3rd Human Challenge Trials

in Vaccine Development

February 6-7, 2020

Pembroke College

Oxford, United Kingdom

Organized by IABS

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About the Conference

This workshop builds on the successes and identified challenges from two prior workshops on the subject of human challenge trials or controlled human infection models (CHIM). When CHIM are used to inform vaccine development, they can add to what is known from natural history, epidemiology, and pathogenesis studies to speed the vaccine development pathway. However, there are significant safety, ethical, operational, environmental, and scientific issues in intentionally infecting humans with infectious organisms in controlled settings of clinical trials. Nonetheless, these trials can be performed safely and ethically both in non-endemic and endemic regions. Attend this workshop to learn more about these challenging issues and to join in the conversation that will lead to progress and recommendations for enhancing CHIM as tools to develop new and improved vaccines

Scientific & Organizing Committees

SCIENTIFIC COMMITTEE

Andrew Pollard, co-Chair Scientific Committee; University of Oxford, United Kingdom
Robert Sauerwein, co-Chair Scientific Committee; Radboud University Medical Center, Nijmegen, The Netherlands
Pieter Neels, Chair Human Vaccine Committee, International Alliance for Biological Standardization (IABS)
Ivana Knezevic, World Health Organization, Geneva, Switzerland
Rebecca Sheets, International Alliance for Biological Standardization (IABS), U.S.A.
Claudia Emerson, McMaster University, Hamilton, Ontario, Canada
Marc Gurwith, San Diego, California, U.S.A.
Anna Durbin, Johns Hopkins Bloomberg School of Public Health, U.S.A.
William Ripley Ballou, GlaxoSmithKline, U.S.A.
Martin Broadstock, Medical Research Council, United Kingdom
Helen McShane, University of Oxford, United Kingdom
Paul Kaye, University of York, United Kingdom
Kirsty E.K Mehring-Le Doare, St. George's, University of London and MRC/UVRI @LSHTM Uganda
Peter J.M. Openshaw, Imperial College of London, United Kingdom
Daniela Ferreira, Liverpool School of Tropical Medicine, United Kingdom
Adrian Wildfire, SGS LIfe Sciences, Belgium

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Scientific Program

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Day 1 Thursday February 6, 2020

8:00 Registration

8:30 Introduction

Andrew POLLARD, co-Chair Scientific Committee; University of Oxford, United Kingdom
Robert SAUERWEIN, Radboud University Medical Center, Nijmegen, The Netherlands
Pieter NEELS, Chair Human Vaccine Committee, International Alliance for Biological Standardization (IABS)

Session 1 - The Role of Challenge Models

Chairperson: **Andrew POLLARD,** University of Oxford, United Kingdom

9:00 Overview: What is the role of challenge studies?
Myron LEVINE, University of Maryland School of Medicine, U.S.A.

9:15 Case study: Group A Streptococcus
Joshua OSOWICKI, Murdoch Children's Research Institute (MCRI), Melbourne, Australia

9:30 The Role of Challenge Models: case study on Typhoid/Paratyphoid
Andrew POLLARD, University of Oxford, United Kingdom

9:45 Case study: RSV
Andrew CATCHPOLE, hVIVO, United Kingdom

10:00 Development, use and refinement of Shigella controlled human infections
Chad PORTER, Naval Medical Research Center, Maryland, U.S.A.

10:15 Discussion
Lynda STUART, Bill & Melinda Gates Foundation, U.S.A.

10:40 Coffee Break

Scientific Program

Session 2- Regulation – GMP and the Trial Challenge

Chairperson: **Pieter NEELS,** Chair Human Vaccine Committee, International Alliance for Biological Standardization (IABS)

11:10 European survey of regulation
Nele BERTHELS, Federal Agency for Medicines and Health Products (FAMHP), Belgium

11:25 Global variation in regulation
Pieter NEELS, Chair Human Vaccine Committee,
International Alliance for Biological Standardization (IABS)

11:40 GMP and the Challenge Agent: Leishmaniasis
Paul KAYE, University of York, United Kingdom

11:55 Case study: Malaria
Robert SAUERWEIN, Radboud University Medical Center, Nijmegen, The Netherlands

12:10 Discussion

12:25 Lunch

Session 3- Ethics (supported by Medical Research Council Hic-Vac network)
This session is sponsored by HIC-Vac

Chairpersons: **Robert SAUERWEIN,** Radboud University Medical Center, Nijmegen, The Netherlands

13:45 Philosophical perspective for HIC and LMIC
Michael SELGELID, Monash University, Australia

14:00 Controlled infection studies: ethical issues and LMICs
Susan BULL, Michael PARKER, University of Oxford, United Kingdom

14:15 Guidelines for ethics committees in HIC
Hugh DAVIES, University of Oxford, United Kingdom

14:30 WHO Roadmap to ethics
Katherine LITTLER, World Health Organization (WHO), Switzerland

14:45 Experimental human gonococcal infection: Advances and challenges
Marcia HOBBS, University of North Carolina, U.S.A.

15:00 Ethics Case Study: Dengue
Anna DURBIN, Johns Hopkins Bloomberg School of Public Health, U.S.A.

15:15 Case study: Schistosomiasis
Meta ROESTENBERG, Leiden University Medical Center, The Netherlands

15:30 Discussion
Led by **Simon KOLSTOE,** University of Portsmouth, United Kingdom

15:50 Tea Break

Scientific Program

Session 4- Children

This session is sponsored by HIC-Vac

Chairperson: **Claudia EMERSON,** McMaster University, Canada

16:15 Human challenge models in Paediatric populations
Kate EMARY, University of Oxford, United Kingdom

16:30 Philosophy & ethics of challenging children
Claudia EMERSON, McMaster University, Canada

16:45 Regulatory perspective
Dominique PLOIN, Hospices Civils de Lyon, France

17:00 Discussion

17:25 Summary of the day
Chairs

17:30 hVIVO - Regulatory guidance for challenge agents
Alex MANN, hVIVO, United Kingdom

17:45 Networking reception

Day 2 Friday February 7, 2020

7:30 Registration

Session 5- Threat to the Community and Environmental Safety Session

Chairpersons: **Adrian WILDFIRE,** SGS Life Sciences, Belgium

8:30 Challenges in safety of enteric challenge in Asia
Cherry KANG, Christian Medical College, Vellore, India

8:45 Containment of respiratory viruses: a case study of unexpected HPIV infection during an A/Belgium/4217/2015 [H3N2] influenza challenge study
Adrian WILDFIRE, SGS Life Sciences, Belgium

9:00 Case study: Norovirus
Robert FRENCK, University of Cincinnati, U.S.A.

9:15 Discussion

Scientific Program

Session 6- Recruitment, Engagement, Advertising and Incentive

Chairpersons: **Helen McShane,** University of Oxford, United Kingdom

9:55 Attitudes towards payment and payment practices in controlled human infection model (CHIM) research
Olivia GRIMWADE, Monash University, Australia

10:10 Factors influencing participation in controlled human infection models: a pooled analysis from six enteric fever studies
Blanché OGUTI, University of Oxford, United Kingdom

10:25 Coffee break

10:55 Community and public engagement for challenge studies in Kenya: Stakeholders, strategies, ethical issues and lessons learnt
Primus CHI, KEMRI Wellcome Trust Research Programme, Kenya

11:10 Risks and challenges in engagement in LMIC
Roma CHILENGI, Center for Infectious Disease Research, Zambia;
Cherry KANG, Christian Medical College, Vellore, India

11:25 Discussion

Session 7- Pre-Existing Immunity

Chairpersons: **Peter OPENSHAW,** Imperial College of London, United Kingdom

11:50 Where should we go for our challenge studies?
Shobana BALASINGAM, Wellcome Trust, United Kingdom

12:05 CA Controlled Human Malaria Infection study to examine naturally-acquired immunity
CHMI – SIKA Study Team
Philip BEJON, KEMRI Wellcome Trust Research Programme, Kenya

12:20 Pre-existing immunity case study: Zika virus
Anna DURBIN, Johns Hopkins Bloomberg School of Public Health, U.S.A.

12:35 Discussion

13:00 Lunch

13:00 The Global Health Network – An Introduction to the knowledge sharing hub for human infection studies
Anna DURBIN, Johns Hopkins Bloomberg School of Public Health, U.S.A.

Scientific Program

Session 8- Clinical, Immunological, and Microbiological Endpoints

Chairpersons: **Anna DURBIN,** Johns Hopkins Bloomberg School of Public Health, U.S.A.
Paul KAYE, University of York, United Kingdom

14:00 Immunological endpoints in challenge studies
Helen McShane, University of Oxford, United Kingdom

14:15 Case study: RSV immunity and human challenge
Peter OPENSHAW, Imperial College of London, United Kingdom

14:30 Microbiological endpoints for a Group B Streptococcal human challenge model
Kirsty E.K MEHRING-LE DOARE, St. George's, University of London and MRC/UVRI @LSHTM, Uganda

14:45 Case study: Influenza; impact of pre-existing immunity on study end points
Rebecca COX, University of Bergen, Norway

15:00 Case study: Malaria
Robert SAUERWEIN, Radboud University Medical Center, Nijmegen, The Netherlands

15:15 Discussion

Session 9- What Is The Future

Chairpersons: **Andrew Pollard,** co-Chair Scientific Committee;
University of Oxford, United Kingdom
Robert Sauerwein, co-Chair Scientific Committee,
Radboud University Medical Center, Nijmegen
Pieter Neels, Chair Human Vaccine Committee,
International Alliance for Biological Standardization (IABS)

15:40 Summing up – Funding challenges
Wellcome Trust, United Kingdom

15:45 Summing up – Ethical and regulatory challenges
Pieter Neels, Chair Human Vaccine Committee,
International Alliance for Biological Standardization (IABS)

15:50 Final word
Chairs

16:00 Tea and Close

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>> 5th Cell & Gene Therapy

February 4-5, 2020– Tokyo, Japan

>> 3rd Human Challenge Trials

February 6-7, 2020 – Oxford, United Kingdom

>> IABS 65th Anniversary: New paths for sustainable solutions to tackle global and emerging infectious threats

February 26-28, 2020 – Lyon, France

>> Cross learning experience human and animal vaccine licensure based on technology platforms

March 16-17, 2020 – Brussels, Belgium

>> Maintaining the quality of vaccines through the use of references standards: Current challenges and future opportunities

June 8-9, 2020 - Ottawa, Canada

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Speaker Abstracts

Dr. Shobana **Balasingam**
Wellcome Trust, United Kingdom

Dr. Philippe **Bejon**
KEMRI-Wellcome, Kilifi County Hospital, Kenya

Dr. Nele **Berthels**
Federal Agency for Medicines and Health Products (FAMHP) Belgium

Dr. Susan **Bull**
University of Oxford United Kingdom

Dr. Primus **Chi**
KEMRI-Wellcome Trust Research Programme, Kenya

Dr. Roma **Chilengi**
Centre for Infectious Disease Research in Zambia, Zambia

Prof. Rebecca **Cox**
University of Bergen, Norway

Dr. Hugh **Davies**
University of Oxford United Kingdom

Prof. Anna **Durbin**
Johns Hopkins Bloomberg School of Public Health, U.S.A.

