Controlled human co-infection with pneumococcus and live attenuated influenza virus
Daniela Ferreira, Liverpool School of Tropical Medicine, United Kingdom

11:10 am What can we learn about human immunity from controlled human malaria infection
Philip Bejon, KEMRI-Wellcome Trust Research Programme, Kenya

11:30 am What have we learnt about immune mechanisms of protection using the human challenge model for (para)typhoid infection?
Andrew J. Pollard, Oxford University, United Kingdom

11:50 am A human challenge trial with wild type Human Metapneumovirus in adults
Kawsar Talaat, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland

12:10 pm **Discussion**
12:20 pm Group photo
12:40 pm Lunch

1:45 pm **Point Counterpoint** - Dengue HCT: a model of infection or disease?
Moderator: Cristina Cassetti, NIH, Bethesda, Maryland

1:50 pm Dengue infection model – **Beth D. Kirkpatrick**, University of Vermont College of Medicine, Burlington, Vermont
2:05 pm Dengue disease model – **Timothy Endy**, SUNY Upstate Medical University, Syracuse, New York
2:20 pm Discussion

Session 6 – Development of New Challenge Models

Chairs:
Beth D. Kirkpatrick, University of Vermont, Burlington, Vermont
Helen McShane, The Jenner Institute, University of Oxford, United Kingdom

2:30 pm Controlled human infection with single-sex *Schistosoma mansoni cercariae*
Meta Roestenberg, Leiden University, The Netherlands

2:50 pm Use of the dengue controlled human infection models to de-risk vaccine development and identify correlate(s) of protection
Anna Durbin, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland

3:10 pm Developing a human mycobacterial challenge model
Helen McShane, The Jenner Institute, University of Oxford, United Kingdom

3:30 pm Rotavirus
Alan Fix, PATH, Washington D.C.

3:50 pm Discussion

4:00 pm Coffee break

Session 7 – Refining and Optimizing Existing Models

Chairs:
Mark Riddle, Uniformed Services University of the Health Sciences, Bethesda, Maryland
David Diemert, George Washington University

4:20 pm Establishing hookworm inoculum size
David Diemert, The George Washington University, Washongton, D.C.

4:40 pm *Plasmodium* nucleic acid testing to replace thick blood smears in malaria human challenge trials
Sean Murphy, University of Washington, Seattle, Washington

5:00 pm Development, use and refinement of enterotoxigenic *Escherichia coli* (ETEC) controlled human infections
Chad Porter, Naval Medical Research Center, Germantown, Maryland

5:20 pm PATH's program to optimize and expand the use of CHIMs
Jorge Flores, PATH (Program for Appropriate Technology in Health until 2016, now PATH)

5:40 pm **Panel discussion** – Key issues in improving challenge models
Chair: Mark Riddle, Uniformed Services University of the Health Sciences, Bethesda, Maryland

Anna Durbin, Johns Hopkins Bloomberg School of Public Health; **Timothy Endy**, SUNY Upstate Medical University; **Ivana Knezevic,** World Health Organization**; Mark Riddle**, Uniformed Services University of the Health Sciences; **Robert Sauerwein**, Radboud University, The Netherlands

Discussion

Optional Session – Discussion of Nomenclature

6:20 pm Optional Session on Nomenclature: Those interested are invited to a brief discussion of terms: Controlled human infections (CHIs); controlled human infection models (CHIMs); human challenge trials (HCT); controlled human [name the pathogen] infection (CH[X]I) (an example of the latter being controlled human malaria infection (CHMI)

7:00 pm End of day 2

Day 3 – Saturday, September 30, 2017

8:00 am **Registration & Coffee**

Introduction
8:20 am **Announcements**
Pieter Neels, Chair, IABS Human Vaccine Committee

8:25 am **Objectives for Day 3**
Thomas L. Richie, The Sanaria Institute for Global Health & Tropical Medicine (SIGHTM), Rockville, Maryland

Session 8 – Human Challenge Trials Guidelines

Chairs:
Anastazia Older Aguilar, Bill & Melinda Gates Foundation, Seattle, Washington
Ivana Knezevic, World Health Organization, Geneva, Switzerland

8:30 am WHO Guidelines
Ivana Knezevic, World Health Organization (WHO)

8:45 am Current Experience from Developing Countries – Adoption of WHO Guidelines
James Southern, Developing Country Vaccine Regulators' Network (DCVRN), West Cape Province, South Africa

9:00 am Discussion

Session 9 – Safety in Human Challenge Trials

Chairs:
Matthew Laurens, University of Maryland School of Medicine, Baltimore, Maryland
David Tribble, Uniformed Services University of the Health Sciences, Bethesda, Maryland

