2nd Human Challenge Trials in Vaccine Development

September 28-30, 2017
Hilton Washington DC / Rockville Hotel
Rockville, Maryland

Agenda as of August 31st

Our world needs safer, more effective drugs and vaccines 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 drugs and 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

Tom Richie	Co-Chair; The Sanaria Institute for Global Health & Tropical Medicine (SIGHTM)
Pieter Neels	Co-Chair; Chair, IABS Human Vaccine Committee
Ana Older Aguilar	Bill & Melinda Gates Foundation
Christina Cassetti	National Institutes of Health
Beth Kirkpatrick	University of Vermont
Ivana Knezevic	World Health Organization
Matthew Laurens	University of Maryland
Mark Riddle	Uniformed Services University of the Health Sciences' F. Edward Hebert School of Medicine
Meta Roestenberg	Leiden University Medical Center
Taryn Rogalski	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
Tom Richie, The Sanaria Institute for Global Health & Tropical Medicine (SIGHTM)

8:40 am **Keynote** – Introduced by **Matt Laurens**
The scope of Human Challenge Trials - historical perspectives & current issues
Myron Levine, University of Maryland School of Medicine

Session 1 –Human Challenge Trials to Support Licensure

Chair: Ivana Knezevic, WHO**; Marco Cavaleri**, European Medicines Agency

9:10 am The story of Vaxchora® cholera vaccine
Marc Gurwith, PaxVax

9:30 am Clinical perspective on accepting HCT data as pivotal
Roshan Ramanathan, FDA

9:50 am Whole sporozoite malaria vaccine – proposed pivotal role for controlled human malaria infection (CHMI)
Tom Richie, SIGHTM

10:10 am Discussion

10:30 am Coffee break

10:50 am TAK-214 norovirus vaccine – proposed pivotal role for HCT
Paul Mendelman, Takeda

11:10 am Bioconjugate vaccine preventing shigellosis: bridge from HCT to field studies
Mark S. Riddle, Uniformed Services University of the Health Sciences, F. Edward Hebert School of Medicine

11:30 am Controlled Human Malaria Infection (CHMI) in Malaria Vaccine Development: A US Regulatory Perspective
Rana Chattopadhyay, CBER / FDA; **Douglas Pratt**, CBER / FDA

11:50 noon **Panel discussion: Human Challenge Trials to Licensure**
Chair: Marco Cavaleri, European Medicines Agency

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

12:30 pm Lunch

Session 2 – Development of Challenge Strains

Chair: Robert Sauerwein, Radboud University, The Netherlands**; James Southern** – TBC

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

2:00 pm Using genomics to define *Plasmodium* diversity
Joana Carneiro da Silva, University of Maryland

2:20 pm Developing wild type influenza strains for HCT
Matthew Memoli, NIAID / NIH

2:40 pm FDA Perspective on CMC section for challenge strain
Scott Stibitz, FDA - OVRR / DBPAP / LESTD

3:00 pm Developing dengue virus strains for HCT
Steve Whitehead, NIAID / NIH

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 University, Bloomberg School of Public Health

Session 3 – Quality Standards for Challenge Strains

Chair: Robert Johnson, NIH / DMID**; Adrian Wildfire,** SGS Belgium NV

4:20 pm The status of challenge material within the EU regulatory framework
Alan Fauconnier, Federal Agency for Medicines and Health Products (FAMHP), 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 Perspective of an FDA audit of a CHI study
Caroline Lyon, University of Vermont School of Medicine

Session 4 - Regulatory framework for Human Challenge Trials

5:20 pm **Panel discussion**
Chair: Ivana Knezevic, World Health Organization**; Pieter Neels,** IABS

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 Break until dinner

7:00 pm Dinner

8:00 pm Point Counterpoint dinner debate - What level of development and qualification should be required for the challenge strains?
Moderator: **Jean-Hugues Trouvin**, IABS Vice-president

8:05 pm Quality standards for challenge strains: the case for full GMP
Nele Berthels, Federal Agency for Medicines and Health Products, Belgium

8:20 pm Quality standards for challenge strains: the case for GMP light/partial compliance
Adrian Wildfire, SGS Belgium NV

8:35 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
Tom Richie, The Sanaria Institute for Global Health & Tropical Medicine (SIGHTM)

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

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

Chair: Andrew J. Pollard, Oxford University; **Philip Bejon,** KEMRI-Wellcome Trust Research Programme, Kenya

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

9:20 am Dissecting immunity to influenza using HCTI
Christopher Chiu, Imperial College London, United Kingdom

9:40 am Predicting susceptibility to norovirus by use of HCM
Robert Frenck, Cincinnati Children's Hospital

10:00 am Quantitative analysis of pathogens and microbiota during controlled human ETEC infection
O. Colin Stine, University of Maryland

10:20 am Discussion

10:30 am Coffee break

10:50 am First Human Challenge Testing of a Pneumococcal Vaccine
Daniela Ferreira, Liverpool School of Tropical Medicine, United Kingdom

11:10 am What can we learn about human immunity from Human Challenge Trials
Philip Bejon, KEMRI-Wellcome Trust Research Programme, Kenya

