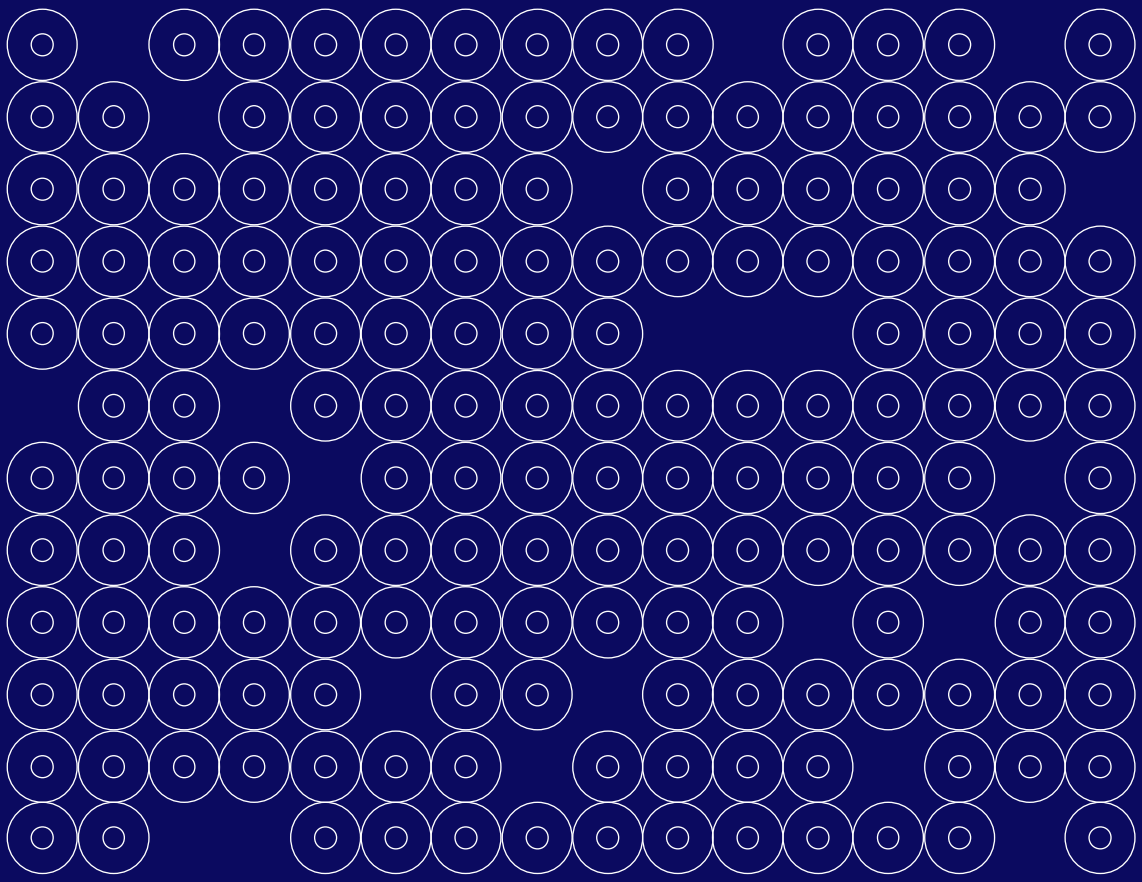
JPIAMR Therapeutics Workshop

Feeding the Antimicrobial Pipeline

20-22 April 2021



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Joint Programming Initiative on Antimicrobial Resistance

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Executive Summary

New strategies for the treatment of infection and identification of resistant microbes are crucial. This virtual workshop "Feeding the Antimicrobial Therapeutics Pipeline", was led by the UK Medical Research Council (MRC) with support from the Swedish Research Council (SRC), the South African Medical Research Council (SAMRC), the National Research Foundation of Korea (NRF), the French National Research Agency (ANR), and the Canadian Institutes of Health Research (CIHR) on behalf of the Joint Programming Initiative on Antimicrobial Research (JPIAMR). The workshop was delivered as part of JPIAMR's mission to enable global coordination of antimicrobial resistance research.

The workshop brought together more than 400 participants from 46 countries, including research experts and agencies collaborating in the antimicrobial therapeutics development field.

The aims of the workshop were to:

- discuss the global antimicrobial development pipeline
- identify gaps and opportunities for therapeutics research and development
- showcase therapeutics research and improve links between academia, industry and policy makers in the context of the wider global antimicrobial therapeutics community
- support collaboration for creative solutions to real-world problems facing therapeutics development in the context of antimicrobial resistance (AMR).

This report provides:

- information relevant to the development of antimicrobial therapeutics
- short summaries of the sessions of the workshop, signposting sources of additional information available to the AMR research community
- abstracts of the research presentations and
- summaries of the major points raised in the panel presentations and discussions
- a description of the challenges and opportunities in the field
- lessons learned to date.

Conclusions:

- The current antimicrobial pipeline is insufficient to tackle the challenges of AMR
- Public health needs and the future reimbursement landscape will shape the future of the therapeutics pipeline
- Understanding how public health priorities are determined and valued is key
- We need solutions that benefit patients
- There are still no licensed novel classes addressing WHO priorities
- A diversity of approaches is required: novelty vs improvements, traditional vs non-traditional.
- Dialogue, collaboration and partnership between all stakeholders (including academia, industry, NGOs, funders, regulators and payers), are essential
- Innovation, access and stewardship are the pillars of a sustainable pipeline
- Global sustainability requires the implementation of pull incentives
- Important to fill gaps in the R&D value chain: new differentiation criteria, clinical trial capacities & capabilities are required.

Introduction

Background and objectives

The Joint Programming Initiative on Antimicrobial Resistance, JPIAMR, is a global collaborative organisation and platform, engaging 28 nations to curb antimicrobial resistance (AMR) with a One Health approach. The JPIAMR coordinates national research funding and supports collaborative action for filling knowledge gaps on AMR with a One Health perspective. Our shared Strategic Research and Innovation Agenda outlines the key areas to be addressed and provides guidance for countries to align their AMR research agendas nationally and internationally. One of the six key priority topics covered is therapeutics and a workshop on therapeutics is identified in the JPIAMR Roadmap of Actions 2019-2024 that guides joint investments and transnational actions of the JPIAMR.

The Medical Research Council (MRC-UK), part of United Kingdom Research and Innovation (UKRI), supports UK participation in the JPIAMR and led the organisation and delivery of Feeding the Antimicrobial Pipeline – JPIAMR Therapeutics Workshop 2021. The Workshop Steering Committee also included JPIAMR members from Canada, France, Korea, South Africa and Sweden as well as scientific advisers from the JPIAMR Scientific Advisory Board (SAB), the Innovative Medicines Initiative (IMI) and the Biotech companies in Europe combating AntiMicrobial Resistance (BEAM Alliance). Please see Annex 3 for further information about the Workshop Organising Committee.

The workshop was designed to provide an overview of the current AMR therapeutics landscape, to showcase therapeutics research and improve links between academia, industry and policy makers in the context of the wider global antimicrobial therapeutics community, and also provide a platform to discuss the current gaps and opportunities in therapeutics research. While originally envisioned as a small-scale face-to-face meeting, the COVID-19 pandemic necessitated a virtual platform; the workshop took place on the 20th, 21st and 22nd of April 2021, providing the opportunity for a much more wide-reaching and inclusive activity. Outcomes from the workshop will support the development of a JPIAMR Research Call in therapeutics that will launch in January 2022 and will also inform the development of a One Health AMR Partnership bid under the Horizon Europe Framework.

The AMR Therapeutics Pipeline

To provide background information for the workshop, upon registration participants were asked to identify gaps in the AMR therapeutics research landscape, potential barriers to research and any research opportunities.

A total of 71 participants responded to the questionnaire: several common themes emerged from participants' responses.

Gaps in AMR Therapeutics Research

The most commonly identified gap in research was novel therapeutics- including phage therapies, novel classes of antibiotic, natural products and biocides (see Figure 1). Other less commonly identified gaps included novel targets, screening methods and vaccines.

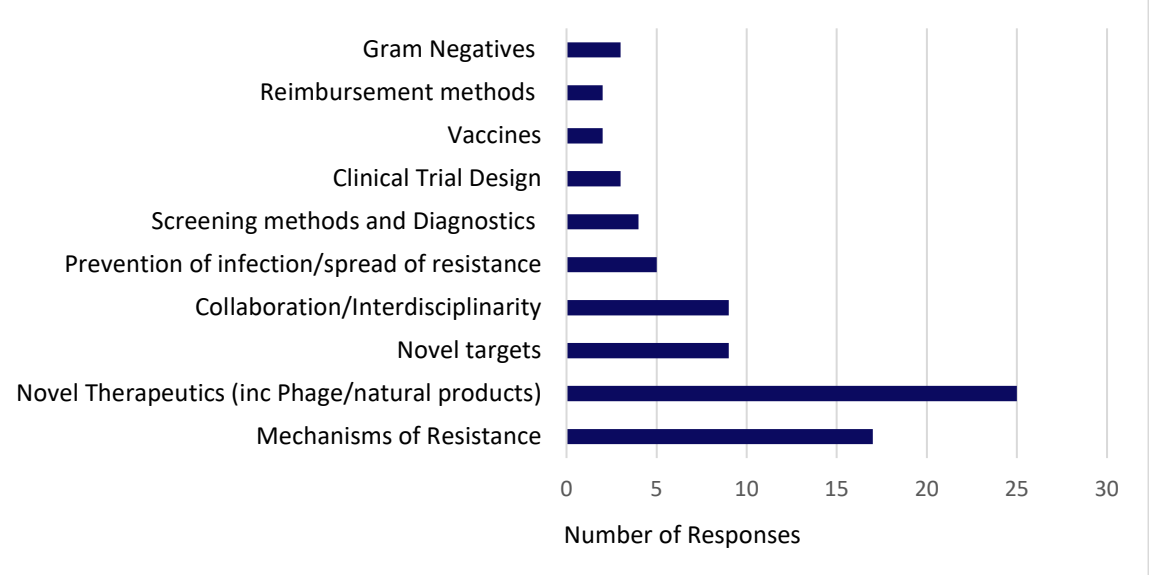


Figure 1. Common Research Gaps identified by participants.

Barriers to AMR therapeutics pipeline

Participants identified a range of barriers, with the most common issue being lack of funding. Other common issues included lack of collaboration and/or interdisciplinarity in the field. Several participants also noted that policy issues could become barriers to research in this field and the ongoing loss of capacity in the bioinformatics field can also be highlighted are a blocker to progress (see Figure 2).

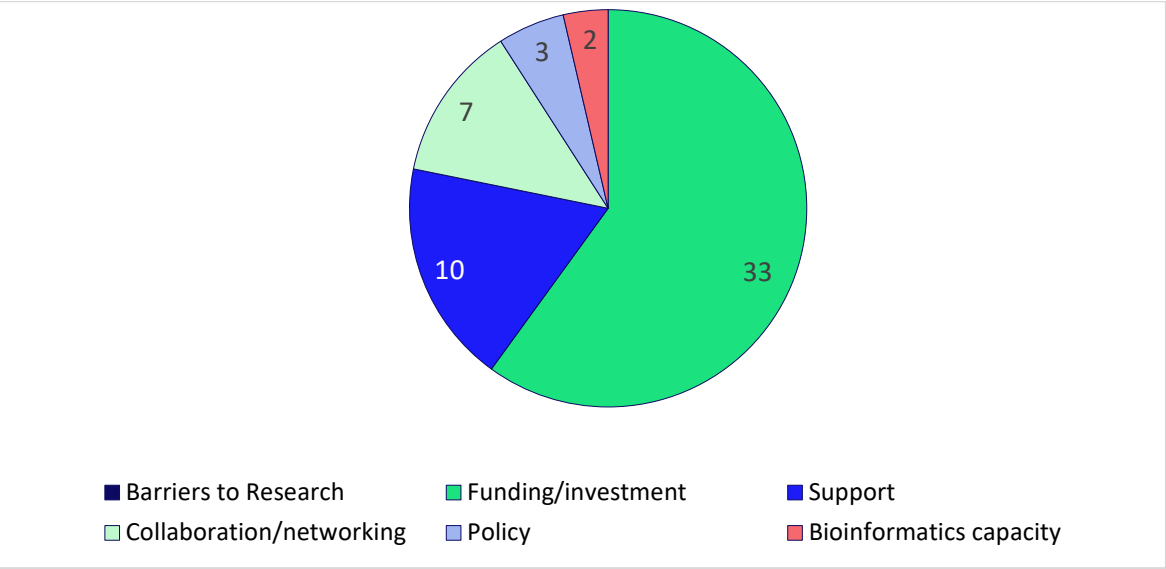


Figure 2. Commonly identified barriers to AMR therapeutics research.

Opportunities for AMR Therapeutics Research

Participants identified a range of opportunities for AMR research; diagnostics, early identification of resistance and screening for resistance genes were the most commonly mentioned opportunities. Design of novel therapeutics, phage therapy and natural products were also popular, as were novel targets and anti-virulence agents (see Figure 3). Participants also highlighted development of bioinformatics tools as an opportunity.