9:20 am Enteric pathogen safety considerations in Human Challenge Trials
David Tribble, Uniformed Services University of the Health Sciences, Bethesda, Maryland

9:40 am Pertussis Human Challenge Models
Tod Merkel, CBER / FDA, Silver Spring, Maryland

10:00 am Managing safety in controlled human malaria infections
Jona Walk, Radboud University Medical Center, The Netherlands

10:20 am From egg to clinical trial: the regulatory considerations of developing the SGS Life Sciences A/BELGIUM/4217/2015 H3N2 challenge agent
Bruno Speder, SGS Life Sciences, Mechelen, Belgium

10:40 am Coffee break

11:00 am Safety in Human Challenge Trials - regulatory aspects of performing HCTs
Nele Berthels, Federal Agency for Medicines and Health Products, Brussels, Belgium

11:20 am **Point counterpoint** – The safe use of HCT
Moderator: Meta Roestenberg, Leiden University Medical Center, The Netherlands

11:25 am Lessons learned from HCT – **Robert Sauerwein**, Radboud University, The Netherlands
11:40 am Assuring safety in HCT - **Michael Pfleiderer**, Biopharma Excellence, Germany
11:55 am Discussion

12:20 pm Lunch

Session 10 – Ethical perspectives

Chairs:
Robert Sauerwein, Radboud University, The Netherlands
David Tribble, Uniformed Services University of the Health Sciences, Bethesda, Maryland

1:30 pm Ethical framework for human challenge studies
Seema Shah, Seattle Children's Research Institute, Seattle, Washington, U.S.A.

1:50 pm Ethical considerations for Human Challenge Trials: the WHO perspective
Abha Saxena, Coordinator, Global Health Ethics, World Health Organization, Geneva, Switzerland

2:10 pm Principles for sponsors and supporters of CHIM studies
Claudia Emerson, Institute on Ethics & Policy for Innovation (IEPI), McMaster University, Hamilton, Ontario, Canada

2:30 pm Ethics and feasibility in CHI studies in The Africa
Joseph Mfutso-Bengo, University of Malawi, College of Medicine, Health Systems & Policy, Malawi

2:50 pm Discussion

Session 11 – Use of Human Challenge Trials in Developing Countries

Chairs:
Roma Chilengi, Centre for Infectious Disease Research, Zambia
Beth D. Kirkpatrick, University of Vermont School of Medicine, Burlington, Vermont

3:10 pm Controlled human malaria infection (CHMI) in Africa using PfSPZ Challenge: introducing a powerful new research tool for evaluating antimalarial drugs and vaccines and for elucidating malaria biology
Said Jongo, Ifakara Health Institute, Dar es salaam, Tanzania

3:30 pm Transitioning the pneumococcal carriage model to Malawi: learning from 'at risk' groups in the UK
Jamie Rylance, Liverpool School of Tropical Medicine, United Kingdom

3:50 pm Dengue model in Vietnam
Bridget Wills, Oxford University Clinical Research Unit, Ho Chi Minh City, Viet Nam

4:10 pm **Panel discussion**
Chair: Anastazia Older Aguilar, Bill & Melinda Gates Foundation, Seattle, Washington

Patricia Njuguna, Chair of Clinical Research, Kenya Medical Research Institute–Wellcome Trust Research Programme, Kenya; **Joseph Mfutso-Bengo**, University of Malawi, College of Medicine, Health Systems & Policy, Malawi; **Roma Chilengi**, Centre for Infectious Disease Research, Zambia; **James Southern**, Developing Country Vaccine Regulators' Network (DCVRN), South Africa

4:40 pm Coffee break

Session 12 – Use of Human Challenge Trials in Vulnerable Populations

Chairs:
Marco Cavaleri, European Medicines Agency, London, United Kingdom
Matthew Laurens, University of Maryland School of Medicine, Baltimore, Maryland

5:00 pm Pediatric influenza and rotavirus challenge models
John Treanor, University of Rochester

5:20 pm Imperative to develop vaccines for children, pregnant women, immunocompromised
Dominique Ploin, Hospices Civils de Lyon, France

5:40 pm Testing Vaccines in an early HIV infection model
Dagna Laufer, The International AIDS Vaccine Initiative (IAVI)

6:00 pm **Panel discussion** – Expanding the boundaries of HCT
Chair: Anna Durbin, Johns Hopkins School of Public Health

Marco Cavaleri, European Medicines Agency; **Abha Saxena,** World Health Organization; **Said Jongo**, Ifakara Health Institute; **Dominique Ploin,** Hospices Civils de Lyon; **Douglas Pratt**, US FDA

6:40 pm Closing remarks
Tom Richie, SIGHTM; **Pieter Neels**, IABS

7:00 pm End of meeting