Dr. Kate **Emary**
University of Oxford United Kingdom

Dr. Claudia **Emerson**
McMaster University, Canada

Dr. Robert **Frenck**
University of Cincinnati, U.S.A.

Dr. Olivia **Grimwade**
University of Oxford United Kingdom

Dr. Marcia **Hobbs**
University of North Carolina U.S.A.

Dr. Gagandeep **Kang**
Translational Health Science and Technology Institute, India

Prof. Paul **Kaye**
University of York United Kingdom

Dr. Kirsty **Le Doare**
St. George's, University of London and MRC/UVRI @LSHTM Uganda

Dr. Mike **Levine**
University of Maryland School of Medicine, U.S.A.

Dr. Katherine **Littler**
World Health Organization Switzerland

Prof. Helen **McShane**
University of Oxford United Kingdom

Prof. Pieter **Neels**
International Alliance for Biological Standardization, Belgium

Dr. Blanche **Oguti**
University of Oxford United Kingdom

Prof. Peter **Openshaw**
Imperial College,United Kingdom

Dr. Joshua **Osowicki**
Murdoch Children's Research Institute (MCRI), Australia

Prof. Michael **Parker**
University of Oxford United Kingdom

Dr. Dominique **Ploin**
Hospices Civils de Lyon France

Prof. Andrew **Pollard**
University of Oxford United Kingdom

Dr. Chad **Porter**
Naval Medical Research Center U.S.A.

Dr. Meta **Roestenberg**
Leiden University Medical Center, The Netherlands

Prof. Robert **Sauerwein**
Radboud University Medical Center, The Netherlands

Prof. Michael **Selgelid**
Monash University, Australia

Mr. Adrian **Wildfire**
SGS LIfe Sciences, Belgium

Speaker Abstracts

Philip Bejon

A Controlled Human Malaria Infection study to examine naturally-acquired immunity

CHMI-SIKA Study Team

Background

A high efficacy vaccine against falciparum malaria would substantially impact global health. Adults in malaria endemic areas are known to acquire clinical immunity that limits parasite growth, and to acquire antibodies to several hundred Plasmodium falciparum (Pf) antigens. We are using the controlled human malaria infection (CHMI) model with malaria-exposed volunteers to identify correlations between immune responses and parasite growth rates in vivo. In this presentation we outline the initial quantitative polymerase chain reaction (qPCR) outcomes and associations with proxies of previous exposure to malaria (i.e. residence and antibody levels to schizont extract).

Methods

We recruited adult volunteers in Kilifi (Coastal Kenya) and Ahero (Western Kenya) who were willing to give fully informed consent for participation in CHMI. We excluded volunteers with significant health problems, including HIV, and excluded volunteers with sickle-cell trait. All volunteers positive for Pf by qPCR were treated with 7 days of artesunate monotherapy prior to CHMI.

We administered 3,200 aseptic, purified, cryopreserved Pf sporozoites (Sanaria® PfSPZ Challenge [NF54]) by direct venous inoculation. Serial qPCR for the falciparum 18s rRNA gene was undertaken during the 21 days following challenge to measure parasite growth in vivo. Participants were treated with anti-malarial drugs when ≥500 parasites per l were detected, or when fever was present at lower parasite counts.

Results

122 of 161 (76%) participants developed parasitemia detectable by PCR. Of the 122 participants with parasitemia, 58 (48%) required treatment, of whom 27 were febrile. 39 participants (24%) were PCR negative throughout monitoring. Prior residence at higher malaria transmission and higher anti-schizont antibody levels were associated with lower risk of needing treatment following CHMI (HR=0.12, 95%CI 0.07 to 0.2 for residence in a moderate transmission versus low transmission area and HR=0.25, 95%CI 0.16-0.38 for increasing anti-schizont antibody concentrations).

Anti-Schizont antibody levels explained 15% of the variability in outcome in CHMI, compared with **0.8% of the variability in previous field-based cohort studies.**

Conclusion

CHMI is a powerful platform for studying host immunity to malaria. Next steps will include high throughput immunological screening of responses. We expect causal correlates to be independently and strongly associated with outcome after adjusting for the non-causal correlates (i.e. schizont antibodies and residence).

Speaker Abstracts

Susan Bull and Michael Parker

Controlled infection studies: ethical issues and LMICs

Introduction: Although controlled infection studies (CIS) fall within the scope of current research ethics guidance, morally significant differences between CIS and other forms of biomedical research, and the implications of conducting CIS in LMIC contexts, require careful consideration. Key values informing such considerations include respect, fairness, and minimisation of research risks and burdens.

Issues: CIS take place within a landscape of commitments to global health justice which recognise the need to address disproportionate burdens of disease and ensure no one is left behind. However, CIS are also an often counter-intuitive, unfamiliar and worrisome research design, taking place against a background of sustained vaccine hesitancy and inconsistent trust in health research. Where CIS appear to offer significant scientific and social value in addressing burdens of infectious disease in LMICs, questions arise about the nature and extent of key stakeholders' obligations relating to: (a) engaging with stakeholders from research councils, health departments, regulatory agencies, ethics committees, communities, and insurers, (b) ensuring that there is a social mandate for such research and that the design and conduct of research has been appropriate informed by engagement activities (c) building capacity to conduct effective, safe and well-governed CIS, (d) appropriate responses to fragile health and sanitation systems which impact risk management and infection control during CIS, (e) addressing tensions between promoting inclusive approaches and ensuring that participants are appropriately protected, and (f) promoting fair collaboration and sharing.

Conclusion: Where CIS are justified in LMICs, such research must be conducted safely, acceptably and appropriately. This requires careful consideration of not just appropriate means of addressing ethical issues arising during the design and conduct of individual CIS, but also of the development of national and international governance frameworks for the appropriate oversight of research.

Speaker Abstracts

Andrew Catchpole

RSV challenge model Case study: Evaluating the efficacy of Janssen's AD26.RSV.PreF vaccine

Background

RSV infection is an increasingly recognized illness in high-risk adults, particularly those aged ≥60 years, with a disease burden similar to that of non-pandemic influenza. There is currently no approved vaccine, and development of an effective RSV vaccine may offer benefits for high-risk adults. RSV vaccine candidates targeting the RSV non-stabilized F protein have proven unsuccessful so far, eliciting poor neutralizing antibody titers, and have failed to protect against LRTI-associated disease

Epitopes specific to the pre-F protein appear to be more potent inducers of neutralizing antibodies than those present on the post-F protein. Ad26.RSV.preF is a recombinant adenovirus serotype 26 vector that encodes and expresses for a full-length RSV-F protein stabilized in the pre-F protein conformation and has demonstrated immunogenicity in older adults aged ≥60 years in stable health, with no significant safety concerns to date and an acceptable tolerability profile.

Method

Janssen Pharmaceutical Companies of Johnson & Johnson contracted hVIVO to conduct a randomized, double-blind, placebo-controlled study to evaluate the efficacy of a single immunization of AD26.RSV.preF against RSV infection in a viral challenge model in healthy adults. Subjects were immunized 28 days prior to inoculation with hVIVO RSV A Memphis 37b challenge virus. Following viral-inoculation subjects were then quarantined in individual en-suite rooms in hVIVO's London-based clinical unit and monitored for 12 further days for RSV infection. Follow up visits were conducted to continue to monitor safety and the immunological response to vaccination.

Results

The Ad26.RSV.preF vaccine met its' primary end point showing a significant reduction in viral load as measured by quantitative PCR. Furthermore, the vaccine showed clear efficacy against a range of secondary endpoints including time to infection, reduction in symptoms, reduction in mucus discharge. RSV disease severity following challenge with RSV-A Memphis 37b were consistently lower in volunteers receiving immunization with Ad26.RSV.preF versus placebo

In addition, Ad26.RSV.preF demonstrated immunogenicity and was well tolerated

Conclusions

The human viral challenge model successfully evaluated the efficacy of the Ad26.RSV.preF vaccine. Ad26.RSV.preF is the first adult RSV vaccine candidate to show functional protection against RSV infection and upper respiratory tract disease. Ad26.RSV.preF may provide promising protection from RSV infection, RSV transmission and RSV disease. Ad26.RSV.preF warrants further evaluation in field trials for efficacy

Speaker Abstracts

Primus Chi

Community and public engagement for challenge studies in Kenya: Stakeholders, strategies, ethical issues and lessons learnt

Considering the unique nature of challenge studies in that they involve deliberately infection participants with an infectious agent that could potentially cause a disease, most stakeholders and the public in many low- and middle-income country (LMIC) settings like Kenya are not familiar with this type of research. It is therefore critical to develop and implement a strong community and public engagement process prior to, during and after conducting a challenge study, especially in the context of changing socio-political issues. The KEMRI-Wellcome Trust Research Programme (KWTRP) has a well-established community engagement platform, with extensive experience in strengthening mutual understanding between community members and the Programme, including for challenge studies. This presentation will dwell on the experience of engaging communities and the public in the context of challenge studies conducted at the KWTRP, with focus on how relevant stakeholders were identified and engaged, ethical issues that arose during the engagement and lessons learnt. The experiences will cut across the initial feasibility study for the controlled human malaria infection (CHMI) model conducted in Nairobi in 2012, through the CHMI study with Semi-immuned Kenyan Adults (CHMI-SIKA) in Kilifi from 2016-2018, to the Shigella human infection study planned for Kilifi and Kericho from 2012-2024. The presentation will draw on secondary and primary data gathered through consultations, and individual and group interviews with targeted stakeholders. The talk will emphasize the importance of identifying the appropriate stakeholders for engagement and adapting the engagement strategies to the target audience.