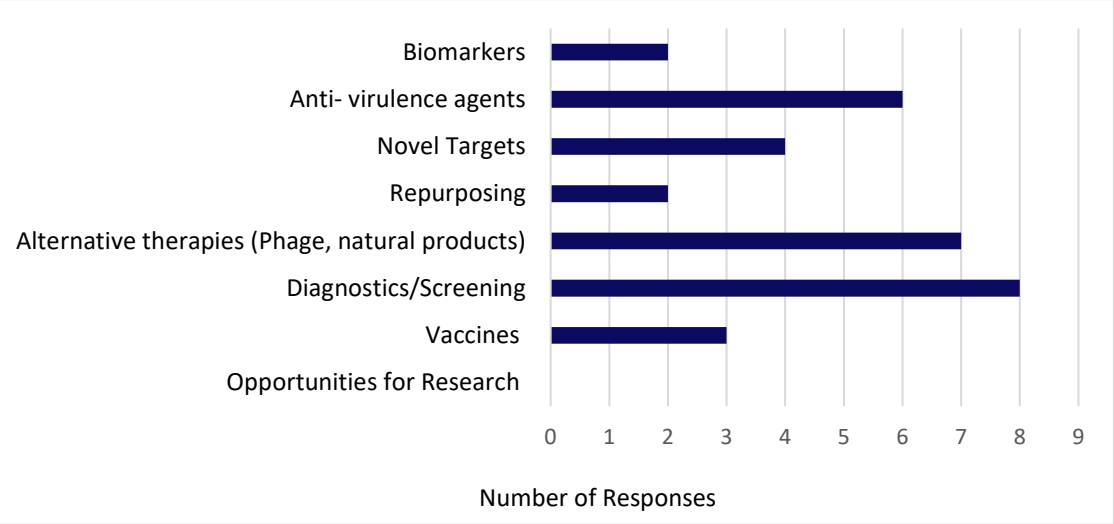


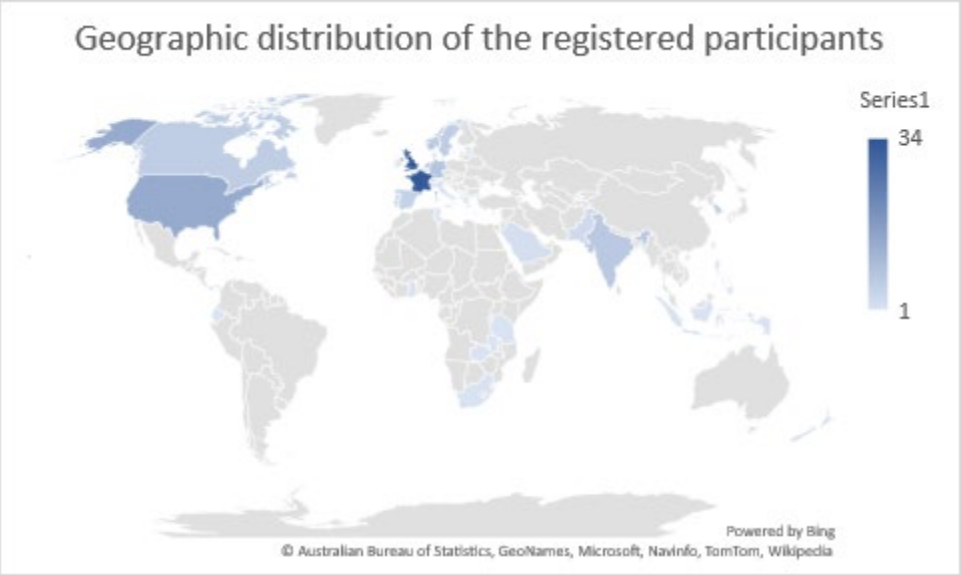
Figure 3. Opportunities for AMR therapeutics research identified by workshop participants.

Workshop Discussions

Gaps, barriers and opportunities identified by the participants were discussed in more depth during the workshop. Workshop speakers identified reimbursement models as a key method over overcoming the funding issues faced by industry.

Key figures

- 12 hours of presentations and scientific discussion over three days and nine sessions:
  - See Annex 1. Workshop Agenda
  - The Session recordings are available here
  - See Annex 2. Photos and Biographies of Moderators, Panel Members and Presenters
  - See Annex 3. Workshop Organising Committee
- The workshop attracted 411 registered participants, with 391 who logged into the workshop
- Participants from 46 countries over 6 continents represented (see Figure 4)
- The total number of participants at any one time peaked at just over 200 (see Figure 5 for an overview of the profile of participants)
- There were 160 connected attendees on average during each session
- A total of 132 scientific inputs and questions were received through the chat



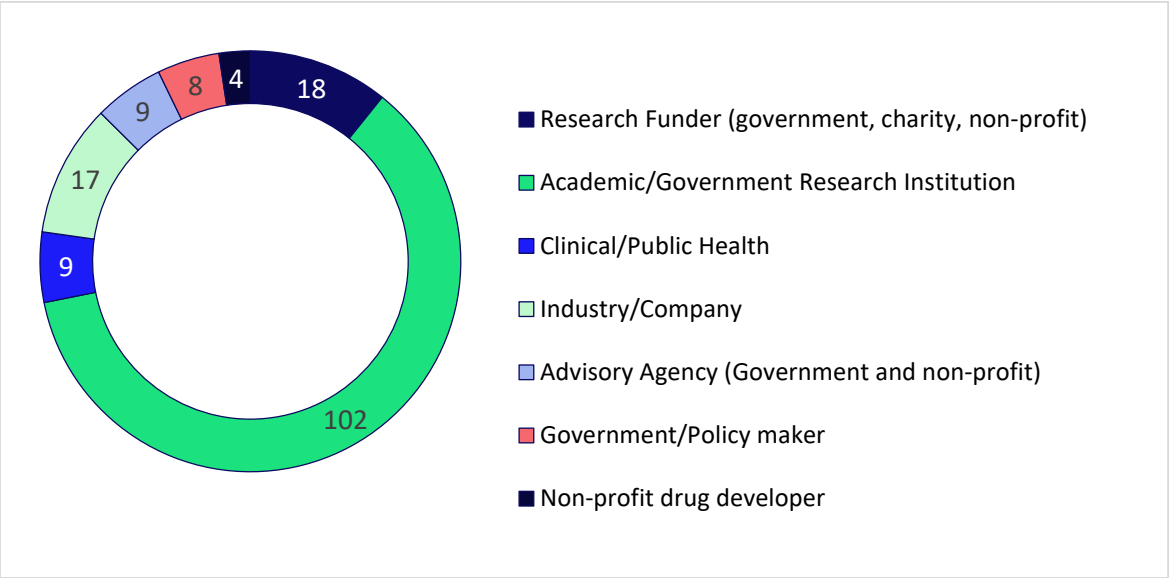


Figure 5. Profile of the registered participants.

Scientific sessions

The Workshop was opened by a welcome from the Chair and a presentation on behalf of MRC-UK and JPIAMR.

Session 1: Antimicrobial Therapeutics Landscape

Session Moderated by Rafael Canton

Professor Canton introduced the session, setting the scene for presentations discussing the current antimicrobial pipeline, funding mechanisms to support the pipeline, and current initiatives to combat AMR.

Keynote Presentation – AMR Therapeutics Landscape, Ursula Theuretzbacher

Dr Theuretzbacher presented the case for the medical need for new antibiotics and provided an overview of recently approved antibiotics. Because of pre-existing resistance and the high geographical variability in resistance patterns, new antibiotics only work in specific regions of the world.

The current clinical pipeline consists mainly of modified old classes of drugs, leading to critical gaps in activity. Trends include pathogen-specific (precision therapy) approaches based in highly developed healthcare systems. There are some new classes of antibiotics being developed as well as some non-traditional approaches.

The preclinical pipeline includes a wide range of activity including both traditional and non-traditional approaches. Targets are well-described, with an increasing number of anti-virulence or adjunctive approaches. These approaches are technically challenging, with long timelines to patient delivery. Given the risks, long-timelines and financial restraints, university academics are delivering this part of the pipeline and therefore grants are shaping drug discovery focus. However, universities can't fill the role of pharmaceutical companies. Dr Theuretzbacher concluded by noting that resistance is not disappearing, that innovation and focus on direct-acting antibacterial therapies is needed and that universities are increasingly the hot-spots of innovation.

The Keynote was followed by short presentations from members of the Panel comprising representatives from global organisations that advocate for a coordinated approach to combating AMR including discovery and development of novel antimicrobials.

1. Hatim Sati, World Health Organization (WHO)
2. Stefano Messori, OIE World Organisation for Animal Health (OIE)
3. Alessandra Martini, European Commission (EC)
4. Tim Jinks, Wellcome Trust
5. Erin Duffy, CARB-X
6. Laura Marin, JPIAMR
7. Florence Séjourné, BEAM Alliance
8. Graham Somers – GlaxoSmithKline (GSK) IMI Portfolio Director

The information presented allowed participants to better understand the role of various organisations in this complex drug development pipeline. In addition, Panel Members presented updates on recent activities and some insight into future plans. The establishment of the AMR Action Fund was noted as an important development for taking promising late-stage products towards registration. But more work is required (end-to-end support) to unlock the whole system including improvements in the regulatory framework and innovation in clinical trial design. A lively, but short discussion with questions from the participants followed the presentations from Session 1.

Key outcomes

- The current antimicrobial pipeline is insufficient to tackle the challenges of AMR. There are still no novel classes addressing WHO priorities.
- Funders are supporting a diversity of approaches: novelty vs improvements, traditional vs non-traditional.
- Universities and small and medium-sized enterprises (SMEs) are playing a critical role in the drug discovery pipeline.
- Important to fill gaps in the research and development (R&D) value chain: new differentiation criteria, clinical trial capacities & capabilities are required.
- Better research coordination is required for seamless development of promising candidates

Horizon Europe will include a variety of initiative

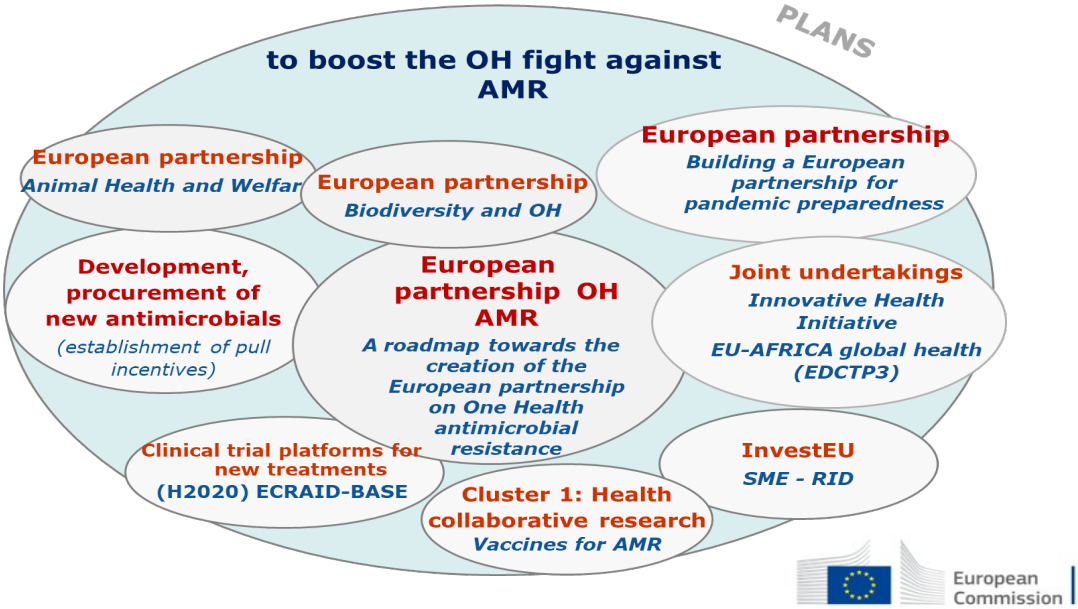


Figure 6. Horizon Europe

Session 2: Choosing wisely – is your product worth developing?

Session Opened and Moderated by John Rex

John Rex opened the session, which was designed to educate the JPIAMR R&D community about stakeholder views on the value of AMR therapies and prevention strategies to avoid pre-clinical development of products with little chance of market success. One of the major considerations is how the reimbursement for human therapeutics to treat infections is changing. Antibiotics are seen as the 'fire extinguishers' of medicine; while good stewardship and infection prevention should limit the use of antibiotics and other novel agents, they should be available in times of need. The COVID-19 pandemic provides a strong example of the utility of this approach.

The UK is implementing the world's first full delinked antibiotic pull incentive. In the pilot scheme, building on the insights from the IMI DRIVE-AB project, NHS England will pay an annual 'subscription fee' which is not linked to product use. The United States and Sweden have followed suit with other incentive models to stimulate R&D in this critical sector.

Following his presentation, John quizzed the discussion panel on the future reimbursement landscape, what product developers and payers what to see. The main messages from the session were:

- Public health needs and the future reimbursement landscape should drive product development choices. Resources exist to guide the research community: WHO priority pathogens list, CDC AMR Threats Report, CARB-X Stewardship and Access Development Guide
- Stakeholders need to consider new mechanisms to reveal the hidden value of antibiotic 'fire extinguishers'
- Developers and evaluators need to consider the added value of new products vs existing products: Payers need to see data on targeted populations
- Individual vs societal benefit (benefit to the population) is difficult to assess, but regulators are open to finding a solution
- Demonstrating superiority over standard care is difficult – good comparators need to be identified
- There is a balance to be struck between what is desirable and what is achievable: push funders are taking a balanced portfolio approach and trying to cover geographical gaps while pull incentives are needed to achieve sustainability

Discussants included:

- Kevin Outterson, Executive Director, CARB-X
- Christine Ardal, Senior Advisor, Norwegian Health Ministry and IMI DRIVE-AB project
- Marco Cavaleri, Head of Anti-Infectives and Vaccines, European Medicines Agency (EMA)
- Laura Piddock, Scientific Director, GARDP
- Camilla Petrycer Hansen, Principal, Novo REPAIR Impact Fund

Sessions 8 and 9 of this Workshop return to this product development theme, exploring economic incentives, antimicrobial stewardship, antimicrobial access and long-term sustainability of the pipeline.

Session 2a: Activities of Potential Interest to the AMR Therapeutics Research Community

Session Moderated by Jess Boname

A short session was added to allow for presentations of general interest to the research community, including large-scale projects which are at or near the initiation phase and would welcome engagement with others. These presentations complemented the previous sessions and provided further links to activities relevant to AMR therapeutics research and development (R&D).

Summary points from the session

- Patient involvement in research helps to determine societal value of products - charities and patient groups can be an important resource for researchers
- Research platforms support research collaboration and coordination – crossing geographic and sectoral boundaries
- Coordinated efforts and information exchange are required to facilitate the transition of innovative products through the AMR therapeutics pipeline and reduce duplication of effort

The following information in this session comes from submitted abstracts. The name of the presenter is underlined.

1. **The Cystic Fibrosis Syndicate in Antimicrobial Resistance: accelerating the translation of CF antimicrobials to the clinic through collaboration.**

   Jessica Lee, Beverley Isherwood, Alessandra Gaeta; Medicines Discovery Catapult, UK; Paula Sommer, Lucy Allen; Cystic Fibrosis Trust, UK

People with Cystic Fibrosis (CF) experience frequent lung infections throughout their lives and are at risk of developing antimicrobial resistance (AMR) due to antibiotic failures. The development of new, effective antimicrobial treatments for infections associated with CF is an urgent unmet need.