11:30 am Correlates of protection typhoid revealed by HCT
Andrew J. Pollard, Oxford University, United Kingdom

11:50 am HCT of Adults With Wild-Type Human Metapneumovirus
Kawsar Talaat, Johns Hopkins Bloomberg School of Public Health

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

1:50 pm Dengue infection model – **Beth Kirkpatrick**, University of Vermont College of Medicine
2:05 pm Dengue disease model – **Timothy Endy,** State University of New York

2:20 pm Discussion

Session 6 – Development of New Challenge Models

Chair: Beth Kirkpatrick, University of Vermont**; Helen McShane,** University of Oxford

2:30 pm Schistosomiasis
Meta Roestenberg, Leiden University, The Netherlands

2:50 pm Zika
Anna Durbin, Johns Hopkins Bloomberg School of Public Health

3:10 pm Tuberculosis
Helen McShane, Nuffield Department of Medicine, University of Oxford, United Kingdom Oxford

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

Chair: Mark Riddle, Uniformed Services University of the Health Sciences' F. Edward Hebert School of Medicine**;**
David Diemert, George Washington University

4:20 pm Establishing hookworm inoculum size
David Diemert, George Washington University

4:40 pm Establishing PCR as primary endpoint for Controlled Human Malaria Infection
Sean Murphy, University of Washington, Seattle

5:00 pm Improving ETEC models
Chad Porter, Naval Medical Research Center

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' F. Edward Hebert School of Medicine

Anna Durbin, Johns Hopkins Bloomberg School of Public Health; **Timothy Endy**, State University of New York
Ivana Knezevic, WHO**; Mark Riddle**, Uniformed Services University of the Health Sciences' F. Edward Hebert School of Medicine; **Robert Sauerwein**, Radboud University, The Netherlands

Discussion

Optional Session – Discussion of Nomenclature

6:20 pm Optional Session on Nomenclature: Those interested are warmly 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))

6:40 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
Tom Richie, The Sanaria Institute for Global Health & Tropical Medicine (SIGHTM)

Session 8 – Human Challenge Trials Guidelines

Chair: Anastazia Older Aguilar, Bill & Melinda Gates Foundation**; Ivana Knezevic,** WHO

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

8:45 am DCVRN perspective on the implementation of WHO Guidelines on HCT into regulatory practice
James Southern, Developing Country Vaccine Regulators' Network (DCVRN)

9:00 am Discussion

Session 9 – Safety in Human Challenge Trials

Chair: Matthew Laurens, University of Maryland**; David Tribble,** Uniformed Services University of the Health Sciences

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

9:40 am Future development of HCT with Bordatella pertussis
Tod Merkel, CBER / FDA

10:00 am Managing safety issues arising with controlled human malaria infection
Jona Walk, Radboud University Medical Center, The Netherlands

10:20 am Regulatory aspects of performing HCTs
Bruno Speder, S.G.S. Life Science Services, Belgium

10:40 am Coffee break

11:00 am Regulatory aspects of performing HCTs
Nele Berthels, Federal Agency for Medicines and Health Products, 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 Univesity, 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

Chair: Matt Laurens, University of Maryland**; David Tribble,** Uniformed Services University of the Health Sciences

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

1:50 pm Ethical considerations from the WHO perspective
Abha Saxena, Coordinator, Global Health Ethics, World Health Organization

2:10 pm Principles for Sponsors and Supporters of CHIM studies
Claudia Emerson, Program on Ethics & Policy for Innovation (PEPI), Ontario, Canada

2:30 pm Ethics of HCT in 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

Chair: Roma Chilengi, Centre for Infectious Disease Research, Zambia; **Beth Kirkpatrick,** University of Vermont

3:20 pm Controlled human malaria infection in Africa
Said Jongo, Ifakara Health Institute, Tanzania

3:40 pm Pneumococcal carriage in Malawi
Jamie Rylance, Liverpool School of Tropical Medicine, United Kingdom

4:00 pm Dengue model in Vietnam
Bridget Wills, Oxford University Clinical Research Unit, Ho Chi Minh City, Viet Nam

4:20 pm **Panel discussion**
Chair: TBD

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, SA….

4:40 pm Coffee break
3:20 pm Controlled human malaria infection in Africa
Said Jongo, Ifakara Health Institute, Tanzania

3:40 pm Pneumococcal carriage in Malawi
Jamie Rylance, Liverpool School of Tropical Medicine, United Kingdom

Session 12 – Use of Human Challenge Trials in Vulnerable Populations

Chair: Marco Cavaleri, European Medicines Agency; **Matthew Laurens,** University of Maryland

5:00 pm Use of replicating influenza vaccine challenge in pediatric populations
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 (short talk)
Frances Priddy, The International AIDS Vaccine Initiative (IAVI) (**Tom Richie** will present)

5:50 pm **Panel discussion** – Expanding the boundaries of HCT

Chair: TBD

Marco Cavaleri, European Medicines Agency (EMA), **Abha Saxena,** World Health Organization **(**WHO)
Dominique Ploin, Hospices Civils de Lyon

6:30 pm Closing remarks, request for feedback
Tom Richie, SIGHTM; **Pieter Neels**, IABS

7:00 pm End of meeting