Speaker Abstracts

Roma Chilengi

Risks and challenges in engagement in LMIC

INTRODUCTION

Compelling ethical and scientific considerations now require that CHIMs are also undertaken in LMICs, but there are challenges posed by this relatively new research methodology in places where policy, culture, and practice is yet to accommodate CHIMs. To engage stakeholders in LMICs, the CHIMs agenda has entirely been driven by investigators who often have to wear multiple hats for any progress to be achieved.

CHALLENGES

Awareness: Investigators not only need to educate themselves and their research teams, they actually have to introduce the basics of the concept to local stakeholders at all levels.

Resources: Nearly always, engagement with stakeholders take the form of workshops and meetings which require specific funding that the investigator must source. Moreover, the actual CHIMs work requires sufficient infrastructure, equipment, staff and logistics that must be in place.

Regulatory environment: In the absence of specific regulations and laws, investigators often have to engage local authorities to help them find "legal loopholes" to facilitate acceptance and review of CHIMs work. Given the lack of awareness and exposure, some level of competence needs to be imparted in order to obtain a meaningful review and guidance.

Technical gaps: Concepts which are "globally unresolved" i.e. the requirement for the challenge agent to be a GMP or GMP-like product, pose exceptionally huge challenges when engaging local regulators in LMICs- they quickly associate this to increased risk.

Researched community: Communicating the lofty idea of CHIMs in societies that are generally research naïve can be difficult. Funders, sponsors and the international community are on the one hand concerned about potential exploitation and the need for individual informed voluntarism against risks; locally, there mere language, how to communicate, community perceptions, and getting the levels of compensation right are critical issues.

APPROACH BEING TAKEN

Our experience has included sustained engagement at every possible contact with gatekeepers including local authorities- ethics committees, ministry of health, regulatory and biosafety authorities, community gate keepers, civic leadership and public media. In parallel, creating a team of motivated scientists kept abreast through key literature and international exposure.

To introduce CHIMs, we had to start with use of Rotarix- a live attenuated vaccine as a challenge agent. Beyond this, we can now look to other possibilities such as shigella.

CONCLUSION

There are real challenges to introducing CHIMs in LMICs but they can be overcome by careful well thought strategies and sustained momentum. It took long to get the international/funding community to accept, and it is taking even longer for the local stakeholders to follow through. Strong indigenous leadership is needed to achieve this in LMIC settings.

Speaker Abstracts

Rebecca Cox

Case study: Influenza; impact of pre-existing immunity on study end points

Influenza Centre, Department of Clinical Science, University of Bergen
Laboratory Building, 5th Floor, Jonas Lies vei 87 N-5021 Bergen, Norway

Adults have experienced a number of influenza infections and may have been immunised with influenza vaccine which will result in heterogeneous immunity. In 1972 Hobson et al. showed that a haemagglutination inhibition (HI) serum antibody titres between 1:18 to 1:36 provided 50% protection against influenza challenge in adult volunteers. Subsequently, an HI titre of 40 has been adopted as a surrogate correlate of protection in adults. The haemagglutination inhibition assay is a good assay for screening research subjects and indicating susceptibility to a given influenza challenge virus. However, the mulitfacated immune response to influenza may require further testing of subjects to improve the challenge model. Recent challenge and cohort studies have shown neuraminidase inhibiting antibodies, nasal wash IgA and stalk specific antibodies can also provide protection from challenge. Furthermore, cellular immune responses including CD4, CD8 and IFN- secreting cells have been shown to correlate with protection from infection. This talk will review the impact of pre-existing immunity on study endpoints and examine how the baseline tests can be used to ensure acceptable homogeneity in the responses to challenge.

Speaker Abstracts

Hugh Davies

Guidelines for ethics committees in HIC

Infecting a healthy volunteer even for the benefit of others rightly causes concern. This exceeds the expected/accepted level of research risk ("minimal risk") and as there is clearly no benefit to the volunteer, it seems to contravene a central tenet of medicine – "First do no harm"

So how should these studies be reviewed and judged?

Oxford A Research Ethics Committee frames its review using the following principles below, recognising two important caveats:-

- "one size won't fit all" as the major risk in these studies is the infection itself which will vary, depending on the infecting agent and
- these studies will be conducted in many different locations under differing circumstances so, while the principles and questions provide an overarching structure for review (and design), there may be local considerations that need to be taken into account.

Particular important principles to frame review of this type of reserch

1. There should be a clear research question and purpose.
2. The research team should be equipped to complete the study.
3. The research should incorporate patient and participant views.
4. Benefits, harms and burdens of the study should be properly addressed.
5. The choice and recruitment of participants must be justified, safe and fair.
6. Participants should be offered a fair choice (Informed consent) and understand what they are agreeing to.
7. There should be fair payments for participation.

Consequent considerations will be discussed in the presentation.

http://www.reviewingresearch.com/human-challenge-studies/

Speaker Abstracts

Anna P. Durbin

Pre-existing Immunity Case Study: Zika Virus

Background: Zika virus (ZIKV) is a member of the Flaviviridae family. It is closely related to the dengue viruses. Following the explosive outbreak of ZIKV in the Americas in 2015-2016, many theories arose as to how ZIKV spread so quickly. Antibody dependent enhancement (ADE) of infection whereby non-neutralizing antibody can bind to a virus and then allow the virus-antibody complex to enter cells via the Fc R is thought to play an important role in the severity of dengue infection. Dengue antibody has been demonstrated to enhance ZIKV infection of Fc R bearing cells in vitro and in immunodeficient mice, but epidemiologic studies have not illustrated ADE of ZIKV in these dengue-endemic areas.

Challenges: It is well documented that any flavivirus antibody can enhance the infection of another flavivirus in vitro. It has been difficult to demonstrate ADE of infection in vivo for flaviviruses other than dengue. Teasing out the protective vs pathologic effects of pre-existing flavivirus antibody on ZIKV is complicated.

Proposed Approach: Review of the epidemiologic data during and following the ZIKV outbreak has not found evidence that pre-existing DENV antibody is responsible for the neurological complications of ZIKV or for the rapid spread of ZIKV through the Americas. In addition, some studies have shown that recent DENV infection may protect against ZIKV infection.

Conclusions: The role of pre-existing flavivirus antibody in ZIKV infection is not well understood. Controlled human infection models may help better characterize the protective and pathologic effects of pre-existing DENV antibody on ZIKV and vice versa.

Speaker Abstracts

Anna P. Durbin

Ethics Case Study: Dengue

Background: Dengue is the most common mosquito-borne viral illness world-wide. There are four different dengue virus (DENV) serotypes, each capable of causing the full spectrum of disease. Dengue is unique in that antibody to one of the 4 serotypes can enhance the severity of disease of a heterotypic DENV upon subsequent secondary DENV infection. This has been termed antibody dependent enhancement of infection and it is thought that the heterotypic antibody can bind to the DENV without inducing neutralization. The antibody-virus complex then enters Fc R bearing cells leading to higher viremia and more severe disease. Epidemiologic studies have identified the greatest risk factor for severe dengue is a second, heterotypic DENV infection.

Challenges: Treatment for DENV infection consists only of supportive care; licensed anti-viral agents for DENV do not exist. In addition, experimentally infecting subjects with a monovalent DENV could potentially put them at risk for more severe dengue should that experience a secondary, heterotypic infection. The risk of this is greater in dengue endemic areas. In addition, there is a risk to third parties if CHIM studies are conducted in areas in which the vector is present.

Proposed Approach: Prior to the conduct of a dengue challenge study the virulence of the proposed challenge virus must be characterized. Two models for dengue challenge exist: a controlled human infection model and a disease model. The objectives of the study should justify the use of a disease model over that of an infection model. Appropriate clinical care must be available to subjects and the risk of mosquito-borne transmission much be mitigated.

Conclusions: Dengue human challenge can be safety and ethically conducted if the risks to volunteers and the risk of transmission to third parties is adequately mitigated.

Speaker Abstracts

Kate Emary

Human challenge models in Paediatric populations

Oguti B[1], Emary KRW[1], Harriss E[2], Khan F[1], Binik A[3], Karron RA[4], Emerson C[3], Pollard AJ[1]

[1] Oxford Vaccine Group, Department of Paediatrics, University of Oxford and the NIHR Oxford Biomedical Research Centre, Oxford, UK
[2] Bodleian Health Care Libraries, University of Oxford, Oxford, UK
[3] Institute on Ethics & Policy for Innovation, Department of Philosophy, McMaster University, Ontario, Canada
[4] Center for Immunization Research, Department of International Health, Johns Hopkins University, Baltimore, Maryland, USA

BACKGROUND – Human infection ('challenge') studies for a variety of pathogens are well accepted models for investigation of vaccine efficacy. While wild-type (wt) organisms were used for paediatric challenge several decades ago, recent paediatric challenge has only been performed with attenuated live vaccines or vaccine candidates. There are complex ethical arguments regarding the inclusion of children in studies where participants are exposed to live infectious agents. This study seeks to systematically review the literature on the involvement of children in challenge studies.

METHODS –Medline, EMBASE and the Cochrane Library were searched without date restriction. Relevant literature was also hand-searched for references. References are being reviewed independently by two researchers for inclusion.

RESULTS – Our search returned a total of 118,341 records for title and abstract screening. From hand-searched literature 74 papers have so far been found.

CONCLUSIONS – Whilst topic such as this involving multiple pathogens and populations without time restriction makes conventional literature searching more difficult, a thorough approach to capture as many examples as possible was felt necessary. There are many different types of human 'challenge' from exposure to wt organisms to challenge with live vaccines. This generates different ethical positions, and for clarity, it may be useful to employ different terms to describe challenge with wt organisms and with vaccines. This review will identify a body of literature that will help to define an ethical framework and shape further conversations around human infection models in a paediatric population.

Speaker Abstracts

Olivia Grimwade

Attitudes towards payment and payment practices in controlled human infection model (CHIM) research

Olivia Grimwade, Julian Savulescu, Alberto Giubilini, Anne-Marie Nussberger, Josh Osowicki, Justin Oakley

Background: The payment of CHIM participants is a controversial issue involving stakeholders across ethics, medicine, and policy-making, with allegations circulating suggesting exploitation, coercion and other violations of ethical principles. To date, little is known of what investigators pay participants or what principles are used to determine payment. Likewise, there have been no empirical studies to assess the public's attitudes on this matter. Here, we survey both the general public and CHIM investigators on their attitudes towards the ethics of payments in CHIM.