The CF Syndicate in AMR is a partnership between the Cystic Fibrosis Trust and Medicines Discovery Catapult, to accelerate the translation of new antimicrobial treatments for CF infections to the clinic. It brings industry leaders and people affected by CF together with academics and clinicians with expertise in CF and pulmonary infection, and, since its launch in September 2019, it has engaged the research community globally on the key challenges in CF antimicrobial development.

Based on these challenges, the Syndicate is driving programmes of research to:

- Enable access to CF-relevant clinical samples and associated data to support robust preclinical validation of antimicrobials for CF.
- Provide guidance on navigating the preclinical pathway in CF antimicrobial development.
- Develop guidance for drug developers through the generation of patient-focused target product profiles.

The CF Syndicate in AMR exemplifies how focused collaborative efforts aligned to a defined area on unmet need can accelerate R&D to bring new treatments to patients, faster.

For more information, please visit the CF Syndicate Website

2. **Pew Evaluates the Global Clinical Pipeline of Antibiotics and Nontraditional Bacterial Products**

   Cara Lepore, Wes Kim, Katie Prosen; The Pew Charitable Trusts, USA

Regulatory, economic, and scientific challenges have contributed to the decline in antibiotic innovation for more than a decade, while the threat of antibiotic resistance continues to grow at an alarming rate. In 2014, Pew's antibiotic resistance project began tracking the global pipeline of small molecule antibiotics in clinical development. The antibiotics pipeline continues to be insufficient to address the growing public health threat of antibiotic resistance.

As of December 2020, 43 new antibiotic candidates were in development, only 15 of which have potential activity against WHO critical threat pathogens. Of concern, the companies developing these drugs have shifted considerably from large to small companies in the last seven years. 36 non-traditional candidates are also in clinical development, consisting of well-known therapies and drugs with innovative mechanisms but little to no precedent in human medicine.

To ensure that we have effective medicines to treat the drug-resistant bacterial infections of today as well as those that emerge in the future, antibacterial innovation must include the discovery and development of novel classes, improvements to existing classes, and innovative non-traditional products. Global action is needed to increase funding for early-stage research and establish new payment solutions for sufficient return on investment for new antibiotics.

Resources for the Research Community:

- Small molecule antibiotics pipeline interactive tool
- Non-traditional pipeline interactive tool
- Historical antibiotic pipeline visualization tool
- Nature Reviews Drug Discovery: The small-molecule antibiotics pipeline: 2014–2018

3. **South Africa-United Kingdom Antimicrobial Drug Discovery Hub**

   Rosemary Dorrington, Perry Kaye, Rui Krause (Rhodes University, SA), Mathew Upton* (University of Plymouth, UK), Hai Deng (University of Aberdeen, UK), Rebecca Goss (University of St Andrews, UK), Karin Jacobs (University of Stellenbosch, SA), Marelize LeRose-Hill (Cape Peniculid University of Technology, SA), Gwynneth Matcher (South African Institute for Aquatic Biodiversity, SA), Derek Ndinteh (University of Johannesburg, SA), Alex O'Neill (University of Leeds, UK), Paul Race (University of Bristol, UK), Stephanie van Heerden (University of Kwazulu-Natal, SA). *SA and UK PIs*

The SA/UK Antimicrobial Drug Discovery (ADD) Hub is a multi-institutional, bilateral consortium that aims to deliver an accelerator programme for the discovery of new antibiotic compounds. Established in July 2020, the UK MRC, the ADD Hub builds on existing expertise and infrastructure to expand cutting-edge research capacity of partner institutions to identify and deliver characterised novel hit compounds that can be progressed to lead optimisation in future projects. Our focus is on natural products (NPs), representing a validated source of chemical diversity capable of delivering a sustained pipeline of novel antibacterial drug candidates. South Africa is one of the most biodiverse countries on the planet, increasing the opportunities for discovery of novel NPs from marine and terrestrial ecosystems. Bilateral research exchanges and training workshops will contribute to capacity building and support future benefit sharing. The ADD Hub activities will include establishment of a NPs Research Network representing fourteen South African partner institutions. Post COVID-19 bilateral research exchanges and training workshops will contribute to capacity building and support future benefit sharing. We will report on first six months of the project, which we have viewed as the inception period for the ADD Hub.

4. **iiCONs role in feeding the AMR pipeline**

   Janet Hemingway, on behalf of the iiCON Partners: Liverpool School of Tropical Medicine, University of Liverpool, Unilever (UK), Evotec (UK), Infex Therapeutics (UK) and the Royal Liverpool and Broadgreen University Hospitals Trust (UK).

Infection Innovation Consortium (iiCON) is playing a unique role in developing and enabling new interventions for combating AMR, covering the translational research cycle from discovery to product placement.

We have developed new resources, such as a vast natural products library to screen for antimicrobial hits and established a hit to leads programme that will enable SMEs to rapidly assess viability of candidates to enter preclinical screening. iiCON will provide

new infection screening platforms, specifically focused on AMR drug discovery, that will include novel in vivo models, physiologically relevant tissue organoid and 3D cell culture systems to expedite development and an expanded offering of human infection challenge models that will radically de-risk first in man studies. We will define the mechanism by which AMR pathogens are disseminated through populations in diverse economic settings and we will model this transmission to propose hygiene and therapeutic intervention opportunities.

iiCONs initiatives will radically impact the landscape of AMR, allowing new antibiotics to be identified, optimised, developed, and implemented in a quicker, cost-effective, and smarter way. We will work collaboratively with the AMR industry to revitalise this neglected, but critically important area of healthcare, to get new antibiotics to market in the shortest possible timeframe.

Please visit the iiCON website for more information.

Session 3: Mtb antimicrobial pipeline

Session Moderated by Mirfin Mpundu

Mirfin Mpundu set the scene for the presentations in this session by describing the scale of the challenge of drug resistance in treating *Mycobacteria tuberculosis* (Mtb) infections. Globally, the WHO estimates that a quarter of the world's population infected by Mycobacterium tuberculosis (TB) and tuberculosis (TB) is one of the world's top 10 causes of death. The disease takes months to diagnose, and without proper treatment, 45% of people with TB will die. Once diagnosed, the approved course of therapy takes months to complete. Multidrug-resistant tuberculosis (MDR-TB) and extensively drug-resistant TB (XDR-TB) are on the increase although XDR-TB remains rare. However, as drug resistance increases, the challenge becomes greater. His introduction was followed by presentations showing how collaboration and coordination of TB R&D has improved the translational drug discovery pathway for novel anti-mycobacterial products.

Key messages

- A simpler, safer and shorter drug regimen is required to treat TB
- Successful drug discovery requires collaboration
- Innovative drug discovery approaches de-risk clinical development and downstream costs
- Early hit triage is based on predicted *in vivo* relevance
- Optimal drug dosing is needed; lesion specific pharmacokinetics (PK) rather than plasma
- Novel strategies and outcomes:
  - High-throughput screening (HTS) and phenotypic screens
  - Blocking efflux pumps
  - Adjunctive agents to boost efficacy of existing drugs

Presentations

1. **Drug discovery to shorten the duration of chemotherapy**

Helena Boshoff, NIAID, USA

Helena Boshoff introduced the TB-Drug accelerator (TBDA). The TBDA is product development partnership (PDP) which is a collaboration of six pharmaceuticals, one biotech company, 15 research institutions and a non-governmental organisation (NGO) that aims to facilitate early TB drug discovery.

Dr Boshoff commented that current TB treatment regimens drive down bacterial levels quickly but require months of treatment to clear all pathogens from the body. The only way to overcome this persistence is through a shorter, more effective treatment regimen. The TBDA was set up to generate multiple, mechanistically different candidates, sufficient to advance a three-drug regimen to a one-month clinical proof-of-concept by 2024.

Dr Boshoff noted that the key to shortening therapy was in understanding the system and using appropriate screening. Early application of counter screens should also be used to increase attrition at early stages of drug development, thereby de-risking costly later stages. Metabolomic analysis of tissue metabolites can also help to identify risks in drug discovery. Dr Boshoff concluded that successful drug discovery requires collaboration.

2. **High throughput screening for Mtb therapeutics**

Vinayak Singh, University of Cape Town, South Africa

This presentation underlined the importance of uptake criteria and identification of relevant screening conditions. The chemical compound collection, assay conditions, and assay technology all contribute to a successful screening programme. Dr Singh noted the particular challenges associated with screening for TB drugs including the requirement for biosafety level 3 (BSL3) facilities, the slow rate of growth of and effect of different microenvironments, and other aspect of the biology of Mtb. These aspects all contributed to the screening programme adopted. He elaborated on the use of the carbon source as a variable, noting that of the millions of compounds that have previously been screened, each compound had 2-3 carbon sources. Dr Singh noted the high early attrition rate for compounds screened and emphasized the importance of secondary screening in the hit triage process; only a few compounds make it from hit to lead and only two series from their screening programme have made it to optimisation.

Historically, limitations with high throughput screening included:

- Low numbers of target families
- promiscuous inhibitors
- high attrition rates
- saturation of chemical libraries

He concluded that there is a requirement for several types of screening to eliminate redundant targets, and researchers need to be aware of promiscuous targets and non-drug like compounds. With the advent of intelligent screening programmes, HTS approaches are delivering candidates to treat TB and Dr Singh noted that more than the 99% of compounds active against TB in the pipeline are outputs of high throughput screening.

3. **Pharmacokinetics and pharmacodynamics of anti-tuberculosis agents**

Rada Savic, University of California at San Francisco, USA

This presentation highlighted the importance of pharmacokinetics and pharmacodynamics (PK/PD) in the development of better TB treatment regimens. Dr Savic described how choice of drug dose, dosing regimen and drug combination all contribute to improved therapy. Indeed, landmark shortening of treatment regimens for TB have recently been achieved; 4 months for patients with drug-susceptible TB and 6 months those with MDR-TB or XDR-TB. There are many new drugs with new mechanisms of action in the pipeline, leading to an opportunity to jointly develop both new drugs and new regimens to improve treatment options with lower drug doses, new combinations and fewer side-effects.

The choice of which drugs to trial is underpinned by work, as shortening treatment to 6 months by using a high dose is controversial. Lesion PK/PD provides us with information about drug delivery specific to where the pathogen is. Patient variability is also important. Hard to treat patients, including those with high smear grade, cavitary TB and low body mass index (BMI), respond differently to other patients. Precision dosing or stratified regimens are required to achieve high TB cure rates.

Take home messages:

- Optimal drug dosing is necessary to balance risk/benefit
- There are lesion specific challenges; some lesions do not have a good blood supply, so drugs are often unable to reach the site of action
- Visualising lesions is important for monitoring success
- Most challenges are drug specific, but some are patient specific
- Modelling, computational and translational tools are essential

4. **Reviving ethionamide. TRICky, but possible**

Modesto J. Remuiñán-Blanco, GSK, Spain

In 2014, TB surpassed HIV as the top infectious disease killer worldwide. The main goals for novel TB drugs are to overcome resistance, shorten treatment time and develop a safer drug profile. Current treatment of MDR-TB includes pro-drugs activated by a TB enzyme which is prone to developing mutations resulting in drug resistance. Limited bioactivation also requires high doses of prodrug which can cause unwelcome side-effects.

TRIC-TB is a focused, agile consortium funded by the IMI AMR Accelerator. TRIC-TB has two partners; one SME, BioVersys, and one big Pharma, GSK. By combining an agile, fast moving SME with the experience and capabilities of a big industry partner, TRIC-TB brings innovation and a new concept of drug development. All the necessary expertise is available within the TRIC-TB consortium, from the end of pre-clinical to clinical development, including microbiology, efficacy and drug metabolism and pharmacokinetics (DMPK), toxicology, chemistry, manufacturing and control (CMC), drug development and clinical trials, and regulatory engagement. This ensures no unnecessary delays as the project is well-focussed, and no unnecessary dilution of intellectual property (IP) which happens with larger consortia.

The TRIC-TB consortium is developing adjunctive therapies which can potentiate the activity of existing TB drugs. One in particular is showing great promise and will be ready for Phase 2a studies in early 2022.

Outcomes:

- Ethionamide (ETO) and prothionamide (PTO) are excellent TB drugs if their full efficacy can be exploited
- BVL-GSK098 is a first-in-class new chemical entity with a novel mechanism of action (MoA)
- *In vitro* and *in vivo* data predict that the addition of BVL-GSK098 to a TB treatment regimen will overcome resistance and reduce the effective dose of ETO, making ETO rapidly bactericidal at very low concentrations

5. **Bedaquiline story**

   Professor Anil Koul, London School of Hygiene and Tropical Medicine and Janssen (UK)

Professor Koul described the development of Bedaquiline, a TB therapeutic reserved for the treatment of MDR-TB. TB is one of the leading causes of death globally, accounting for 1.4 million deaths in 2019. An estimated 10 million people fall ill with TB each year. While TB is a curable disease, its unique pathogenesis requires prolonged treatment with many antimycobacterial agents, that can preclude treatment compliance. Added to this, drug resistance is an alarming concern, with around a 10% increase in MDR or rifampicin resistant TB reported year on year.

New discoveries for TB drugs: while it's promising to see how many new drugs are in pipeline, we always need new TB drugs, and a lot of drug discovery is serendipity – essentially finding a needle in haystack. The key for successful TB drug discovery is novel targets and chemical matter that is strongly bactericidal. The discovery of Bedaquiline, a drug which over 300,000 patients have received to date, has highlighted bacterial energy metabolism as a source for novel drug targets in the treatment of tuberculosis. Bedaquiline is a slow bactericidal but the latest data shows that Bedaquiline kills dormant TB. Killing dormant bacteria is critical as it shortens treatment. Drug resistance is linked to efflux pumps, so countering drug resistance requires blocking efflux pumps. Bedaquiline downregulates the ATP efflux pump, therefore, is an effective treatment for

MDR-TB. Bedaquiline is on the list of essential medicines and has recently been approved by the US for paediatric use.

Barriers to overcome:

- Sharing libraries can be hard as these are the crown jewels of pharma.

Session 4: Novel Antimicrobial Targets

Session moderated by Jordi Vila

Professor Vila introduced the session, covering novel antimicrobial targets. Presentations covered targets from the innate immune system to preventing gene transfer.

Key messages

- Stimulation of the innate immune system as a non-traditional target to quench infection and reduce treatment failure
- Chemical and antibody screens are being used to assess compounds in a variety of bacterial species against novel targets including:
  - quorum sensing
  - biofilm formatio
  - anti-virulence approaches
  - gene transfer
  - non-coding RNA eg: targeting thiamine pyrophosphate (TPP) riboswitches
  - resistance mechanisms

The following information in this session comes from submitted abstracts. The name of the presenter is underlined.

1. **Boosting innate immunity to treat bacterial pneumonia – ABIMMUNE**

   Jean-Claude Sirard, Institut Pasteur de Lille - Inserm, France, Tom van der Poll, University of Amsterdam, Netherlands, Mustapha SI-TAHAR, Inserm, Tours, France, Charlotte KLOFT, Freie Universität Berlin, Germany, Martin RUMBO, National University of La Plata, Argentina

Alternative treatment strategies against bacterial infections are required to decrease the use of antibiotics. Our studies tested the hypothesis whereby stimulation of the innate immune receptor Toll-like receptor 4 (TLR4) or TLR5 can be combined with antibiotics to ameliorate the treatment of invasive pneumonia. The efficacy of amoxicillin (AMX), the monophosphoryl lipid A (MPLA, a clinically-approved TLR4 activator), a recombinant flagellin (a TLR5 activator) or a combination of AMX and MPLA or AMX and flagellin was tested in a mouse model of Streptococcus pneumoniae respiratory infection. A single oral low-dose of AMX or the systemic injection of MPLA decreased 100 to 5,000-fold the bacterial load in lung and spleen but did not enhance survival compared to mock treatment. The combination of MPLA and AMX further reduced the bacterial colonization and invasion and significantly improved protection

against lethal disease. Similar findings were obtained by combining AMX and respiratory administration of flagellin. Our proof-of-concept study demonstrated that leveraging host innate immunity via TLR or TLR5 can synergize with antibiotics in order to increase the efficacy of therapy of bacterial pneumonia.

Outcomes and Outputs:

- Proof-of concept of the targeting of innate immunity to improve antibiotic treatment
- 5 articles (Talanta, Front Immunol, Mucosal Immunol, ACS Infect Dis, Pharmaceutics)
- New European Union (EU) project as a follow-up

2. **Fighting antimicrobial resistant infections by high-throughput discovery of biofilm-disrupting agents and mechanisms – DISRUPT**

   Morten Kjos, Norwegian University of Life Sciences, Nassos Typas, EMBL Heidelberg, Germany, Jan-Willem Veening, University of Lausanne, Switzerland, Christoph Merten, EMBL Heidelberg, Germany and EPFL Lausanne, Switzerland

Bacterial infections that are related to biofilms are difficult to treat with current antibiotic strategies. All the more so when drug resistant bacteria are involved. By developing novel approaches, we aim to identify novel targets and agents for understanding and treating biofilm-associated infections in four major antimicrobial resistant pathogens: staphylococci, pneumococci, E. coli and Pseudomonas.

In the DISRUPT consortium, we are constructing new genome-wide genetic tools and resources for these bacterial pathogens. These include CRISPRi-based and transposon-based mutant libraries, which is used to identify the full repertoire of anti-biofilm targets. Furthermore, we are using high-throughput screens for anti-biofilm substances, including chemicals and antibodies. By combining these approaches, we further characterise the mechanisms of action of novel anti-biofilm agents.

Outcomes and Outputs:

- Genome-wide genetic resources for studying biofilm-forming drug-resistant pathogens
- Novel anti-biofilm targets and agents

3. **Exploration of the TPP riboswitch as a new target for antibiotics - EXPLORE**

   Vipul Panchal, Ruth Brenk, U Bergen, Norway, Matthias Mack, Hochschule Mannheim, Germany, Gints Smits, Latvian Institute of Organic Synthesis, Daniel Lafontaine, Université de Sherbrooke, Canada

Riboswitches belong to a novel class of anti-bacterial drug targets as they regulate biosynthesis and transport of essential metabolites in bacteria by binding small molecules and are absent in humans. Residing in the 5' untranslated region of mRNA, these cis-regulatory elements are structured non-coding RNAs that adopt alternative

3D-conformations in response to cognate ligand and thereby function as genetic switches.

The high prevalence of thiamine pyrophosphate (TPP)-riboswitch among pathogenic bacteria and its regulation of essential genes involved in biosynthesis and transport of the essential cofactor TPP, makes it a promising target for a novel antibiotic. To facilitate drug discovery, we aim at screening tens of thousands of compounds against the TPP riboswitch using a high-throughput (HTS) assay followed by structure-based lead-optimization approach. We are currently developing a novel fluorescence based HTS compatible assay to identify ligands that bind to the TPP riboswitch and thereby inhibit transcription of a reporter gene. We have already established the proof of principle of this assay and expect to employ it to screen the CZ-Openscreen compound library. To further investigate the drug like property, mode of action and efficacy of the resultant hits against ESKAPE pathogens, we have also developed an *in vivo* reporter gene assay.

Outcomes and Outputs:

- Proof of principle of a novel HTS assay
- Optimization of the assay for HTS
- Preliminary screen

4. **Novel antimicrobials specific against Helicobacter pylori – FLAV4AMR**

   Javier Sancho, University of Zaragoza, Spain, Eliette Touati, Institut Pasteur, Paris, Ulrich E. Schaible, Research Center Borstel, Germany, Alain Bousquet-Melou, INRA, ENVT, France

Helicobacter pylori (Hp) infection is one of the leading causes of peptic ulcer, MALT lymphoma, and gastric cancer. About 50% of the human population is infected with Hp. The efficacy of antimicrobials in use is declining and no Hp-specific antimicrobial has been described so far. Current eradication therapies are based on a quadruple treatment with simultaneous administration of three broad-spectrum antibiotics/antimicrobials plus a proton pump inhibitor.

We are developing Hp-specific antimicrobials targeting flavodoxin, an essential Hp protein. These flavodoxin inhibitors are quite specific against the Helicobacter genus, which can reduce the damage to the microbiota often associated with antimicrobial treatment. The flavodoxin inhibitors have demonstrated in vitro efficacy according to EUCAST criteria against Hp clinical strains resistant to Mnz, Cla and rifampicin. Furthermore, some of them have been able to eradicate Hp infection from up to 50% of infected mice after administration for a week of a single daily dose without combining with any other antimicrobial or proton pump inhibitors (PPI). More sophisticated dosing regimens or combinations have not yet been attempted. Currently, we are determining their PK/PD properties, improving their bioavailability, studying their influence on the mouse microbiota, and testing their efficacy in combination with a PPI.

Outcomes and Outputs:

- Patented, novel, small-molecule, Helicobacter-specific flavodoxin inhibitors effective against Hp-resistant clinical strains and partly effective for Hp-eradication from infected mice.

5. **Sensitising Pseudomonas aeruginosa biofilms to antibiotics and reducing virulence through novel target inhibition – SENBIOTAR**

   Miguel Cámara, University of Nottingham, UK, Peter Nielsen, University of Copenhagen, Denmark, Roger Levesque, University of Laval, Canada, Christel Bergström, Uppsala University, Sweden, Fadi Soukarieh, University of Nottingham, UK

Pseudomonas aeruginosa (PA) continues to pose a threat public health due to its high levels of antimicrobial resistance (AMR) and limited options for effective treatment. The SENBIOTAR programme pursued a novel approach to tackle AMR in this organism through targeting bacterial virulence and restoring the efficacy of antibiotics. PA controls the production of virulence traits at the bacterial population level through quorum sensing (QS). The PA Pseudomonas Quinolone System (pqs) QS system controls the production of virulence factors and biofilm maturation through the activation of the transcriptional regulator PqsR by the QS molecule PQS. The pqs system has been validated as a drug target for virulence attenuation. Using *in silico* screening combined with structure activity relationship studies we have identified 4 non-toxic lead compounds from different chemical classes which can antagonise the interaction of PQS with PqsR attenuating PA virulence and sensitizing biofilms to antibiotics. They could also synergise the action of antisense peptide nucleic acids developed by our consortium and designed to inhibit the expression of the pqs system.

Overall, SENBIOTAR delivered one of the most effective strategies to inhibit the PA pqs QS system to date paving the path for future preclinical development.

Outcomes and Outputs:

- Delivery of novel potent inhibitors of the PA pqs QS system to attenuate PA virulence and sensitise biofilms to antibiotics
- 4 peer reviewed manuscripts and 4 in preparation.
- Training of 3 Postdoctoral researchers, 4 PhD students and 7 MSc students.

Session 5: Non-traditional antimicrobials

Session Moderated by Richard Gordon

Dr Gordon introduced the session, which covered non-traditional antimicrobials, including repurposed anti-parasitics, antimicrobial peptides and bacteriocins, host-directed therapies and tolerance inhibitors.

Key messages

- Tolerance inhibitors sensitize Mtb to stress, improve the function of Isoniazid, and re-sensitize Isoniazid-resistant isolates
- Repurposed Nitazoxanide shows potential to be an anti-staphylococcal lead alone or in combination
- Antimicrobial peptides and bacteriocins:
  - highly potent agents with potential for reduced antimicrobial resistance
  - opportunities for directed delivery to improve patient management and compliance
  - Understanding PK/PD, *in vivo* relevance, innate immunity and resistance critical to develop antimicrobial peptides that can be delivered systemically

The following information in this session comes from submitted abstracts. The name of the presenter is underlined.

1. **Development of novel Mycobacterial Tolerance Inhibitors (MTIs) against MDR/XDR tuberculosis (MTI4MDR-TB)**

   Tahira Riaz, Siva Krishna Vagolu, Tone Tønjum, Håvard Homberset, Umeå University, Sweden, and Souvik Sarkar, Mari Støen, Fredrik Almqvist, University of Oslo, Oslo University Hospital, Norway

The focus of this project is a new class of drugs, named Mycobacterial Tolerance Inhibitors (MTIs), discovered by partners in the MTI4MDR-TB consortium. MTIs hold great potential to be used as drugs in treatment against tuberculosis (TB). Mycobacterium tuberculosis (Mtb) is the bacterial cause of TB, which is the leading cause of death from a single infectious agent worldwide. According to the WHO's "Global Tuberculosis report 2020", 7.1 million new TB cases were notified in 2019. Additionally, 22% of the world's population is estimated to have latent TB infection and being at risk for developing active disease. Globally, 8% of new TB cases and 11.6% of previously treated TB cases are resistant against isoniazid (INH). Previous results of the MTI C10 have shown that C10 prevents biofilm formation of Mtb laboratory strains. Mtb cells form a biofilm to resist the stressors it encounters in the body, and the biofilm can also counteract the effect of antibiotics. MTI C10 has also demonstrated the ability to re-sensitize INH-resistant katG laboratory Mtb strain, when used in combination with INH. Here, we have tested the effect of a new collection of MTIs alone and in combination with other antibiotics in clinical Mtb strains with various combinations of antibiotic resistance. Cultures of clinical Mtb strains subjected to treatment with MTIs are compared to non-treated cultures by high end mass spectrometry analysis of lysed Mtb cells.

Outcomes:

- Inhibition of growth in combination with INH in INH-resistant clinical Mtb strains
- Changes in the Mtb proteome of clinical strains with and without MTIs are detected to help dissecting the exact MTI mode of action

2. **Systemically delivered bactericidal antimicrobial peptides to treat bacterial lung infections**

James Mason, Chris Lorenz, Clive Page, Simon Pitchford, Richard Amison, King's College London, UK, Mark Sutton, Charlotte Hind, Public Health England, UK, David Phoenix, London South Bank University, UK

Antimicrobial peptides (AMPs) are a potential alternative to classical antibiotics that are yet to achieve a therapeutic breakthrough for treatment of systemic infections. The antibacterial potency of pleurocidin, an AMP from Winter Flounder, is linked to its ability to cross bacterial plasma membranes and seek intracellular targets while also causing membrane damage. Here we describe modification strategies that generate pleurocidin analogues with substantially improved, broad spectrum, antibacterial properties, which are effective in murine models of bacterial lung infection. Increasing peptide–lipid intermolecular hydrogen bonding capabilities enhances conformational flexibility, associated with membrane translocation, but also membrane damage and potency, most notably against Gram-positive bacteria. This negates their ability to metabolically adapt to the AMP threat. An analogue comprising D-amino acids was well tolerated at an intravenous dose of 15 mg/kg and similarly effective as vancomycin in reducing EMRSA-15 lung CFU. This highlights the therapeutic potential of systemically delivered, bactericidal AMPs.

Outcomes and Outputs:

- Mechanism of antibacterial activity of AMPs is dependent on bacterial metabolism which may vary according to nutrient availability e.g. killing of Staphylococcus aureus more efficient when it is fermenting
- Modification of naturally occurring AMPs can not only enhance activity but also alter mechanisms of action, affecting suitability
- Suitably potent bactericidal AMPs can be delivered intravenously, are tolerated, reach the lung and effect a therapeutic reduction in lung CFU
- PHE Open Innovation Platform for AMR to encourage collaboration in the development on non-traditional antimicrobials[1]

3. **A novel best in class agent for prevention of post-surgical infections**

Gordon Barker, Mat Upton, Aprologix Ltd, UK, Ian Fotheringham, Ingenza Ltd, UK

At Amprologix, we are developing novel bacteriocin candidates for use against topical infections. Our lead candidate is a low-toxicity bacteriocin, epidermicin NI01, being developed for nasal decolonization (ND) of MRSA - a leading cause of hospital acquired infections. NI01 exhibits high potency against priority Gram positive pathogens, with no emergence of resistance. We have demonstrated that the peptide sequence can be modified, adapting the spectrum of activity.

In a mouse model of nasal MRSA carriage, a single dose of 0.8% NI01 was as effective as three days of twice daily dosing with 2% mupirocin (the current standard of care), giving

[1] *Contact charlotte.hind@phe.gov.uk or mark.sutton@phe.gov.uk*

potential for single-dose or short course therapy in humans. We have developed a high yield and flexible recombinant expression system for production of NI01 at a very low cost of goods.

Epidermicin NI01 has been formulated into a vehicle for delivery to the nasal cavity and evaluated in an IND enabling study. Data from this work indicate that NI01 is very well tolerated, with no clinical signs or adverse reactions following treatment with up to 240ug twice daily per animal for 14 days. Epidermicin NI01 has excellent potential for use ND and we are developing it for larger clinical indications.