Methods: A representative sample of the UK public was surveyed online to assess public attitudes towards payment in CHIM. This will be complemented by a survey of CHIM investigators, which also explores payment practices. The survey presents respondents with CHIM scenarios in which type of risk (severe side effects; death as result of a severe side effect) and magnitude of risk (1 in 1,000,000 to 1 in 1,000) are varied systematically. For each scenario, the respondents indicate required payment for participation and the willingness to allow participation in the given study.

Results: We surveyed 264 members of the public, who required higher payments for CHIM participants exposed to more severe types of risk as well as greater risk magnitude. Furthermore, 86.7% of respondents ranked risk as the most important factor to consider in determining payment for CHIM. Respondents' ratings of willingness to allow participation in CHIM similarly followed the nature and level of risk. These results on public attitudes towards CHIM payment should be complemented by CHIM investigators' attitudes and practices by the time we present at IABS.

Conclusions: A representative sample of the UK general public requires CHIM payments to compensate for risk type and level of risk involved in such studies. Although many research guidelines do not condone paying for risk, our findings provide empirical support to the growing number of ethical arguments challenging this status quo. We suggest that a Wage and Risk Payment Model, which considers a number of different payment factors such as time requirements, study location, pain experienced and risk, would be the best model to deliver just and ethical payment to CHIM participants.

Speaker Abstracts

Marcia M. Hobbs

Experimental human gonococcal infection: Advances and challenges.

Marcia M. Hobbs, PhD, Andreea Waltmann, PhD and Joseph A. Duncan, MD, PhD
Department of Medicine, University of North Carolina, Chapel Hill, NC, USA

Introduction: Neisseria gonorrhoeae (Ng) is a human-specific pathogen that has co-evolved with us for centuries. Experimental infection of male volunteers with Ng is safe and reproduces the features of naturally acquired gonococcal urethritis. Human studies have defined the natural history of experimental infection, and the controlled human infection model (CHIM) has proved useful for testing the importance of putative gonococcal virulence factors for urethral infection in men. The model also presents opportunities to examine host immune responses that may be exploited or improved in development of gonococcal vaccines.

Challenges: In addition to ethical challenges inherent in all CHIMs, in which individuals are deliberately exposed to microbial pathogens, the gonococcal model faces additional barriers, including stigma regarding the natural route of sexual transmission and the theoretical potential for adverse reproductive consequences of infection.

Approach Being Taken: The human Ng infection model is limited to men to avoid the potential for complications from ascendant infection in women. Risks are explained in detail; participants must pass a test of understanding, and written informed consent is obtained twice: before screening and immediately before inoculation. Bacteria used for inoculation have demonstrated susceptibility to antibiotics used to treat all participants; tests of cure have been negative in 100% of participants enrolled to date.

Conclusions: More than 240 volunteers have been enrolled in studies using this CHIM since the 1990s with no serious adverse events. Experimental gonococcal infection in men is safe, reproducible, and has contributed significantly to our understanding of Ng pathogenesis and vaccine development.

Speaker Abstracts

Paul Kaye

GMP and the Challenge Agent: Leishmaniasis

Paul Kaye[1], Eli Schwartz[2], Charle Jaffe[3], Jovana Sadlova[4], Charles Lacey[1], Vivak Parkash[1], Greg Matleshewski[5] and Kai Lipinski[6].
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Background: Leishmaniasis is a globally important but neglected disease, for which no vaccines for human use are currently available. Reflecting the folklore practice in endemic countries of deliberately inoculating lesion scrapings to induce natural immunity ("leishmanization"), almost two million people were inoculated with Leishmania parasites during the 20th century. In 1989, the WHO recommended this practice be ceased except as a last resort. In 2000, WHO supported a proof of concept study of leishmanization as a tool for vaccine evaluation, the first modern-day leishmaniasis controlled human infection model (CHIM; Mohebali et al Acta Tropica. 2019. 200:105173). This program was not continued for a combination of scientific and political reasons.

Challenges: Early consultation with the UK Medicines and Healthcare products Regulatory Agency (MHRA) provided the framework for a successful funding application to MRC to support development of a new CHIM involving transmission by sand fly bite. Major discussion points included: provenance of the challenge agent; manufacturing standard (GMP or GMP-like); release and stability assays; mitigation of risks to participants.

Approach: Consideration of all factors indicated that the best option was to source and characterise fresh clinical isolates of Leishmania major and to produce a challenge agent under GMP using a contract development & manufacturing organisation (CDMO). The chosen CDMO had no prior experience of working with Leishmania but experience with other Category 2 pathogens. Safety documentation was provided and an iterative process of developing SOPs adopted. For two parasite donors, full clinical histories were obtained along with HIV, HTLV1, HBV, HCV and Mycoplasma pneumoniae status and donors were followed for 6 months post cure. Parasites were isolated and cultured using GMP grade materials, genotyped, tested for virulence and drug sensitivity in mice and for transmission competence in two sand fly species. Pre-GMP expansion ("research banks") is underway and virulence will be re-confirmed in mice prior to GMP production. A stability plan for the GMP bank has been developed.

Conclusions: Although GMP-like production of this challenge agent might have been possible in an academic setting, the use of an experienced CDMO has had tangible benefits in terms of i) ensuring maximal compliance with our desired product specification, ii) cost, iii) GMP compliance and iv) time to completion.

Speaker Abstracts

Kirsty Le Doare

Microbiological endpoints for a Group B Streptococcal human challenge model

Background: Group B Streptococcus (GBS) is commonly found in the gut or lower vaginal tract, where it resides harmlessly in both men and women. The immunological and protective role of GBS carriage is unknown, but carriage in pregnancy is associated with ascending infection that can result in chorioamnionitis, preterm, stillbirth and early onset neonatal sepsis (first 7 days of life). Approximately 20% of pregnant women carry GBS globally. As GBS is the leading cause of neonatal infection worldwide, and carriage is critical in this process, a human challenge model could be developed to study the immunizing effect of an experimental carriage episode and its role in sustaining protective immunity in healthy non-pregnant women in preparation for a maternal GBS vaccine.

Challenges: Several studies highlight the transient nature of GBS carriage during pregnancy. Women who are intermittent carriers are often found to carry the same GBS type on recolonization, highlighting the possibility that low levels of GBS are missed due to insensitive microbiological methods or low density of carriage. Two African studies (South African and the Gambia) identified reduced rates of carriage associated with high antibody concentrations, implying an immunizing effect of exposure to GBS. However, the relative contribution of anticapsular and antiprotein responses in protection against carriage are still unclear, as is the correlation between mucosal and systemic immunity to colonisation.

Proposed Approach: The primary objective of a human challenge study would be to evaluate the association between natural serotype-specific serum CPS IgG antibody in relation to an experimental GBS carriage episode in non-pregnant women and the association between CPS antibody and clearance of GBS colonization.

Conclusion: Our hypothesis is that carriage would boost the pre-exiting anti-GBS antibody responses, and that these altered responses would be protective against reacquisition of carriage and thus protect against passage of GBS from mother to child at birth.

Speaker Abstracts

Helen McShane

Immunological endpoints in challenge studies

Helen McShane[1], Rachel Tanner[1], Julia Marshall[1], Magali Matsumiya[1], Rachel Wittenberg[1], Raquel Ramom-Lopez[1], Stephanie Harris[1], Iman Satti[1], Henry Bettinson[2].
[1] The Jenner Institute, University of Oxford
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Background

Controlled human infection models provide a useful experimental medicine model to demonstrate a biological signal of efficacy in humans, prior to undertaking large, expensive field efficacy trials. Necessarily, the primary endpoint in such studies is usually microbiological, to allow the demonstration of a reduction in pathogen burden with vaccination. However controlled human infection models also allow the identification of potential immune correlates of protection, which can subsequently be validated in field efficacy trials. For tuberculosis vaccine development, the identification of immune correlates of protection would be game changing. In developing a controlled human infection model for tuberculosis, it is not possible to ethically infect healthy volunteers with virulent Mycobacterium tuberculosis. However, using BCG as a model mycobacterial challenge agent which is licensed for human use, we have established controlled human infection models using intradermal and aerosol delivered BCG.

Experimental Approach

Using an intradermal infection model, we have identified gene expression signatures and cytokine profiles that correlated with mycobacterial growth. We have also used an in vitro mycobacterial growth inhibition assay to demonstrate that it is possible to detect the same vaccine response using in vivo and in vitro challenge assays.

An additional potential use of controlled human infection models is to interrogate the immunobiology of a controlled time point infection. Such studies complement field studies where it is not possible to precisely time infection. Using an aerosol BCG infection model, we are currently using bronchoalveolar lavage fluid, lung biopsies and blood taken at different time points post-infection to define the immunobiology of mycobacterial infection in humans. Parallel studies in non-human primates allow us to use these immunological outcomes to bridge to efficacy and furthermore to confirm the relevance of such animal models.

Speaker Abstracts

Blanche Oguti

Factors influencing participation in controlled human infection models: a pooled analysis from six enteric fever studies

B Oguti, MM Gibani, C Darlow, CS Waddington, C Jin, E Plested, D Campbell, C Jones, TC Darton, AJ Pollard

BACKGROUND: Enteric fever is an acute febrile-illness caused by infection with the human-restricted Salmonella serovars Typhi and Paratyphi. Controlled human infection models (CHIM) of S. Typhi and Paratyphi infection are used to accelerate vaccine development and to better understand host-pathogen interactions. The primary motivations for participants to take part in these studies are unknown. We studied participant motivations, attitudes and the factors influencing CHIM study participation.

METHODS: Participant surveys were nested in six enteric fever CHIM studies conducted at a single centre in Oxford, UK, between 2011 and 2017. All eligible participants received one invitation to complete an anonymous, self-administered paper or online survey on either day 28 or 60 after challenge. A descriptive analysis was performed on these pooled data. All studies were included, to minimize selection bias.