Outcomes and Outputs:

- A novel low-toxicity bacteriocin candidate with potent activity against Gram positive pathogens on the WHO/CDC priority lists
- Potential for single dose efficacy in nasal decolonization
- A bespoke formulation for delivery to the nasal cavity
- Demonstrated low in vivo toxicity and positive PK data
- A proprietary, GMP compliant, scalable 'plug-and-play' recombinant production system for delivery of drug at a very competitive cost of goods

4. **Repurposing an antiparasitic as an anti-staphylococcal agent**

Sidharth Chopra, Grace Kaul, CSIR-Central Drug Research Institute, Lucknow, India

Drug Repurposing has emerged as a suitable alternative to the tedious conventional drug development against infectious diseases caused by resistant bacterial pathogens. With the same approach, while screening non antibiotics for activity against ESKAPE pathogens, we discovered Nitazoxanide, originally an antiparasitic drug, having significant activity against Staphylococcus aureus (SA) ATCC 29213 with an MIC of 16 mg/L. Nitazoxanide exhibited its potent anti-staphylococcal profile with similar activity against MDR SA strains including MRSA and VRSA. It is a synthetic nitrothiazolyl salicylamide derivative prodrug that is reported to get converted into its active metabolite tizoxanide upon deacetylation in stomach. Nitazoxanide's activity was further ascertained by its time kill kinetics study against SA ATCC 29213 where it demonstrated ~4 Log reduction at 24 hours at 10X MIC concentration compared to untreated SA. Nitazoxanide was also able to synergize with Linezolid and Ceftazidime in vitro with ~10 log and ~6 log reduction in bacterial load at 24 hours respectively. Nitazoxanide also exhibited an in vitro Post antibiotic effect of ~1 hour at 10X MIC concentration comparable to vancomycin. The in vivo efficacy against Staphylococcal infections is currently being determined. Taken together, Nitazoxanide shows potential to be an anti-staphylococcal lead alone or in combination therapy.

Outcomes and Outputs:

- Nitazoxanide exhibits potent in vitro anti-staphylococcal activity.
- Nitazoxanide shows in vitro synergistic activity with Linezolid and Ceftazidime against Staphylococcus aureus (SA).
- Nitazoxanide has an in vitro post antibiotic effect of ~1 hour against SA.

- Nitazoxanide shows potential to be an anti-staphylococcal lead alone or in combination therapy.

5. **Host Targeted Drug therapy in TB**

   Sandra Peña-Diaz, Celine Rens, Sahile Henok, Tirosh Shapira, Joseph D Chao, Tom Pfeifer, Clement K.M. Tsui, Flavia Sorrentino, Gagandeep Narula, Abraham Lopez, Adama Bojang, Xingji Zheng, Adrian Richter and Yossef Av-Gay, University of British Columbia, Canada

There is a growing need for new and better drugs to treat Tuberculosis (TB), stemming from the rapid development of drug-resistant strains of Mycobacterium tuberculosis (Mtb), the causative agent of TB. Drug-resistance in Mtb can be attributed to the long duration of current antibacterial regimens. The challenges in reducing duration of treatment and combating bacterial infection have given rise to a new approach termed Host Directed Therapy (HDT), whereby compounds that target host immunity can assist with the eradication of bacteria or shorten the duration of treatment. Almost 90 percent of new TB drugs in development target bacterial pathways, while sporadic attempts to develop HDTs are still in their infancy. We have developed a High Throughput, High Content screening approach for identifying of compounds that inhibit Mtb growth in an intracellular model of infection. Our assay enables identification of compounds that are active in the macrophage environment, and not in broth. We have identified potential HDT compounds targeting Mtb intracellularly in THP-1 cells: some are published, and others are under development. Our hits shown to be active in killing intracellular Mtb included repurposed drugs, signalling modifiers, immunomodulators, and infection control related inhibitors. Genetic validation of identified host targets was performed using RNAi and CRISPR knock out methods.

Outcomes and Outputs:
- Developed a High Content High Throughput assay to monitor Mtb growth in infected macrophages
- Identified several hit compounds that kill Mtb intracellularly at dose dependent low uM concentrations
- Identified and validated novel host targeted drug targets using RNAi and CRISPR

Session 6: Novel Strategies

Session moderated by Kyeong-Kyu Kim

Professor Kyeong-Kyu Kim introduced the session, in which novel strategies to overcome AMR were discussed, including computational modelling strategies, novel target identification and use of adjuvants.

Key messages

- Computational modelling approaches can capture biological context and complexity to identify novel targets for antibacterial therapies
- Microbial metabolism is an attractive novel target for drug development

- Novel artificial siderophores are "Trojan Horses" - tools for the detection (bioluminescence) and treatment of gram-negative infections
- Adjuvants inhibiting bacterial pump efflux maximise the intrabacterial concentration of antibiotics
- Combinations of antibiotics and antibiotic/ adjunctive agents show *in vitro* activity and have the potential for treating resistant pathogens

The following information in this session comes from submitted abstracts. The name of the presenter is underlined.

1. **Targeting microbial metabolism to combat the AMR in Staphylococcus aureus**

   Akhilesh K. Chaurasia, Nayab Batool, Kyeong Kyu Kim Sungkyunkwan University School of Medicine, South Korea

Due to the scarcity of effective antibiotics against antimicrobial-resistant (AMR) *Staphylococcus aureus* (SA), novel targets are urgently required to develop next-generation antibiotics. We investigated the accessory and exclusive microbial metabolic key genes as targets to identify their interacting drug partners. In this context, we explored the mannitol and methylglyoxylase pathways wherein mannitol-1-phosphate dehydrogenase (SaM1PDH) and aldo-keto reductases (SaAKRs) were targeted which are responsible for regulating intracellular mannitol and methylglyoxal levels, respectively. Since mannitol is necessary for maintaining the cellular redox and osmotic potential, the homeostatic imbalance caused by treatment with a SaM1PDH inhibitor or knockout of the gene encoding SaM1PDH (mtlD) results in bacterial cell death through oxidative and/or mannitol-dependent cytolysis. To further validate the use of SaM1PDH as an antibacterial target, we identified dihydrocelastrol (DHCL) as a competitive inhibitor of SaM1PDH and confirmed that DHCL effectively reduces bacterial cell viability during host infection. Similarly, the role of SaAKR as target was explored both in virulence and AMR. Chemical-genetic screening approach identified flufenamic acid (FLF) which inhibits transcriptional regulators, SaeRS two-component systems & agr resulting in the inhibition of offensive toxins, and defensive biofilm & staphyloxanthin. FLF specifically binds to SaAKRs and inhibits their activities. SaAKRs are involved in the conversion of triose phosphate sugars to methylglyoxal; and thereby FLF diverts the glycolysis pay-off phase towards energy-deficient methylglyoxylase pathway due to the accumulation of bacteriostatic methylglyoxal. The metabolic imbalance and targeting master transcriptional virulence regulators reversed AMR and blocked *S. aureus* pathogenesis in mouse infection models. Our results strongly support the concept that targeting of SaM1PDH and SaAKRs represents alternative strategies for developing a new class of antibiotics which cause bacterial cell death not by blocking the central dogma but by inducing cytolysis and intracellular methylglyoxal toxicity, respectively.

Outcomes:
- SaM1PDH and SaAKRs as novel targets
- DHCL as a competitive inhibitor of SaM1PDH
- FLF specifically binds to SaAKRs, and inhibits their activities
- Bacterial cell death by inducing cytolysis and intracellular methylglyoxal toxicity

2. **Design, Synthesis and Lead Generation of Novel Siderophore Conjugates for the Detection and Treatment of Infections by Gram-Negative Pathogens**

   Mark Brönstrup, Helmholtz Centre for Infection Research, Germany, Isabelle Schalk, CNRS, University of Strasbourg, France, Doron Shabat, Tel Aviv University, Israel

In the so-called Trojan Horse Strategy, antibiotics are conjugated to siderophores to hijack the bacterial siderophore transport system, and thereby enhance the intracellular accumulation of drugs. We synthesized novel artificial siderophores, characterized their transport, resistance and bacterial adaptation mechanisms, and their efficacy when coupled to antibiotic natural products. We also describe first applications of siderophore conjugates for chemiluminescent imaging and PET imaging, in order to enable the noninvasive visualization of infections in humans. We also report a theranostic agent that combines both diagnostic and antibiotic modalities.

Outcomes:

- New artificial siderophores discovered that confer high antibiotic activity
- Uptake, resistance and bacterial adaptation mechanisms characterized
- Coupling of siderophores with triggerable chemiluminescent moieties
- First PET probe for imaging of infections in large animals

3. **Development of a First-in-Class Antibacterial Drug Using a High-Resolution Computational Model of the Biosynthesis of the Outer Envelope of E. coli**

   Ajay Mistry, John George, Ed Siegwart, Tony Raynham Oppilotech Ltd, UK

The cell envelope of Gram-negative bacteria represents a barrier to chemical or physical attack. During growth, bacterial cells need to carefully synchronise all 3 components (Lipopolysaccharide; phospholipids and peptidoglycan) in order to maintain integrity. Dysregulation of any one of the components can result in membrane instability leading often to cell death. However, many of the regulatory processes underlying membrane biosynthesis are largely unknown. We have used systems biology and Machine Learning to build a highly detailed dynamic computational model of the biosynthesis of the outer envelope. The model is validated experimentally in the lab. The model was used to identify a target involved in the biosynthesis of Lipid A. We then undertook an in-silico docking study against the target crystal structure, purchased molecules and identified several structurally distinct active Hit compounds. Further chemical analogues of the Hit compounds were generated and exhibited improved antibacterial activities across a range of Gram-negative bacteria, with no cross resistance. We now intend to undertake a comprehensive Hit-to-Lead and Lead Optimisation campaign to further improve the activities of the compounds and develop towards the clinic.

Outcomes:

- Identification of drug target involved in biosynthesis of LPS
- Identification of Hits against target

- Generation of analogues of Hits exhibiting activities against priority Gram-negative pathogens

4. **Antibiotic translocation across bacterial membranes and bacterial susceptibility, concepts & methods**

   Jean-Marie Pages, Anne Davin, Jean-Michel Bolla; INSERM, Aix-Marseille University, France Muriel Masi, Matthieu Refregiers; Synchrotron SOLEIL, Gif-sur-Yvette, France; Paolo Ruggerone; University of Cagliari, Italy ; Mathias Winterhalter; JUB, Bremen, Germany.

In Gram-negative bacteria, antibiotic resistance is mostly associated with the presence of mutations and enzymatic barriers that can be anticipated and magnified by a decreased penetration and an increased active efflux. Consequently, the ability of an antibiotic to reach effective internal concentrations is a key factor for their antimicrobial activity. This is illustrated by three definitions, the SICAR (Structure Intracellular Concentration Activity Relationship), the RTC2T (Resident Time Concentration Close to Target) and the DEK (Dose for Early Killing) that have been proposed for quantifying the dose-activity of antibiotics. These concepts have been recently applied by using various methods and protocols allowing us to follow the accumulation and killing rate on strains exhibiting various membrane phenotypes. By using this method, we have ranked fluoroquinolone molecules for influx-efficiency and efflux-sensitivity and correlated with their respective activity. All these efforts pave the way for rational chemical-pharmaceutical modulations of antibiotics making them more permeable to Gram-negative membranes and less efflux-sensitive, thus more effective to attack resistant bacteria exhibiting membrane-associated mechanisms of resistance.

Outcomes:

- Translocation across bacterial membrane
- Resident Time Concentration Close to Target
- Structure Intracellular Concentration Activity Relationship
- Dose for Early Killing
- Real time correlation intracellular antibiotic concentration - antibacterial activity

5. **Developing combinations of CO-ACTIVE antimicrobials and non-antimicrobials (CO-ACTION)**

   Johan Mouton, Joseph Meletiadis, Erasmus University Medical Center, Netherlands, Lena Friberg, Thomas Tängdén, Uppsala University, Sweden, Françoise Van Bambeke, Université Catholique de Louvain, Belgium, William Couet, Université de Poitiers, France,Alain Bousquet-Mélou, INRAE, France

As resistance rates are increasing worldwide and too few antibiotics are being developed, effective treatment is lacking especially against infections caused by gram-negative bacteria. Antibiotic combination therapy holds great promise to restore the activity of available drugs by synergistic interactions. Yet, data is insufficient on which antibiotics and non-antibiotics should be combined to optimize bacterial killing and

prevent emergence of resistance. There is need for well-defined methods to efficiently screen and identify promising combinations and validating these *in vitro* and *in vivo*. By applying pharmacokinetic/pharmacodynamic (PKPD) modelling, preclinical and human pharmacokinetic data are integrated to inform effective dosing regimens.

The purpose of the CO-ACTION project was 1) to develop and provide a framework for evaluating and validating the effectiveness of antibiotic and non-antibiotic combinations in the preclinical setting based on pharmacokinetic/pharmacodynamic principles and 2) to develop useful combinations of against multidrug-resistant gram-negative bacteria, e.g. Pseudomonas aeruginosa and Klebsiella pneumoniae. The project was carried out in six work-packages that were executed partly sequentially, partly in parallel: screening for combinations against strains with well described resistance mechanisms, selecting potential synergistic combinations, subsequent validation using PKPD *in vitro* experiments and mathematical modelling and finally testing combinations in animal models. Interaction between the participating research groups and work-packages was key to accelerating the search for the most co-active combinations.

Outcomes:

- A novel method for efficient screening of antibiotic combinations was validated by screening multiple antibiotic combinations against a large set of clinical isolates.
- Synergistic combinations of polymyxin B with rifampicin, minocycline, aztreonam, meropenem were identified.

Session 7: Economic Incentives

Session moderated by Katherine Payne

Professor Payne introduced the topic of economic incentives, covering the UK reimbursement model, open science initiatives, the Swedish pilot reimbursement model and ending with an industry perspective.

Session Outcomes

- Existing models of reimbursement don't work for antimicrobial therapeutics
- Current and future value to the health system needs to be assessed
- Pilot payments/ reimbursement modes are being tested in the UK and Sweden
- Payments are delinked from the volume of use (sales)
- Critical that more countries develop their own models in order to achieve global impact (eg: Pasteur Act in US Congress)
- Open Science partnerships to speed-up drug discovery and translation
- Regulatory data protection supports broad freedom-to-operate and provides private sector incentives

The following information in this session is a brief synopsis of the content of each presentation.