RESULTS: Survey response rates varied from 33.0%-86.1%, yielding 201 participants. In the cohort, 113/198(57.0%) were educated to bachelor's level, 61.6% were employed, 30.3% were students and 4.6% were unemployed. The most commonly cited motivations for CHIM study participation were a desire to contribute to the progression of medicine (170/201; 84.6%); the prospect of financial reimbursement (166/201; 82.6%) and curiosity about clinical trials (117/201; 57.2%). The majority of respondents (139/197; 70.6%) reported that most people advised them against participation.

CONCLUSION: Motivation to participate in a CHIM study was multi-factorial and heavily influenced by internal drivers beyond monetary reimbursement alone. High educational attainment and employment may be protective factors against financial inducement; however, further research is needed, particularly with CHIM studies expanding to low-income and middle-income countries

Speaker Abstracts

Andrew J Pollard

The Role of Challenge Models: Case study on Typhoid/Paratyphoid

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There are more than 11 million cases of enteric fever every year, mainly affecting children and young adults in regions of the world where there is inadequate access to clean water and sanitation infrastructure is poor. The spread of highly resistant strains of Salmonella Typhi has caused recent public health concern. New typhoid conjugate vaccines (TCVs) developed over the past decade are immunogenic but there were only limited efficacy data from a prototype TCV 20 from years ago to support widespread introduction. We used a human challenge model of typhoid infection to demonstrate efficacy of the new vaccine and simultaneously showed efficacy in the model of a licensed plain polysaccharide vaccine, which had previously been found to be efficacious in field studies. Results from the challenge model showed that the new TCV was at least as potent as the licensed vaccine and that it induced memory B cell production (unlike the licensed product), supporting global policy recommendations in 2017. Data are now emerging from analysis of challenge model samples on potential correlates of protection, which will inform introduction in different regions and the ongoing development of vaccines by other manufacturers. These data also supported release of funding for field studies to evaluate implementation approaches, which have now confirmed efficacy in an interim analysis.

For paratyphoid vaccines, there are no licensed products and disease burden is currently very much lower than it is for typhoid. For this reason, field efficacy studies may not be feasible. Thus, establishing efficacy data for licensure of a novel paratyphoid vaccine, and identifying potential correlates of protection, might best be undertaken through the use of a human challenge model, supported by field data on immunogenicity. Possible routes to licensure will be discussed.

A bivalent vaccine, developed with the use of a human challenge model, providing protection against typhoid and paratyphoid could have a considerable impact on the burden of enteric fever among some of the world's most vulnerable children and help in the fight against antimicrobial resistance.

Speaker Abstracts

Chad Porter

Development, use and refinement of Shigella controlled human infections

Background. Since 1946 the controlled human infection model (CHIM) for Shigella has been used to improve understanding of disease pathogenesis, describe clinical and immunologic responses to infection and as a tool for vaccine development. As the frequency and intent for use in product development and down-/up-selection increases, standardization and consistency in the methods utilized is necessary.

Challenges. As the frequency and sample size of controlled human infections with Shigella increase, there is a need to standardize methods, endpoints and sample collection. To date institutional and investigator variability has led to inconsistencies in model application and reported endpoints. Harmonization of the methods utilized is needed to minimize variability in the host, ensure consistency in inoculum preparation and refine clinical endpoints to account for the complex of signs and symptoms arising from experimental Shigella infection. These refinements may be integral to the future use of these models to support vaccine licensure.

Approaches. Several recent advancements have been attempted to standardize the Shigella challenge model ensure consistency in attack rates and disease characterization over time and across institutions. The first is the transition from utilizing freshly harvested plate-grown organisms to lyophilized lots of product that can be directly administered to minimize potential variability in administered doses and subsequently disease attack rates. Additionally, efforts to establish and standardize the primary endpoint for utilization across institutions has been an area of increased focus to ensure consistent assessments of preliminary efficacy in potential vaccine candidates. In addition to the primary endpoints, harmonizing secondary endpoints characterizing shigellosis severity will enable a more robust assessment of vaccine candidates. Many of these methods, in addition to consensus recommendations regarding sample collection and testing, have recently been published in a Clinical Infectious Disease supplement and will be detailed.

Conclusions. Refinement and harmonization of the Shigella human challenge model will ensure consistency in its use and application in early stage clinical trials of prototype Shigella vaccines and enhance our understanding of the host response to infection and potentially assist in the identification of immune correlates of protection.

Speaker Abstracts

Meta Roestenberg

Case study – schistosomiasis

Background: Schistosomiasis, a WHO-appointed neglected tropical disease, is caused by multicellular parasites transmitted by fresh water snails. Its treatment relies on the use of one drug only, praziquantel, which is insufficient to control transmission in highly endemic areas. Novel medicines and vaccines are urgently needed to expand the toolbox for schistomiasis control. An experimental human model for schistosomiasis could accelerate the development of these products.

Materials & Methods: We performed a dose-escalating clinical safety trial in 17 volunteers who were dermally exposed to male Schistosoma mansoni (Sm) cercariae, which do not produce eggs at the Leiden University Medical Center, the Netherlands. The safety as well as the infectivity and kinetics of worm-derived circulating anodic antigen (CAA), the primary biomarker readout for infection, was studied.

Results: We found a dose-related increase in adverse events related to acute schistosomiasis syndrome. This syndrome had previously been attributed to egg formation. Overall there seemed to be a dose-response relationship between adverse events and challenge dose. Symptoms could not be predicted from baseline characteristics. Serum CAA peaked above detection levels in the majority of volunteers several weeks after exposure. All volunteers showed IgM and IgG1 seroconversion and worm-specific cytokine production by CD4+ T-cells. All volunteers were cured with praziquantel provided at 12 weeks after exposure.

Conclusions: Infection with 20 Sm cercariae leads to severe adverse events in a minority of volunteers and provides high infection rates, paving the way for fast-track product development for treatment and prevention of schistosomiasis.

Speaker Abstracts

Michael Selgelid

This paper outlines and analyses ethical issues associated with human (infection) challenge studies. Responding to the concern that challenge studies might be considered ethically objectional because they involve intentional harm of research participants, it demonstrates why there should be no in-principle ethical objection to human challenge studies--and argues that this kind of research might even be ethically required. While numerous infamous historical examples of research involving human subjects involved the direct infection (and/or microbial exposure) of human participants, it was not intentional infection (and/or microbial exposure) of participants per se that made these studies wrong. Human infection challenge studies are nonetheless ethically sensitive, and thus warrant additional ethical vigilance—e.g. via establishment of specific research ethics guidelines and/or special review procedures

Speaker Abstracts

Adian Wildfire

Containment of respiratory viruses: a case study of unexpected HPIV infection during an A/Belgium/4217/2015 [H3N2] influenza challenge study

SGS LS

BACKGROUND—An unexpected diagnosis of hPIV was made in a subject prior to discharge (day 10) from a commercial isolation unit during a phase IIb influenza challenge study to assess the safety and efficacy of an inhaled, antiviral drug in healthy volunteers (primary endpoint was a statistically significant reduction in the viral AUC). All subjects had previously been pre-screened (d-2) against a panel of upper-respiratory tract pathogens including hPIV and found to be negative by multiplex PCR (BioFireTM). Root cause analysis offered three possible scenarios for undiagnosed infection. Following discussion, the subject's data was subsequently removed from the efficacy dataset but was included in follow-up and SDTM database for the general and safety analyses.

METHODS— 80 subjects were enrolled in the study. Subject suitability was primarily based upon a pre-screening MNT value of <10, as part of the protocol's IC/EC criteria. Subjects were admitted to a human challenge (containment) unit in cohorts of 20 at d-2 for randomisation. The challenge unit incorporated negative pressure HVAC systems appropriate for CL3 and HCU staff employed reverse barrier-nursing techniques, including appropriate PPE, to minimise the possibility of cross-infection between staff and subjects. Subjects were required to wear an FP3 mask at all times when in communal areas. Subject screening at d-2 included a multiplex PCR for common URT pathogens inclusive of hPIV. Subjects were subsequently inoculated on d1 with an influenza challenge agent (A/Belgium/4217/2015, H3N2) before being dosed with drug or placebo daily over a 5-day period. Subjects were monitored for shedding (qRT-PCR and TCID50 x2 daily) and symptoms (Symptom Scorecard x2 daily) from d1 to d10. Subjects were released at d10 pending a satisfactory physical examination and a negative BioFireTM test.

RESULTS— A mild to moderate ARI or ILI was noted in a proportion of subjects from d3 to d6 with an uneventful recovery by d8. NP testing for virus showed H3N2 shedding consistent with previous studies using A/Belgium. Upon testing for URT pathogens prior to discharge at d10 it was discovered that one subject was positive for hPIV. This was confirmed by PCR testing at Erasmus MC who further identified the pathogen as hPIV-1. The subject confirmed to be shedding hPIV-1 was positive from d1 until d11 with only minor variations in viral load (normal variation: 1log10 = 3.3 Ct).

CONCLUSIONS— It is possible that the hPIV-1 positive subject became infected in one of three scenarios: 1. d-2 sample was already positive for HPIV-1 but it was not detected; 2. The subject became infected between d-2 and d1 or 3. The subject was in the incubation period on d-2 and commenced shedding on day 1. Given the sensitivity of the BioFireTM assay, the short incubation period of hPIV-1 (2-7 days) and the duration of shedding (11 days), scenarios 2. and 3. are most probable. Since this incident additional BioFireTM testing at d-1 has been introduced.

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I began working on Phase I and IIb clinical trials of a candidate malaria vaccine based on viral vectors between the Jenner at University of Oxford and KEMRI-Wellcome in Kilif, Kenya in 2002. I returned to Oxford in 2006 to complete specialist clinical training as a clinical lecturer, and was appointed as a senior fellow in the NIHR Oxford Biomedical Research Centre in 2009. I remained active in malaria research during these posts, leading further trials of GSK's candidate malaria vaccine "RTS,S", and as a member of the Malaria Vectored Vaccine Consortium funded to test viral vectored malaria vaccines in several sites in Africa including Kilifi. An MRC Clinician-Scientist Fellowship, allowed me to return to be resident full-time in Kilifi in 2013, working on heterogeneity of malaria transmission. I became Executive Director of the KEMRI-Wellcome Trust Research Programme in September 2014. My current interests still include malaria vaccines, as well as Yellow Fever and Ebola vaccines, studies of malaria transmission dynamics including genotyping and work on a human malaria challenge model to study acquired immunity.

Biosketch

Nele Berthels, Ph.D.

Clinical Assessor

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Nele Berthels is a clinical assessor at the Federal Agency for Medicines and Health Products in Belgium contributing to the marketing authorization of vaccines for human use in Europe and beyond. As Therapeutic Area Coordinator, she is responsible for the benefit-risk analysis of vaccines during their development and lifecycle.
She contributes to the agency's Innovation Office by advising industry and academic groups on their clinical development plans for new vaccines. She also contributes to scientific advices at the European level through the Scientific Advice Working Party of the European Medicines Agency (EMA).
She is a member of the Vaccines Working Party, the EMA body that provides recommendations to the Committee for Medicinal Products for Human Use (CHMP) on matters relating directly or indirectly to vaccines including the drafting of guidance documents.
Within the Belgian agency she is also involved in the activities of the Centre of Excellence of Vaccines. One project concerns the scientific and regulatory aspects of controlled human infection models and human challenge studies.
She obtained a MSc degree in bio-engineering and a PhD in biochemistry from KU Leuven (Belgium) in collaboration with Stellenbosch University (South Africa).

Biosketch

Susan Bull BSc, LLB, MA, PhD

Senior Researcher in the Ethics of Genomics and Global Health

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Susan has a longstanding research interest in international health research ethics, with a focus on both novel and enduring ethically complex issues. Prior to her current role she was Deputy Director of the Nuffield Council on Bioethics and managed the working party addressing ethical issues associated with health research in LMICs. In conjunction with colleagues in Ghana, Kenya, India, Mali, Malawi, South Africa, Thailand, Vietnam, Susan has led multi-national research collaborations addressing ethical issues associated with genomic research, data sharing, and seeking consent to research. In addition to her research interests, Susan heads Global Health Bioethics, Research Ethics and Review, and has been involved in the development and implementation of multiple online and in-person training and capacity building programmes in research ethics. Susan is the Rapporteur for the WHO Ethics Guidance on controlled human infection studies, which is currently under development.

Biosketch

Andrew Catchpole BSc DPhil

Chief Scientist hVIVO

Andrew Catchpole first studied as a virologist as the University of Warwick before then further his education with postgraduate studies in influenza replication at Oxford University. Since then he has applied his scientific knowledge in a commercial setting. After working as part of a multidisciplinary R and D team developing nuclear medicine research tools at GE Heathcare he then returned to the field of virology to work for hVIVO, an industry-leading providing of human viral challenge studies. Andrew is now considered an expert in human viral challenge studies (controlled human infection studies) having played key roles in the development of influenza, RSV and hRV models at hVIVO. He has overseen the design and conduct of numerous antiviral and vaccine product efficacy studies and now works as Chief Scientist in the company providing both internal consultancy as well as advising hVIVO's clients and collaborators on challenge study design. In addition, he was PI on a recent successfully completed DARPA-sponsored research project to utilise the challenge model to identity human biomarkers and algorithms prognostic of influenza contagiousness.

Biosketch

Primus Che Chi, PhD

Mid-Level Social Scientist

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Primus is a social scientist with a background in health systems and bioethics, committed to and passionate about promoting maternal and child health and ethical conduct of research in low- and middle-income country (LMIC) settings. With basic and postgraduate training in microbiology and parasitology, Primus went on to complete additional graduate trainings in Public Health and Bioethics. Upon completing his PhD in International Health, Primus served as a postdoctoral research fellow with Centre for Research on HealthCare in Disasters, a WHO Collaborating Centre at Karolinska Institute (Sweden). Leveraging his skills and experiences in the fields of microbiology/parasitology, bioethics and public health, Primus joined the KEMRI-Wellcome Trust Research Programme (KWTRP) in July 2018 as social science lead (Mid-level Social Scientist) for Controlled Human Infection Model (CHIM)/ challenges studies – trials that have the potential of fast-tracking the development of drugs and vaccines for important infectious diseases affecting maternal and child health. He currently leads a small team of researchers exploring the social and ethical implications of CHIM studies in a LMIC context like Kenya, using an empirical ethics approach, with the goal of contributing to policy and practice. Their empirical ethics work is embedded within ongoing and planned challenge studies for malaria and Shigella at the KWTRP.

Biosketch

Roma Chilengi, MD

Chief Scientific Officer

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I am a Zambian physician, epidemiologist and vaccinologist currently employed as Chief Scientific Officer at the Centre for Infectious Disease Research in Zambia (CIDRZ). My research career has spanned roles as study physician on clinical studies in Zambia while at Tropical Diseases Research Centre; as sponsor based central study manager for malaria vaccine trials while at the African Malaria Network Trust in Tanzania; and as head of clinical trials facility at the University of Oxford/KEMRI-Wellcome Trust Programme in Kenya. In the course of this career, I have gained much experience as a clinical investigator as well as manager for numerous studies in Africa and have also competed for and managed various research grants. My research work is on enteric disease vaccines including rotavirus, ETEC, cholera and Shigella, as well HIV vaccine research. Presently, i am working to validate a human infection challenge model using live oral rotavirus vaccine as the infection agent and simultaneously studying to understand differences in between natural infection in Zambia and exposure through infection challenge to naïve volunteers. My goal is to establish a robust human infection studies site in Zambia for evaluating enteric vaccines.
I am also the Site Leader for the current CIDRZ Clinical Trials Unit within the HVTN network. I have an adjunct faculty position as Assistant Professor, University of Alabama at Birmingham school of Medicine as well as honorary lecturer appointment at the University of Zambia, School of Public Health

Biosketch

Rebecca Cox

Rebecca Cox is professor in medical virology and head of the Influenza Centre at the University of Bergen, Norway leading a team of 14 scientists. Rebecca Cox completed her PhD in 1995 at the London Hospital Medical College, University of London, UK before post doc positions at Guys Hospital, UK and the University of Bergen, Norway. She has >25 years of experience of influenza work particularly in development and evaluation of influenza vaccines. She has serves as advisor to the WHO SAGE Immunization Working Group on Influenza, the Norwegian epidemic and pandemic committee, European Medicines Agency (EMA) and the vaccine industry on influenza vaccines. She has led EU funded preclinical and phase I trials of pandemic/universal vaccines. Her research focuses on development and evaluation of influenza vaccine with particular focus on human immune responses to infection and vaccination. She is deputy chair of Influenza and Other Respiratory Viruses and senior editor for the journal Influenza and Other Respiratory Viruses and associate editor of the journals human vaccines and immunotherapeutics and Vaccines and Molecular Therapeutics (specialty section of Frontiers in Immunology and Frontiers in Public Health). She is author of more than 100 peer-reviewed papers and regularly contributes to the public debate on Influenza and vaccines through multi-media channels.

Biosketch

Dr. Claudia Emerson

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Claudia Emerson is the founding Director of the Institute on Ethics & Policy for Innovation at McMaster University, and Associate Professor in the Department of Philosophy. Her work in applied ethics considers issues and policy gaps in global health research. She is particularly interested in ethics issues related to data sharing and models of data governance, the introduction and adoption of novel technologies, and the management of infectious disease. She is the Principal Investigator of the ESC (Ethical, Social, and Cultural) Thinking Program that supports the Global Health division of the Bill & Melinda Gates Foundation address normative issues encountered along the discovery-to-delivery pathway for potential life-saving interventions. Currently, she is leading the development of Funder's Principles for human infection studies and collaborating on the development of ethics guidance for these studies.
Dr. Emerson serves in several advisory capacities related to public health and evidence-informed policymaking. She is a member of the Malaria Strategic Advisory Panel (MSAP) of the Bill & Melinda Gates Foundation, a member of the LEEDR (Legal, Ethical, Environmental, Dual-Use and Responsible innovation) Panel for DARPA's Safe Genes Program, and serves on the Steering Committee of the Outreach Network for Gene Drive Research, and the Scientific Committee of the Cochrane Colloquium 2020.

Biosketch

Olivia Grimwade BMedSc(Hons)

MD Candidate

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Olivia Grimwade is currently completing her final year of the Doctor of Medicine at Monash University in Melbourne, Australia. In 2019, Olivia undertook a BMedSc(Hons) at the Oxford Uehiro Centre for Practical Ethics under the supervision of Prof Julian Savulescu, Dr Alberto Giubilini (Oxford) and A/Prof Justin Oakley (Monash). The focus of her research was the ethical issues surrounding the financial compensation of participants of controlled human infection model (CHIM) research. Olivia presented the findings of this research at the European Association of Centres of Medical Ethics (EACME) 2019 Conference. Olivia was the recipient of a Cabrini Summer Research Scholarship in 2017/2018 based in the Intensive Care Unit at Cabrini Hospital. Olivia is also a second and third year medical tutor at Mannix College, Monash University.

Biosketch

Marcia M. Hobbs, PhD

Professor of Medicine

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Marcia M. Hobbs, PhD is Professor of Medicine and Microbiology & Immunology in the School of Medicine at the University of North Carolina at Chapel Hill, where her research program includes the Neisseria gonorrhoeae controlled human infection model. She is also an associate director of the HIV/STD Laboratory Core of the UNC Center for AIDS Research. Core laboratory activities support a variety of research projects aimed directly at diagnosis, treatment and prevention of sexually transmitted infections or the use of these infections as bio-markers in evaluating biomedical or behavioral interventions aimed at prevention of HIV and other sexually transmitted infections. In addition, Dr. Hobbs is active in medical school education and has received several teaching awards.

Biosketch

Gagandeep Kang, MD, PhD, FRCPath, FAAM, FASc, FNASc, FNA, FFPH

Executive Director

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Professor Kang is the Executive Director, Translational Health Science Technology Institute (THSTI), an autonomous institute of the Department of Biotechnology. Prior to joining DBT, Prof. Kang was Professor and Head of the Wellcome Trust Research Laboratory, and the Division of Gastrointestinal Sciences at the Christian Medical College (CMC) in Vellore.
Professor Kang has built a strong inter-disciplinary research program that has demonstrated the complex relationships between infection, gut function and physical and cognitive development. Based first at an outstanding medical college and now at the THSTI, she has established a strong training program for students and young faculty in clinical translational medicine aiming to build a cadre of clinical researchers studying relevant problems in India.
With over 350 publications, she is internationally recognized for her contributions to biomedical research. She serves on or has served on the scientific advisory committee of several national and international institutions, including the Wellcome Trust, UK, the DBT-Wellcome Trust India Alliance, the International Vaccine Institute, International Center for Genetic Engineering and Biotechnology and the World Health Organization.