Presentations

1. **UK antibiotic reimbursement model**

   Mark Sculpher, University of York, UK

Professor Sculpher discussed the UK delinked reimbursement model, and implications for assessing value (see Figure 8). The UK model is based on societal value. Payment for access rather than volume; payments are made over time, irrespective of volumes used. Two 'test evaluations' for NICE are currently underway for ceftazidime with avibactam and cefiderocol. Dr Sculpher presented the key principals of value assessment and the challenges associated with assessing the value of a product to the health system at the level of the population rather than at the level of the individual.

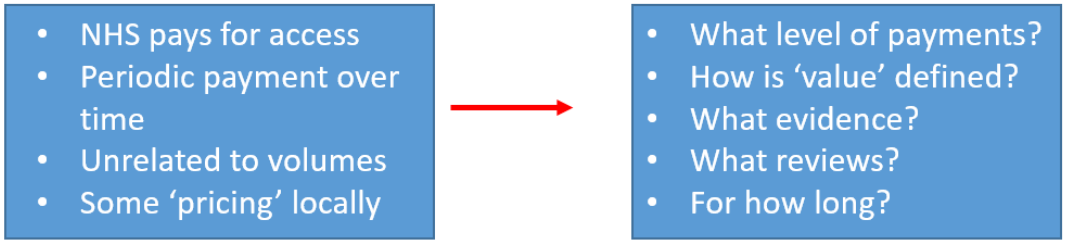


Figure 8. UK Model and Value Assessment.

Dr Sculpher summarized his presentation, pointing out that:

- There are policy challenges in how to appropriately incentivise the development of new antimicrobials
- Any policy will need to determine how much funding a health system should devote to newly available product
- Standard approaches to value assessment are unlikely to be suitable
- A fuller methods framework is needed
- Evidential uncertainty is a major challenge

2. **Sweden antibiotic reimbursement model**

Jenny Hellman, Public Health Agency, Sweden

Ms Jenny Hellman introduced the need to act and the need to develop new reimbursement models, noting that Sweden faces a risk of insufficient availability of antimicrobial therapeutics, in part due to high resistance rates, restrictive use of therapeutics and the small market. Ms Hellman discussed the Swedish pilot study, which runs from 2018-2022. The study involves a contract for availability of therapeutics and a partially de-linked model. The pilot study will evaluate 5 products, with three new to the Swedish market. The goal of the pilot study is to give the government a recommendation if, and in what way, the model should be extended.

The suggested principles for the pilot study are:

- A minimum annual revenue to the pharmaceutical company should be guaranteed from the national level. In return the company deliver a certain amount in specified time limits.
- Regional healthcare, will continue to pay for their usage as usual
- Annual reconciliation should be done. If the revenue of companies is lower than the guaranteed level, the difference will be paid from national level.
- If the revenue of companies from regions is higher than the guaranteed level, the companies will keep the income and be paid up 10% of the value of the security stock as compensation for the security stock, paid at national level.

The pilot study has led to contracts for five products, three of which were new for the Swedish market. Ms Hellman suggested that more pilot studies are needed, but the models need to be adjusted to the requirements of other countries. There is also a need to consider antibiotics that target different pathogens. Ms Hellman also noted that political involvement is essential and suggested the creation of an international network to collaborate and to share experiences.

3. **Open science for sustainable AMR therapeutics development**

   Richard Gold, McGill University

Professor Gold discussed the economic problems faced by the therapeutics pipeline noting that large pharmaceutical companies have moved away from the development of anti-infectives and that two start-ups with drugs in development failed (Achaogen and Aradigm). Professor Gold commented that innovation in AMR faces similar challenges to other areas of drug discovery, such as pandemic preparedness, rare diseases, paediatric diseases, where the market does not supply an adequate incentive to invest.

Professor Gold went on to discuss the challenges and barriers facing the drug discovery innovation system.

Challenges:

- decreasing productivity per unit (however measured)
- exponentially increasing costs
- a decline in risk-taking

Barriers:

- Increasing complexity of science, leading to larger teams and, hence, expenses
- Misaligned incentives in both the academic and industrial sectors
- Balkanization of knowledge

Professor Gold suggested that models of drug discovery that we have used thus far have hit their limits, particularly where the market fails to provide an incentive, and noted that there is a need to develop new models.

4. **Sustaining a pipeline of new antibiotics; a UK industry perspective*:***

   Bryan Deane, Association of the British Pharmaceutical Industry

Dr Bryan Deane introduced the AMR Action Fund, noting that the subscription payment model should:

- Value a new antibiotic on preventing the AMR public health challenge
- Be based on agreed annual payment separated from volume usage
- Be under a stewardship plan so that use is in the patients who need it

Dr Deane conclude that no one country can solve this issue: the UK pilot and the AMR Action Fund may add significantly to the landscape, but the global challenge remains – to create the environment for a sustainable development pipeline for future antibiotic needs.

Session 8: Antimicrobial Stewardship, Access and Sustainability

Session moderated by Patrick Stewart, Director General, Health Canada.

Professor Patrick Stewart introduced the session, which began with a keynote presentation from Professor Dame Sally Davies, introduced by Pierre Sabourin, Assistant Deputy Minister, Health Canada. This was followed by a round table discussion, panel moderated by Patrick Stewart. Panellists discussed gaps in access to antibiotics in low- and middle-income countries; existing stewardship barriers; the impact of COVID-19 on antimicrobial resistance; and new opportunities to track patterns of resistance and ensure novel medicines and vaccines aimed at fighting drug-resistant infections reach those most in need.

Session outcomes

- Health systems can be rescued if we act collectively now
- The global disparity in access to antimicrobials needs to be addressed
- We need innovation, access and security across the whole value chain of antimicrobials
- Stewardship and access are the cornerstones of medicine - aim to treat everyone everywhere
- Lack of incentives for antimicrobial stewardship
- Work needed to implement national action plans and implement IACG recommendations

Keynote presentation – Antimicrobial Stewardship Access and Sustainability, Dame Sally Davies

With an introduction by Pierre Sabourin, Assistant Deputy Minister, Health Canada

Professor Dame Sally Davies positioned AMR in the context of the current COVID-19 pandemic. She noted that science, research and economic stimuli are needed to get us out of the concurrent pandemics of COVID-19 and AMR. She likened COVID-19 to a

lobster being dropped into a pot of boiling water (immediate, obvious and noisy) and AMR to a lobster being put into cold water which is heated up very slowly (it will take a while to die and won't make any noise). If we act now, we can rescue the disruption and devastation that will occur in a world without active antibiotics.

She provided an excellent introduction to the panel discussion that followed her presentation, highlighting the need for better global access to antibiotics so that they can be used when they will be effective. She described the need for innovation, access and security across the whole value chain. She reiterated the need for a global reimbursement system that recognises societal value of antibiotics, to create an ecosystem that will demonstrate the power of collaboration.

She closed her talk by coming back to COVID-19 and how the viral pandemic was a great challenge but also an opportunity to raise the profile of AMR and capitalise on the public appetite for real time data. The value of rapid diagnostics has been demonstrated; wouldn't they be a game-changer for antimicrobial stewardship. Knowledge empowers individuals to understand what they can do to conserve antimicrobials. She noted that a key priority for the UK G7 presidency in 2021 is better antimicrobial stewardship, a reinvigorated antimicrobial development pipeline and a safe, secure and transparent antibiotic supply chain, and invited other G7 countries to help move this agenda forward.

The Keynote was followed by short presentations from members of the Panel comprising representatives from global organisations that advocate for better antimicrobial stewardship including improved access and a sustainable antibiotic supply chain.

- **Oliver Williams** described how the Wellcome Trust is working in partnership with other global organisations to improve stewardship and access to antimicrobials. He introduced the voluntary guidance recently published by CARB-X to support all antibiotic developers that sets a new benchmark for what can reasonably be expected from product developers and provides a comprehensive overview of strategies to support stewardship access.
- **Yann Ferrisse** described the GARDP programme to transform care of babies with sepsis, with the aim of making vital treatment available to everyone everywhere. They are working to ensure sustainable access and a dynamic portfolio of therapeutics and the evidence to support their use in babies and children.
- **Margo Warren** introduced the Access to Medicine Foundation and their flagship Access to Medicine Index and AMR Benchmark. She noted that the Foundation seeks to guide and stimulate pharma to improve global access to medicine and limit treatment-resistant bacterial and fungal diseases. They too were involved in the development of the CARB-X voluntary guidance noted above and encourage early consideration of stewardship and access when developing new antimicrobials. The Benchmark is more than just comparing companies and includes key findings, best practice and an analysis of the drug pipeline. The Benchmark is published on a 2-year cycle with the release of the next Benchmark scheduled for the end of this year.

- **Mirfin Mpundu**, ReAct Africa highlighted the COVID-19 pandemic as an example of what happens when effective treatment and vaccines are unavailable to treat infections. He noted that low- and middle-income countries are more susceptible to the consequences of rising antimicrobial resistance because these countries carry a higher burden of infection. While the responsibility for improving weak health systems falls on national governments, the protection of lifesaving antibiotics is also a global responsibility. Countries need to take collective action as well as taking national responsibility to support the implementation of National Action Plans for AMR. High income countries should set an example and mobilise resources to support countries with weaker economies.

Future JPIAMR Therapeutics call scoping discussion

Laura Plant introduced the 14th JPIAMR transnational call for research projects. The next call will support research and therapeutic/agricultural interventions based on the improvement of the efficacy, specificity, delivery, combinations and/or repurposing of drugs and plant protection agents to treat bacterial or fungal infections in One Health settings. The DRUID Call aims to improve the treatment of bacterial and fungal infections and/or the prevention of the emergence/spread of resistance in humans, animals or plants through the improvement of efficacy, specificity, delivery, combinations and/or repurposing of drugs and plant protection agents.

Workshop participants were invited to comment on priority areas of focus for the DRUID call, and future JPIAMR calls.

Conclusions

The workshop Chair, Dr Marc Lemonnier, closed the workshop, with a discussion of the major outcomes. Dr Lemonnier then gave a brief concluding message, noting that public health needs (WHO priorities) and the future reimbursement landscape will be key issues in shaping the future antimicrobial therapeutics pipeline. Understanding how public health priorities are detected, measured and valued is essential. There is a balance to be struck between what is desirable and what is achievable. While identification and development of novel drug classes is the goal, in the current climate of increasing development of antimicrobial resistant, improvement of existing classes (including adjunct therapies) should not be neglected. Both traditional and non-traditional approaches are required; we need solutions that provide benefit to patients!

Dr Lemonnier discussed the need for dialogue, collaboration and partnerships between all stakeholders including academia, SMEs, Pharma, Funders, NGOs, Regulators, payers and end users. JPIAMR has an important role to play in coordinating these interactions. There was general consensus that antimicrobial therapeutics pipeline is underpinned by innovation. To truly reduce global antimicrobial resistance, better access and stewardship must be taken into consideration early in the development process. It is important to fill gaps in the R&D value chain: new differentiation criteria, clinical trial capacities and capabilities are required.

Global sustainability requires governments to work together. A thriving antimicrobial drug development pipeline will require both research funding and the implementation of pull incentives.

Dr Lemonnier thanked the speakers, moderators and participants.

Table of Acronyms

ADD: South Africa-United Kingdom Antimicrobial Drug Discovery
AMPs: Antimicrobial peptides
AMR: Antimicrobial Resistance
AMX: amoxicillin
ATCC: American Type Culture Collection
BEAM: Biotech companies in Europe combating AntiMicrobial Resistance
BMI: body mass index
CARB-X: Combating Antibiotic-Resistant Bacteria Biopharmaceutical Accelerator
CDC: Centers for Disease Control and Prevention, USA
CFU: colony forming units
Cla: Clavulanic acid (antibiotic)
CMC: chemistry, manufacturing and controls
COVID-19: pandemic disease caused by the SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) that was first reported in December 2019
CRISPR: clustered regularly interspaced short palindromic repeats
CRISPRi: CRISPR interference
DEK: Dose for Early Killing
DHCL: dihydrocelastrol
DMPK: drug metabolism and pharmacokinetics
DRUID: Disrupting drug resistance using innovative design – JPIAMR Call 14
EMA: European Medicines Agency
ERA-NET: European Research Area Network
EC: European Commission
E. coli: *Escherichia coli*
EMRSA-15: a multidrug-susceptible strain of *Staphylococcus aureus*
ESCMID: European Society of Clinical Microbiology and Infectious Diseases
ESKAPE pathogens: *Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa,* and Enterobacter species
EU: European Union
EUCAST: European Committee on Antimicrobial Susceptibility Testing
FLF: flufenamic acid
G7: The Group of Seven is an intergovernmental organisation made up of the world's largest developed economies
GARDP: Global Antibiotic Research and Development Partnership
GSK: GlaxoSmithKline
HDT: Host directed therapy
HTS: High-Throughput Screening
Hp: *Helicobacter pylori*
IACG: Interagency Coordination Group on Antimicrobial Resistance
iiCON: Infection Innovation Consortium
IMI: Innovative Medicines Initiative
IND: intranasal delivery
INH: isoniazid
IP: Intellectual property

JPIAMR: Joint Programming Initiative on Antimicrobial Resistance
MD: Medical Doctor
MDR: Multi-Drug Resistance
MIC: minimum inhibitory concentration
Mnz: metrobidazole (antibiotic)
MoA: Mechanism of action
MPLA: monophosphoryl lipid A
MRC-UK: Medical Research Council (part of United Kingdom Research and Innovation)
MRSA: Methicillin-Resistant Staphylococcus Aureus
Mtb: *Mycobacterium tuberculosis* (pathogen causing tuberculosis)
MTI: Mycobacterial Tolerance Inhibitors
ND: nasal decolonization
NGO: Non-governmental organisation with a social mission
NHS: National Health Service (UK)
NICE: National Institute for Health and Care Excellence (UK)
OIE: World Organisation for Animal Health
PA: *Pseudomonas aeruginosa*
PDP: Product Development Partnership
PhD: Doctor of Philosophy or Doctorate degree
PK: Pharmacokinetics
PK/PD: Pharmacokinetics and pharmacodynamics
Pqs: Pseudomonas Quinolone System
PPI: proton pump inhibitors
QS: quorum sensing
R&D: Research and Development
RNAi: RNA interference
RTC2T: Resident Time Concentration Close to Target
SA: *Staphylococcus aureus*
SAB: Scientific Advisory Board
SaAKRs: *Staphylococcus aureus* aldo-keto reductases
SaM1PDH: *Staphylococcus aureus* mannitol-1-phosphate dehydrogenase
SAMRC: South African Medical Research Council
SICAR: Structure Intracellular Concentration Activity Relationship
SME: Small and medium-sized enterprise
TB: tuberculosis (disease)
TLR: Toll-like receptor
TPP: thiamine pyrophosphate
UK: United Kingdom of Great Britain and Northern Ireland
UKRI: United Kingdom Research and Innovation
VRSA: vancomycin-resistant *Staphylococcus aureus*
WHO: World Health Organization
XDR: Extremely drug-resistant

Links to websites referenced in the workshop

- https://accesstomedicinefoundation.org/
- http://amr.solutions
- https://beam-alliance.eu/
- https://carb-x.org/
- CDC AMR Threats Report
- Cystic Fibrosis Syndicate in Antimicrobial Resistance | Medicines Discovery Catapult
- https://ec.europa.eu/info/research-and-innovation/funding/funding-opportunities/funding-programmes-and-open-calls/horizon-europe_en
- https://www.ema.europa.eu/en
- https://gardp.org/
- https://www.imi.europa.eu/projects-results/project-factsheets?keywords=AMR&status=All&call=All&programmes=All&disease_areas=All&products=All&tools=All
- https://www.jpiamr.eu/
- https://www.lstmed.ac.uk/iicon
- https://www.oie.int/en/what-we-do/global-initiatives/antimicrobial-resistance/
- https://www.pewtrusts.org/en/projects/antibiotic-resistance-project
- https://www.repair-impact-fund.com/
- https://www.samrc.ac.za/media-release/international-research-collaboration-tackle-antimicrobial-resistance-tapping-south
- https://www.ukri.org/councils/mrc/
- Ursula Theuretzbacher, Ph.D. | Antibiotic expert – Antibacterial drug R&D strategies and public health
- https://wellcome.org/what-we-do/our-work/drug-resistant-infections
- WHO priority pathogens list
- https://www.who.int/publications/i/item/WHO-EMP-IAU-2017.12

Annex 1. Workshop Agenda

Feeding the AMR Therapeutics Pipeline - JPIAMR Therapeutics Workshop 2021

Day 1 – Tuesday April 20th

Time (CET)	Session Details	Moderators and Speakers
13:00 – 13:05	Welcome from the Chair	Workshop Chair – Marc Lemonnier
13:05 – 13:10	Funder presentation	UK MRC/ JPIAMR – Jess Boname
13:10 – 14:40	Session 1 - Antimicrobial Therapeutics Landscape	Moderator – Rafael Canton
13:10 – 13:30	Keynote presentation - AMR Therapeutics Landscape	Ursula Theuretzbacher
13:30 – 14:40	Panel Discussion with Q&A from workshop participants	Hatim Sati – WHO Stefano Messori – OIE/STAR-IDAZ Alessandra Martini – EC Tim Jinks – Wellcome Trust Erin Duffy – CARB-X Laura Marin – JPIAMR Florence Séjourné – BEAM Graham Somers – GSK IMI Portfolio Director
14:40 – 14:50	Break	
14:50 – 15:50	Session 2 - Choosing wisely — is your product worth developing?	Moderator - John Rex

Time (CET)	Session Details	Moderators and Speakers
14:50 – 15:00	Invited speaker	John Rex
15:00 – 15:50	Panel Discussion with Q&A from workshop participants	Kevin Outterson – CARB-X Christine Årdal – IMI DRIVE-AB and EU-JAMRAI Marco Cavaleri – EMA Laura Piddock – GARDP Camilla Petrycer Hansen – Novo REPAIR Impact Fund
15:50 – 16:00	Break	
16:00 – 16:50	Session 2a – Activities to support the AMR therapeutics research community	Moderator – Jess Boname
16:00 – 16:10	CF Syndicate in AMR	Jessica Lee[1], Paula Sommer[2], Beverley Isherwood[1], Lucy Allen[2], Alessandra Gaeta[1] 1. Medicines Discovery Catapult, UK 2. Cystic Fibrosis Trust, UK
16:10 – 16:20	Pew Evaluates the Global Clinical Pipeline of Antibiotics and Non-traditional Bacterial Products	Cara Lepore, Wes Kim, Katie Prosen, The Pew Charitable Trusts, USA

Time (CET)	Session Details	Moderators and Speakers
16:20 – 16:30	South Africa/UK Antimicrobial Drug Discovery Hub	Rosemary Dorrington[1*], Mathew Upton[2*], Hai Deng[3], Rebecca Goss[4], Karin Jacobs[5], Perry Kaye[1], Rui Krause[1], Marelize LeRose-Hill[6], Gwynneth Matcher[7], Derek Ndinteh[8], Alex O'Neill[9], Paul Race[10], Stephanie van Heerden[11] 1. Rhodes University, SA; University of Plymouth, UK; 2. University of Plymouth, UK 3. University of Aberdeen, UK 4. University of St Andrews, UK 5. University of Stellenbosch, SA 6. Cape Peniculid University of Technology, SA 7. South African Institute for Aquatic Biodiversity, SA 8. University of Johannesburg, SA 9. University of Leeds, UK 10. University of Bristol, UK 11. University of Kwazulu-Natal, SA * SA and UK Pis
16:30 – 16:40	Delivering integrated solutions for human infections – iicon infection innovation consortium	Janet Hemingway, Liverpool School of Tropical Medicine, UK, Peter Jackson, Infex Therapeutics UK, with partners from Evotec UK, Unilever UK, Royal Liverpool and Broadgreen University Hospitals Trust, UK
16:40 – 16:50	10-minute Q&A and with all speakers as panel	
16:50 – 17:00	Short wrap-up from the Workshop Chair	Marc Lemonnier

Day 2 – Wednesday April 21st

Time (CET)	Session Details	Moderators and Speakers
13:00 – 13:05	Opening remarks	Marc Lemonnier
13:05 – 14:15	Session 3 - Mtb antimicrobial pipeline	Moderator - Mirfin Mpundu
13:05 – 13:15	Drug discovery to shorten the duration of chemotherapy	Helena Boshoff, NIAID, USA
13:15 – 13:25	High throughput screening for Mtb therapeutics	Vinayak Singh, University of Cape Town, South Africa
13:25 – 13:35	Pharmacokinetics and pharmacodynamics of anti-tuberculosis agents.	Rada Savic, University of California at San Francisco, USA
13:35 – 13:45	Reviving ethionamide. TRICky, but possible	Modesto Jesus Remuiñán-Blanco, GSK
13:45 – 13:55	Bedaquiline story	Professor Anil Koul, London School of Hygiene and Tropical Medicine, UK and Janssen, Belgium
13:55 – 14:15	20-minute Q&A with all speakers as panel	
14:15 – 14:25	Break	
14:25 – 15:35	Session 4 - Novel antimicrobial targets	Moderator - Jordi Vila
14:25 – 14:35	Boosting innate immunity to treat bacterial pneumonia - ABIMMUNE	Jean-Claude Sirard, Institut Pasteur de Lille, France Tom van der Poll, University of Amsterdam, Netherlands Mustapha SI-TAHAR, INSERM, Tours, France Charlotte KLOFT, Freie Universität Berlin, Germany Martin RUMBO, National University of La Plata, Argentina

Time (CET)	Session Details	Moderators and Speakers
14:35 – 14:45	Fighting antimicrobial resistant infections by high-throughput discovery of biofilm-disrupting agents and mechanisms - DISRUPT	Morten Kjos, Norwegian University of Life Sciences Nassos Typas, EMBL Heidelberg, Germany Jan-Willem Veening, University of Lausanne, Switzerland Christoph Merten, EMBL Heidelberg, Germany and EPFL Lausanne, Switzerland
14:45 – 14:55	Exploration of the TPP riboswitch as a new target for antibiotics - EXPLORE	Vipul Panchal, Ruth Brenk, U Bergen, Norway Matthias Mack, Hochschule Mannheim, Germany Gints Smits, Latvian Institute of Organic Synthesis Daniel Lafontaine, Université de Sherbrooke, Canada
14:55 – 15:05	Novel antimicrobials specific against *Helicobacter pylori* – FLAV4AMR	Javier Sancho, University of Zaragoza, Spain Eliette Touati, Institut Pasteur, Paris Ulrich E. Schaible, Research Center Borstel, Germany Alain Bousquet-Melou, INRA, ENVT, France
15:05 – 15:15	Sensitising *Pseudomonas aeruginosa* biofilms to antibiotics and reducing virulence through novel target inhibition - SENBIOTAR	Miguel Cámara, University of Nottingham, UK Peter Nielsen, University of Copenhagen, Denmark Roger Levesque, University of Laval, Canada Christel Bergström, Uppsala University, Sweden Fadi Soukarieh, University of Nottingham, UK
15:15 – 15:35	20-minute Q&A and discussion with speakers as panel	
15:35 – 15:45	Break	
15:45 – 16:55	Session 5 - Non-traditional antimicrobials	Moderator – Richard Gordon

Time (CET)	Session Details	Moderators and Speakers
15:45 – 15:55	Development of novel Mycobacterial Tolerance Inhibitors (MTIs) against MDR/XDR tuberculosis - MTI4MDR-TB	Tahira Riaz[2], Siva Krishna Vagolu[2], Souvik Sarkar[1], Håvard Homberset[2], Mari Støen[2], Fredrik Almqvist[1] and Tone Tønjum[2] 1. Umeå University, Sweden 2. University of Oslo, Oslo University Hospital, Norway
15:55 – 16:05	Systemically delivered bactericidal antimicrobial peptides to treat bacterial lung infections	James Mason[1], Mark Sutton[2], Charlotte Hind[2], Chris Lorenz[1], Clive Page[1], Simon Pitchford[1], Richard Amison[1], David Phoenix[3] 1. King's College London, UK 2. Public Health England, UK 3. London South Bank University, UK
16:05 – 16:15	A novel best in class agent for prevention of post-surgical infections - AMPND	Gordon Barker, Amprologix Ltd, UK Ian Fotheringham, Ingenza Ltd, UK Mat Upton, Amprologix Ltd, UK
16:15 – 16:25	Repurposing an antiparasitic as an anti-staphylococcal agent	Sidharth Chopra, Grace Kaul, CSIR-Central Drug Research Institute, Lucknow, India
16:25 – 16:35	Host directed therapy in Tuberculosis	Sandra Peña-Diaz, Celine Rens, Sahile Henok, Tirosh Shapira, Joseph D Chao, Tom Pfeifer, Clement K.M. Tsui, Flavia Sorrentino, Gagandeep Narula, Abraham Lopez, Adama Bojang, Xingji Zheng, Adrian Richter and Yossef Av-Gay, University of British Columbia, Canada
16:35 – 16:55	20-minute Q&A and discussion with speakers as panel	
16:55 – 17:00	Short wrap-up from the Workshop Chair	Marc Lemonnier

Day 3 – Thursday April 22nd

Time (CET)	Session Details	Moderators and Speakers
13:00 – 13:05	Opening remarks from the Chair to welcome everyone back and summarise previous day for newcomers (slides from end of day 2)	Marc Lemonnier
13:05 – 14:15	Session 6 - Novel strategies	Moderator - Kyeong Kyu Kim
13:05 – 13:15	Targeting microbial metabolism to combat the AMR in *Staphylococcus aureus*	Akhilesh K. Chaurasia, Nayab Batool, Kyeong Kyu Kim Sungkyunkwan University School of Medicine, South Korea
13:15 – 13:25	Design, Synthesis and Lead Generation of Novel Siderophore Conjugates for the Detection and Treatment of Infections by Gram-Negative Pathogens - SCAN	Mark Brönstrup, Helmholtz Centre for Infection Research, Germany Isabelle Schalk, CNRS, University of Strasbourg, France Doron Shabat, Tel Aviv University, Israel
13:25 – 13:35	Development of a First-in-Class Antibacterial Drug Using a High-Resolution Computational Model of the Biosynthesis of the Outer Envelope of *E.coli*	Ajay Mistry, John George, Ed Siegwart, Tony Raynham Oppilotech Ltd, UK
13:35 – 13:45	Antibiotic translocation across bacterial membranes and bacterial susceptibility, concepts & methods - Antabs	Jean-Marie Pages[1], Anne Davin[1], Jean-Michel Bolla[1], Muriel Masi[2], Matthieu Refregiers[2], Paolo Ruggerone[3], Mathias Winterhalter[4] 1. INSERM, Aix-Marseille University, France 2. Synchrotron SOLEIL, Gif-sur-Yvette, France 3. University of Cagliari, Italy 4. JUB, Bremen, Germany

Time (CET)	Session Details	Moderators and Speakers
13:45 – 13:55	Developing combinations of CO-ACTIVE antimicrobials and non-antimicrobials – CO-ACTION	Johan Mouton, Joseph Meletiadis, Erasmus University Medical Center, Netherlands Lena Friberg, Thomas Tängdén, Uppsala University, Sweden Françoise Van Bambeke, Université Catholique de Louvain, Belgium William Couet, Université de Poitiers, France Alain Bousquet-Mélou, INRAE, France
13:55 – 14:15	20-minute Q&A and discussion with speakers as panel	
14:15 – 14:25	Break	
14:25 – 15:25	Session 7 - Economic incentives	Moderator - Katherine Payne
14:25 – 14:35	UK antibiotic reimbursement model	Mark Sculpher, Professor of Health Economics, York UK
14:35 – 14:45	Sweden antibiotic reimbursement model	Jenny Hellman, Public Health Agency, Sweden
14:45 – 14:55	Open science for sustainable AMR therapeutics development	Richard Gold, McGill University
14:55 – 15:05	Sustaining a pipeline of new antibiotics; a UK industry perspective	Bryan Deane, Association of the British Pharmaceutical Industry
15:05 – 15:25	20-minute Q&A and discussion with speakers as panel members	
15:25 – 15:35	Break	

Time (CET)	Session Details	Moderators and Speakers
15:35 – 16:40	Session 8 – Antimicrobial Stewardship, Access and Sustainability	Moderator – Patrick Stewart, Director General, Health Canada
15:35 – 16:00	Keynote presentation with questions – Introduction by Pierre Sabourin, Assistant Deputy Minister, Health Canada	Professor Dame Sally Davies
16:00 – 16:40	Panel Discussion with Q&A from workshop participants	Oliver Williams, Wellcome Trust Yann Ferrisse, GARDP Margo Warren, Access to Medicine Foundation Mirfin Mpundu, ReAct Africa
16:40 – 16:55	Scoping the next JPIAMR call	Laura Plant, JPIAMR Emily Brown, UK Medical Research Council
16:55 – 17:00	Workshop wrap-up	Workshop Chair- Marc Lemonnier, Funders - Jess Boname, UK Medical Research Council

Annex 2. Photos and Biographies of Moderators, Panel Members and Presenters

Christine Årdal (Panel Member- Session 2) is Senior Advisor, Institute of Public Health, Norway. She has worked for over 20 years on access to medicines through different sectors, including research institutes, governmental development assistance, pharmacy, national health service and insurance. At the Norwegian Institute of Public Health, her research focuses on the policy aspects of antimicrobial access and innovation. Årdal was a co-lead in the DRIVE-AB research project which aimed to transform the way policymakers stimulate innovation, the sustainable use, and the equitable availability of novel antibiotics to meet unmet public health needs. She is currently the co-lead of the research and innovation work package for the European Union's Joint Action on Antimicrobial Resistance and Healthcare-Associated Infections (EU-JAMRAI), which aims to detail European strategies to implement mechanisms to increase antibiotic and alternative therapeutic innovation. Previously she was a member of the World Health Organization expert review panel for the overall programme review of the Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property. She led the Norwegian Agency for Development Cooperation's (Norad) efforts within the UN Commission on Life-Saving Commodities for Women and Children.