Biosketch

Paul Kaye, PhD, FRCPath, FMedSci.

Professor of Immunology

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Paul Kaye is Professor of Immunology at the Hull York Medical School, University of York. He trained in zoology (BSc) and immunology (PhD) and has worked for over 30 years on the immunology and immunopathology of the neglected tropical disease leishmaniasis. In addition to his work in leishmaniasis, he is internationally recognized for his research on macrophages and dendritic cells, contributing to a fundamental understanding of their biology in health and disease, and for his work on lymphoid tissue remodeling and granulomatous inflammation during chronic infection. Paul is a Wellcome Trust Senior Investigator and an elected Fellow of the UK Academy of Medical Sciences. He was awarded FRCPath in 2004. He has extensive links with leishmaniasis-endemic countries and is currently leading two Phase II therapeutic vaccine trials in Sudan, developing a digital pathology network to enhance data sharing and establishing a controlled human infection model of sand fly transmitted cutaneous leishmaniasis. Paul has published over 120 articles including Nature Medicine, Immunity, J. Clin. Invest., and PNAS, and has received funding as principal investigator or co-investigator of >£35M. Paul is currently Chair of the MRC Infections and Immunity Board and a member of MRC Strategy Board.

Biosketch

Simon Kolstoe, Ph.D.

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Originally a Biochemist working in pre-clinical drug development, Dr Simon Kolstoe is now a senior lecturer in Evidence Based Healthcare at the University of Portsmouth and chair of both the Hampshire A NHS and MOD research ethics committees. He has recently contributed to the UK House of Commons select committee inquiry on research integrity, published on the issues of reporting bias and clinical trial transparency, and been appointed to the Department of Health's Confidentiality Advisory Group (CAG). One particular area of interest is the governance of research ethics committees where he has acted as a policy advisor to Universities, Government departments and independent organisations seeking to establish robust research ethics processes. Along with a PhD in Biochemistry he holds degrees in Philosophy and Research Ethics.

Biosketch

Kirsty Le Doare, MD, Ph.D.

KRI Future Leaders Fellow

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Dr Le Doare is UKRI Future Leaders Fellow and Professor of Global Health within the Paediatric Infectious Diseases Research Group at St. George's, University of London.

Her research interests are age-related immune responses to infectious diseases, in particular to Group B-streptococcus (GBS). She is interested in improving our knowledge of how maternal antibody in vaginal fluid, blood and breast milk is passed to babies and how this protects them from colonisation and disease. Her focus is on harnessing these tools of nature (basic pathophysiology and immunity) to improve vaccines and prevention strategies, coupled with clinical vaccine studies at her maternal vaccination platform site in Kampala, Uganda.

She leads the GASTON initiative to determine serocorrelates of protection against GBS and is part of the WHO task-force to defeat meningitis by 2030 and develop the pathway for licensing the GBS vaccine. She has close collaborations with colleagues at the CDC, FDA and academic and industrial groups both in the UK and overseas. She is currently working on a pilot study to understand vaginal mucosal immunity to GBS colonisation in preparation for a Human Challenge Study.

She is passionate about training the next generation of female scientists working in Africa to improve maternal and child health. She receives funding from the EDCTP, MRC and the Bill and Melinda Gates Foundation.

Biosketch

Katherine Littler

Katherine has extensive experience in global health ethics, research, governance and policy. In October 2018, Katherine joined the Global Health Ethics Team at the World Health Organization in Geneva as Senior Ethics Specialist and Co-lead. Current areas of focus, include: emerging technologies, particularly human genome editing; genomics; human challenge studies; and epidemic preparedness and response. Prior to this, Katherine co-led the Global Policy Team at Wellcome. She has a background in medical law and ethics and during her time at Wellcome provided strategic advice on regulatory, governance and ethical issues. She led a programme of work focusing on research ethics, global governance and advocacy, epidemic preparedness, genomics and emerging technologies, and evidence into policy. She has sat on many oversight bodies, including: the PHE Ebola Governance Group; the IDDO Ebola Platform Steering Committee; the H3Africa Ethics and Regulatory Working Group and she was the chair of the GLOPID-R data sharing working group.

Biosketch

Helen McShane, FRCP PhD FMedSci

Professor of Vaccinology

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Helen McShane is currently Director of the Oxford NIHR Biomedical Research Centre; Professor of Vaccinology at Oxford University; Deputy Head (Translation and Personnel), Medical Sciences Division; and an Honorary Consultant Physician in infectious diseases.

Helen obtained an intercalated BSc in 1988, followed by a degree in medicine in 1991 (both University of London). In 1997 She was awarded an MRC Clinical Training Fellowship to undertake a PhD with Adrian Hill in Oxford, and was later awarded a PhD in 2001 (University of London). In 2001 she was awarded a Wellcome Clinician Scientist Fellowship, allowing her to complete her clinical training and subsequently awarded a CCST in HIV and GU Medicine in 2003. In 2005 and 2010, she was awarded a Wellcome Senior Clinical Research Fellowship. She currently holds a Wellcome Trust Investigator Award. Helen was elected to be a fellow of the Academy of Medical Sciences in 2019.

Since 2001, Helen has lead a TB vaccine research group at the University of Oxford. She led the development of MVA85A, the first new TB vaccine candidate to enter efficacy testing. Current areas of focus include the development of controlled human mycobacterial challenge models, aerosol delivery of vaccines and immunomonitoring in clinical trials. She collaborates with several research groups across Africa in TB vaccine clinical trials.

Biosketch

Pieter Neels, MD

Chair

IABS Human Vaccine Committee
Ex-CHMP member
Ex-EMA Vaccine Working Party Vice-chair
Vaccine-Advice BVBA
Founder
Associate Professor University of Namur

Dr Pieter Neels is a native of Belgium where he trained as an MD (University of Antwerp, 1985) and was boarded as a general practitioner. In 1994, his interest for medical research led him to work for a pharmaceutical company.
In 1997, he joined the Belgian Ministry of Public Health as a senior evaluator of the clinical part of registration files in the field of cardiology, nephrology, endocrinology (diabetes), ...
In 2001 he was appointed CPMP member. In 2002 he was asked to take over all Belgian central vaccine rapporteurships. During this year he became infected by the world of vaccines and until June 2013 he was the rapporteur of more than 15 vaccines.
After being an observer for more than 5 years at the Vaccine Working Party, he was elected vice-chair of this CHMP Working Party for discussion on development and evaluation of registration files for vaccines until June 2013.
The Belgian agency started a spearhead policy in 2007 and Dr Neels was appointed co-ordinator for the spearhead domain vaccines.
EMA/CHMP has asked Dr Neels has be an observer at the SAGE/WHO meetings and to attend several scientific meetings on vaccines until June 2013.
WHO has asked Dr Neels to attend many meetings on vaccine development all over the world in order to share the EU regulatory requirements/competence in vaccinology.
Dr. Neels is also a member of the world wide network on vaccine promotion as he is asked to attend the ADVAC course (Foundation Mérieux) and the IABS conferences.
In 2013 Dr. Neels was nominated associate Professor at the Namur University for a course in Vaccinology.
In June 2013 Dr Neels stepped down from the CHMP and left the Belgian Federal Agency to start his own consultancy company “Vaccine-Advice” in order to be able to support vaccine development in a more efficacious way.
In 2014 Dr Neels was elected board member of IABS-EU and in 2016 he accepted to chair the Human Vaccine committee of IABS.

Biosketch

Blanché Oguti , MBChB DTMH MRCP MSc

Clinical Research Fellow

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Dr. Blanché Oguti is currently a Clinical Research Fellow at the Oxford Vaccine Group, working on Meningococcal B, Ebola Virus Disease and Plague phase I clinical trials. Her research group has expertise in typhoid challenge studies and she is part of the clinical team on these trials. After graduating from medical school she moved to India for 6 months to do an internship in tropical dermatology, which sparked her interest in tropical medicine. She returned to the UK to complete foundation training in various specialties including infectious diseases, emergency medicine and medical microbiology. She spent 7 months at the Institute of Tropical Medicine in Belgium, learning about microscopy, parasitology and public health. Subsequently, she enrolled at the London School of Hygiene and Tropical Medicine to do a Masters in Tropical Medicine and International Health, followed by a Masters in Epidemiology, where she gained skills in advanced statistics. At the London School she had the opportunity to go to Ghana to carry out a survey-based research project on Yaws in the rural communities; a community engagement project designed to support the WHO Yaws Eradication Programme. Blanché then spent 2 years as a Core Medical Trainee in North West London and passed the examinations to become a Member of the Royal College of Physicians in 2018, before entering the field of adult vaccinology at Oxford University.

Biosketch

Peter JM Openshaw FMedSci

Professor

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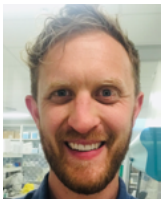
Peter Openshaw is a respiratory physician and mucosal immunologist, studying how the immune system both protects against infection but also causes disease. He has worked on RSV and influenza since the mid-1980s, leading a large Wellcome Trust funded consortium ('MOSAIC') to investigate the pathogenesis of human influenza in 2009-12. He is vice-Chair or NERVTAG, a Department of Health committee horizon-scanning for emerging respiratory threats; he directs MRC and EU-funded studies of human volunteers infected with RSV and influenza and directs HIC-Vac, an international consortium that promotes the use of human challenge to accelerate vaccine development. He is the inaugural President of the International RSV Society (under the auspices of isirv). He is Theme Lead for Infection in Imperial Biomedical Research Centre, Respiratory Infections Section Head within the National Heart and Lung Institute and Senior Consul at Imperial College London.

Biosketch



Joshua Osowicki, MBBS BMedSci FRACP

Paediatric Infectious Diseases physician

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Josh is a Paediatric Infectious Diseases physician trained in Melbourne and Darwin in Australia, and Vancouver in Canada. He works clinically at the Royal Children's Hospital Melbourne and is nearing completion of a PhD in the Tropical Diseases research group at Murdoch Children's Research Institute, supervised by Profs. Andrew Steer, Pierre Smeesters, Jonathan Carapetis, and Dr. Paul Licciardi, establishing a group A Streptococcus (GAS, Streptococcus pyogenes) pharyngitis human infection study in healthy adults, based in Melbourne. Plans for vaccine evaluation using the model are an important part of a growing global push to accelerate GAS vaccine development, including WHO-supported efforts leading to establishment of a global Strep A VAccine Consortium (SAVAC) with funding from the Wellcome Trust, and a major investment by the Australian federal government's Medical Research Future Fund (MRFF) in a new Australian Strep A Vaccine Initiative (ASAVI).

Biosketch

Chad K. Porter, Ph.D.

Head, Clinical Studies and Epidemiology

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Chad Porter received his BS in Clinical Laboratory Science from the University of North Carolina, Chapel Hill in 1999, his MPH from George Washington University in 2004 and his PhD in epidemiology also from George Washington University in 2011. He is the Head of the Clinical Studies and Epidemiology Division in the Enteric Diseases Department at the Naval Medical Research Center where he oversees the conduct of early phase clinical trials to evaluate vaccines (and other products targeting primary and secondary prevention) against the pathogens of travelers' diarrhea in deployed military populations including: Shigella, Campylobacter and enterotoxigenic Escherichia coli. These studies include first-in-human trials of subunit, live-attenuated and conjugate vaccines and non-vaccine based products to assess safety as well as expanded phase 1/2 trials to obtain expanded safety and immunogenicity data. As part of those product development efforts, he is actively involved in the use and assessment of controlled human infection models for those three pathogens to improve understanding of host response to infection and to assess the efficacy of products targeting primary prevention. He is also involved in multiple field studies in travel populations that are designed to inform clinical practice guidelines on travelers' diarrhea treatment and management as well as to guide product acquisition strategies for the US military. Additionally, he is actively engaged in conducting studies on the epidemiology and acute/chronic morbidity associated with travelers' diarrhea to inform primary prevention strategies.

Biosketch

Andrew J POLLARD, BSc MA MBBS MRCP(UK) FRCPCH PhD DIC FHEA FIDSA FMedSci

Professor of Paediatric Infection and Immunity
University of Oxford
Honorary Consultant Paediatrician
Oxford Children's Hospital
Vice Master
St Cross College, Oxford

He obtained his medical degree at St Bartholomew's Hospital Medical School, University of London in 1989 and trained in Paediatrics at Birmingham Children's Hospital, UK, specialising in Paediatric Infectious Diseases at St Mary's Hospital, London, UK and at British Columbia Children's Hospital, Vancouver, Canada. He obtained his PhD at St Mary's Hospital, London, UK in 1999 studying immunity to Neisseria meningitidis in children and proceeded to work on anti-bacterial innate immune responses in children in Canada before returning to his current position at the University of Oxford, UK in 2001. He chaired the UK's NICE meningitis guidelines development group, the NICE topic expert group developing quality standards for management of meningitis and meningococcal septicaemia. His research includes the design, development and clinical evaluation of vaccines including those for meningococcal disease and enteric fever and leads studies using a human challenge model of (para)typhoid. He runs surveillance for invasive bacterial diseases and studies the impact of pneumococcal vaccines in children in Nepal and leads a project on burden and transmission of typhoid in Nepal, Bangladesh and Malawi, and co-leads typhoid vaccine impact studies at these sites. He has supervised 37 PhD students and his publications includes over 500 manuscripts and books on various topics in paediatrics and infectious diseases. He chairs the UK Department of Health and Social Care's Joint Committee on Vaccination and Immunisation and the European Medicines Agency scientific advisory group on vaccines and is a member of WHO's SAGE. He received the Bill Marshall award of the European Society for Paediatric Infectious Disease (ESPID) in 2013, the ESPID Distinguished Award for Education & Communication in 2015 and the Rosén von Rosenstein medal in 2019 awarded by the Swedish Paediatric Society and the Swedish Society of Medicine. He was elected to the Academy of Medical Sciences in 2016 and is an NIHR Senior Investigator. He made the first British ascent of Jaonli (6632m) in 1988 and Chamlang in 1991 (7309m) and was the Deputy leader of the successful 1994 British Medical Everest Expedition.

Biosketch

Robert Sauerwein, MD; Ph.D.

Professor

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Trained as medical specialist in clinical microbiology and immunology, I have a vested interest in translational research, more specifically the clinical development of Plasmodium falciparum malaria vaccines. For this purpose we improved, standardized and expanded the portfolio of the Controlled Human Malaria Infection (CHMI) models (Sauerwein, NRI 2011, Reuling eLife 2018) and studied immune responses after CHMI showing long lasting (semi-innate) T- and B cell responses (Teirlinck, PLoS Pathog 2013, Walk Nat Com 2019). In addition, we developed an immunization regime so called CPS, that induces complete protection in the CHMI model with unprecedented potency and longevity (Roestenberg, Lancet 2011). We have been able to generate a large bio-bank of valuable blood samples and clinical data in more than 10 years of CHMI and CPS studies. Stringent CHMI protocols have been developed (Bijker, E Soc Stud Sci 2016) and CHMI was improved by modeling parasitaemia and by the use of qPCR for parasite detection (Coffeng, Plos Comp Biol 2017; Roestenberg, JID 2012; Hermsen AJTMH 2004). A panel of P. falciparum clones from different genetic and geographic background has been developed for use in CHMI (Teirlinck, JID 2013; McCall, Sc Transl Med 2017 ,Langenberg AJTMH 2018). The combined activities have strengthened the CHMI as a strong model for understanding of malaria immunity with a well-accepted role on the critical path of clinical malaria vaccine and drug development.

Biosketch

Michael Selgelid

Michael Selgelid is Professor of Bioethics and Director of the World Health Organization Collaborating Centre for Bioethics in the Monash University Bioethics Centre in Melbourne, Australia. He is a member of the Scientific Committee of the Brocher Foundation in Geneva/ Switzerland and a member of the General Ethical Issues Sub-committee of the Alfred Hospital Ethics Committee in Melbourne. He was previously a Member of the Board of Directors of the International Association of Bioethics; the Ethics Review Board of Médecins Sans Frontières; and the Ethics Advisory Group of the International Union Against Tuberculosis and Lung Disease. He was Chair of the Global Network of WHO Collaborating Centres for Bioethics from 2016 to 2018.
His research primarily focuses on public health ethics (especially regarding infectious disease) and ethical issues associated with biotechnology. Michael edits a book series in "Public Health Ethics Analysis" for Springer-Nature, and he is Co-Editor of Monash Bioethics Review. Among numerous other engagements with the World Health Organisation he has served on WHO International Health Regulations (IHR) emergency committees regarding Ebola and Zika. In 2015 he was commissioned by the US National Institutes of Health (NIH) to produce a White Paper on ethical issues associated with gain-of-function research; and he led a recently completed project, commissioned by The Wellcome Trust, on ethical issues associated with human challenge studies in endemic settings. Michael earned a BS in Biomedical Engineering from Duke University; and a PhD in Philosophy from the University of California, San Diego.

Biosketch

Lynda Stuart, MD; Ph.D.

Deputy Director

Bill and Melinda Gates Foundation
Seattle, Washington 98109
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Dr. Lynda Stuart is an academic and physician-scientist. She currently leads the Vaccine and Host Pathogen Biology domain of Discovery and Translational Sciences at the Bill & Melinda Gates Foundation. This group works across all infectious diseases of interest to the Foundation and aims to **source novel approaches and accelerate the discovery, development and translation of new passive and active immunization strategies for Foundation priority diseases**. The key initiatives supported include novel live and whole-cell vaccines candidates, replicating viral vectors, antigen identification and immunogen design, adjuvants and formulation, monoclonal antibody identification, generation and analysis, and vaccine correlates of protection. In addition they manage a number of best-in-class integrated service and research platforms for vaccine R&D as well as a translational platform for exploratory clinical studies.

Her research career has focused on the role of the innate immune system in control of autoimmune and infectious diseases, the interplay between innate and adaptive immunity and on host-pathogen biology. She was a recipient of numerous academic awards including a Wellcome Trust Clinical Research Fellowship, Wellcome Trust Clinician Scientist Award, Howard M. Goodman Award, and the Massachusetts General Hospital Research Scholars Award. She is a member of the Royal College of Physicians in the United Kingdom and a Fellow of the American Society of Clinical Investigation. Prior to joining the Bill & Melinda Gates Foundation, Dr. Stuart was a member of the faculty at the Massachusetts General Hospital and Harvard Medical School where she was co-director of the Laboratory of Developmental Immunology, a member of the Center for Computational and Integrative Biology, an affiliate of the Broad Institute of Harvard and MIT, and served on the Massachusetts General Hospital Executive Committee for Research. She remains actively involved in basic research with an RO1-funded program and affiliated appointment at the Benaroya Research Institute in Seattle. Dr. Stuart earned an MD from the University of Cambridge and the University of London and a PhD from the University of Edinburgh. She completed residency training in Internal Medicine in the United Kingdom.

Biosketch

Adrian Wildfire

Scientific Director

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Adrian Wildfire, Scientific Director is a Master, Fellow and accredited specialist in the fields of Virology, Medical Microbiology and Parasitology. He is a subject matter expert in the controlled human infection modelling (CHIM) primarily for diseases of the upper and lower respiratory tract. Adrian started his career in 1987 as a Clinical Scientist, working with antimicrobial resistant isolates of tuberculosis under the tutelage of Professor Denis Mitchison within the Wolfson Research Institute (Royal Postgraduate Medical School), Hammersmith Hospital, London before going on to take a microbiology Fellowship at St. Mary's Hospital. Becoming a Senior Medical Microbiologist, he worked overseeing diverse diagnostic services and research projects. A Parasitology Masters from the London School of Hygiene and Tropical Medicine followed before joining Professor Brian Gazzard's HIV Research team at the Chelsea and Westminster Hospital – working primarily with HIV, Hepatitis and Sexual Health cohorts and acting as a subject matter expert (e.g. the Academic Health Science Centre, SAGE and the NHS Diagnostic Pathology Group) and obtaining a DMS as well as Project Management (PRINCE2) and Leadership (Harvard Leadership Program) qualifications. Recently Adrian was employed in designing challenge studies as Director of Research Services at Retroscreen (hVIVO) before joining a multidisciplinary team within SGS Life Sciences manufacturing wild-type challenge agents for use in clinical trials, designing and performing CHIM and CHMIs and leading on infectious disease strategy and training. He has authored papers and articles relating to HIV, Ethics, Immunology and Human Challenge amongst others.