Yossef Av-gay (Invited Speaker – Session 5) is a professor of microbiology and immunology at the university of British Columbia. Prof. Av-Gay research focuses on chronic microbial lung diseases, primarily tuberculosis (TB), followed by nontuberculous mycobacteria (NTM) diseases. He explores molecular events that govern host-pathogen interactions and the ability of mycobacteria to block the immune response to infection. Dr. Av-Gay's research is geared towards the identification and characterization of novel drugs and drug targets in Mycobacterium tuberculosis and intracellular high-throughput screening (HTS) and high content microscopy screening (HCS) assays detecting Mtb growth in human macrophages. Prof. Av-Gay research was translated into a clinical drug development program through establishment of Start-up companies. One of them, Beyond Air, listed at the NASDAQ stock exchange, pioneers the development of novel treatments for bronchiolitis, viral infections and NTM's in cystic fibrosis patients.

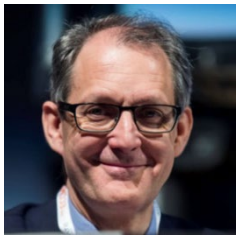
Jessica Boname (Moderator- Session 2) is Head of Programme for AMR at MRC-UK. She is leading a portfolio of strategic research and support activities to both reduce our reliance on antibiotics and develop novel antimicrobial therapies. These activities are based on partnerships with other Research Councils within UKRI, and wider partnerships within the UK and globally, coordinated through the UK AMR Funders Forum and the Joint Programming Initiative on AMR (JPIAMR). Jess is a Management Board member within the JPIAMR and led the organisation and delivery of this AMR Therapeutics Workshop. She is a virologist by training, working at Universities around the world including Stanford, McMaster, Oregon Health Sciences

University and the University of Cambridge, helping to elucidate the often complex pathways exploited by viruses to evade the immune system.

Helena Boshoff (Invited Speaker – Session 3) acquired her PhD at the University of the Witwatersrand, South Africa and completed her postdoctoral studies at the National Institutes of Health in the United States. She moved on to a staff scientist position later becoming an associate scientist at the National Institutes of Health in the Tuberculosis Research Section. She has published on DNA repair, cellular metabolism as well as drug discovery against Mycobacterium tuberculosis. Her current projects include formal hit assessment of inhibitors identified by high-throughput screening against whole Mycobacterium tuberculosis under in vivo relevant conditions, unravelling the mechanism of action of hits of interest as well as the mechanisms by which the pathogen adapts to the xenobiotic stress.

Mark Brönstrup (Invited Speaker – Session 6) studied Chemistry at the Philipps-Universität Marburg and at the Imperial College in London. In 1999 he received his doctorate from the Technical University Berlin in Organic Chemistry. After his graduation, he worked from 2000 to 2013 for Aventis, Sanofi-Aventis and Sanofi, complemented by a research sabbatical in 2003 at Harvard Medical School. He led the Natural Product Sciences with the goal of discovering leads from natural sources and optimising them to clinical candidates, and he dealt with translational research projects as a domain head for Biomarkers, Bioimaging & Biological Assays. Since December 2013, he heads the department Chemical Biology at the Helmholtz Centre for Infection Research. Additionally, he holds a Professorship (W3) at the Leibniz Universität Hannover. His research is focused on the discovery and the characterization of novel antibacterial and antiviral drugs. This also includes the establishment of novel analytical and diagnostic methods.

Rafael Cantón, PhD (Moderator- Session 1) is the Head of the Clinical Microbiology Department at the University Hospital Ramón y Cajal (Madrid, Spain) and is associated Professor of Clinical Microbiology at School of Pharmacy at Complutense University (Madrid, Spain). His research activity is developed within the Spanish Network for Research in Infectious Diseases and Institute Ramón y Cajal for Health Research and is focussed on antimicrobial susceptibility testing and surveillance, characterization of antimicrobial resistance mechanisms and interplay with high-risk clones, and respiratory tract infections. He is currently Clinical Data Coordinator and past Chairman of the European Committee for Antimicrobial Susceptibility Testing (EUCAST), a member of the Spanish Antimicrobial Committee (COESANT), Past President of Spanish Society of Infectious Diseases and Clinical Microbiology (SEIMC), Associate Editor of Clinical Microbiology and Infection and member of the editorial board of Journal of Clinical Microbiology. He is co-editor of the Clinical Microbiology Procedures of the SEIMC (www.seimc.org) and a member of the Scientific Advisory Board of JPIAMR.



Marco Cavaleri (Panel Member- Session 2) is Head of Office, Biological Health Threats and vaccines strategy at the European Medicine Agency (EMA). He is the Chair of EMA COVID Task force and responsible for EMA activities for emergent pathogens, vaccines and AMR. Marco Cavaleri is a Pharmacologist who spent several years in industry in R&D mainly in the area of anti-infectives covering different positions in preclinical and clinical development. In 2005 he joined the EMEA as Scientific Administrator in the Scientific Advice and Orphan Drugs Sector, specifically being in charge of anti- infectives and vaccines scientific advice procedures. In 2009 he was appointed as Head of Section for Anti-infectives and vaccines in the Safety & Efficacy Sector, Human Medicines Development and Evaluation Unit.

Akhilesh K. Chaurasia (Invited Speaker – Session 6) carried out his Ph.D. work at Bhabha Atomic Research Centre, Mumbai and obtained Ph.D. degree in Microbiology from University of Mumbai, India. After finishing Ph.D., Dr. Chaurasia worked as a postdoctoral fellow at Department of Microbiology, University of Massachusetts (UMASS). At UMASS, he used functional genomics and synthetic biology approach to carry out various basic and applied research projects. Currently, Dr. Chaurasia works at School of Medicine, Sungkyunkwan University (SKKU) and affiliated with Institute of Antimicrobial Resistance Research and Therapeutics (IAMRT). His current area of research is to study host-pathogen interaction, mechanism of bacterial pathogenesis and diseases progression, various strategies to inhibit drug resistance and pathogenesis using novel target and its interacting drug partner. We apply omics and forward and reverse - chemical genetics to identify novel drug targets and their interacting drug partners for highly virulent and antimicrobial resistant (AMR) bacterial pathogens i.e. Vibrio vulnificus, uropathogenic Escherichia coli (UPEC) and various community and hospital associated Staphylococcus aureus strains.

Professor Dame Sally Davies (Keynote Presenter – Session 8) is UK Special Envoy on Antimicrobial Resistance. Before this, she was Chief Medical Officer (CMO) for England and Chief Medical Adviser to the UK government from March 2011 to September 2019, having held the post on an interim basis since June 2010. Dame Sally advocates globally on AMR. She has spoken on AMR at numerous events including the World Health Assembly side events, the G8 science ministers' meeting in 2015, the Global Health Security Initiative in 2015, and the UN General Assembly side event in 2016. She was chair of the 2013 AMR forum at the World Innovation Summit for Health (WISH) and was for three years the chair of the WHO Strategic and Technical Advisory Group on AMR. Most recently, Dame Sally has been appointed a co-convener of the UN Inter-Agency Co-ordination Group on AMR, set up in response to the AMR declaration made at UNGA 2016.

Bryan Deane (Invited Speaker – Session 7) is the New Medicines & Data Policy Director

of the Association of the British Pharmaceutical Industry (ABPI). Bryan has a degree in Pharmacology and a PhD in Neuropathology, and over twenty- five years' experience in the pharmaceutical industry. This covered development and launch of new medicines in a variety of therapy areas including infectious diseases, and a wide range of countries and regions. Bryan joined the ABPI's Research, Medical & Innovation Team in May 2018, covering all aspects of New Medicines discovery, development, and manufacturing including a focus on AMR, vaccines, advanced therapies, and harnessing health data.

Rosemary Dorrington PhD (Invited Speaker – Session 2a) holds the DST/NRF SARChI

Chair in Marine natural Products Research at Rhodes University, Makhanda, South Africa. Prof Dorrington is the South African Principal Investigator of the SA/UK Antimicrobial Drug Discovery Hub funded by the South African Department of Health and the UK Newton Fund through the South African and UK Medical Research Councils. She leads a multidisciplinary team engaged in research across the broad field of marine biodiscovery focusing on the potential of bioactive small molecules as molecular probes for drug development.

Erin Duffy (Panel Member- Session 1) is the Chief of Research & Development at CARB-

X. CARB-X is a global non-profit partnership dedicated to accelerating antibacterial research to tackle the global rising threat of drug-resistant bacteria. With up to US$480 million to invest in 2016-21, CARB-X funds the world's largest early development pipeline of new antibiotics, vaccines, rapid diagnostics, and other products to prevent, diagnose and treat life-threatening bacterial infections. Prior to CARB-X, she worked at Melinta Therapeutics (fka Rib-XPharmaceuticals) where she became EVP, Chief Scientific Officer.

Yann Ferrisse (Invited Speaker –Session 8) is Head of Business Development at GARDP.

Yann joined GARDP in January 2018 to lead all business development activities, from scouting of opportunities to defining market access strategies for the GARDP portfolio. His main mission now is to define, in collaboration with other partners, how to expand and accelerate access to essential antibiotics to prepare countries for the silent pandemic of drug-resistant bacterial infections. The aim is to bridge the gap between late (or final) product development and established adoption. Prior to joining GARDP, Yann was Partner at Alcimed - an innovation and new business consulting firm - and Managing Director of the Singapore regional office. At Alcimed, Yann was instrumental in setting up country offices throughout Europe as well as in Asia. There, Yann built a network of industry contacts, established strong partnerships with life sciences companies, and assessed several market opportunities.

Richard Gold (Invited Speaker – Session 7) is a James McGill Professor at McGill University's Faculty of Law and Faculty of Medicine. Teaching in the area of intellectual property and innovation, he currently serves as the Director of the Centre for Intellectual Property Policy. His research centers on models of innovation and novel intellectual property strategies, particularly those relying on open science. Prof. Gold has been an expert for the Royal Society of Canada, the Council of Canadian Academies, Health Canada, Industry Canada, the Canadian Biotechnology Advisory Committee, the Ontario Ministry of Health and Long-Term Care, the Organisation for Economic Cooperation and Development (where he was the lead author of the OECD Guidelines on the Licensing of Genetic Inventions and a report on Collaborative Mechanisms in Life Science Intellectual Property), the World Health Organization, the World Intellectual Property Organization and UNITAID.

Richard Gordon (Moderator- Session 5) was the Executive Director of the Grants, Innovation and Product Development groups at the South African Medical Research Council (SAMRC) until the end of 2020. During this time, his team managed more than 200 grants ranging from small independent research awards to major international programs seeking to develop new drugs vaccines and medical devices. It is the largest African based funder of Research. The majority of the SAMRC programs focus on HIV, Tuberculosis and Malaria – including drug resistance. Collaboration partners include: GARD-P, the WHO, the Bill and Melinda Gates Foundation, The UK Newton Fund and several others. Dr Gordon has held a number of international positions and specializes in establishing international research partnerships. These range from drug discovery (target discovery, high throughput screening, medicinal chemistry, ADMET and pharmacology for a wide range of therapeutic areas), medical devices and vaccines.

Jenny Hellman (Invited Speaker – Session 7) has a Master of Science of Pharmacy and works as an Analyst at the Public Health Agency of Sweden. She has been working at the national level within the antibiotic resistance and antibiotic use area since 2009. She started her career at the national STRAMA office, with focuses on rational use of antibiotic and antibiotic stewardship programs. Since 2014 she has been the project leader for the Public Health Agency's work regarding availability of antibiotics at the Swedish market. She is now the project leader of the Swedish pilot study of a new reimbursement model to ensure the availability of antibiotics in Sweden.

Peter Jackson (Invited Speaker – Session 2a) is an experienced UK-based serial entrepreneur in the life sciences sector. Over the past ten years, he has created six new companies, targeting novel therapeutics across infection, oncology and immunology, as well as in agrochemicals and life sciences services. Dr Jackson has over 25 years' experience in the sector, previously holding senior executive roles as commercial director then VP of Avecia's Pharmaceutical Products business unit, following senior commercial and R&D positions at predecessor companies Zeneca and

ICI. During 2015-16, Dr Jackson was chairman of the steering committee created to establish the UK's translational R&D centre focused on antimicrobial resistance, the AMR Centre, and now runs Infex Therapeutics as its executive director.

Timothy Jinks PhD (Panel Member- Session 1) is the Head of Wellcome Trust's Drug Resistant Infections Priority Program, leading Wellcome's efforts directed at reducing the threat of antimicrobial resistance. In his preceding role he led development of Wellcome's strategic plan to address drug resistant infections. Previously in Wellcome's Innovations Division, he was responsible for a portfolio of over a dozen early-stage product development projects covering therapeutics, diagnostics and devices spanning across therapeutic areas such as infectious diseases and oncology. He is a member of the CARB-X Joint Oversight Committee, the Longitude Prize Committee and is Non-Executive Director of Reviral Ltd. Prior to joining the Trust in 2012 he has over a decade of industry experience, most recently as a consultant providing business development, licensing and commercial research services. His scientific background is as a chemist turned molecular biologist having studied at University of Georgia and Princeton University, with academic research experience at Harvard Medical School, Dana Farber Cancer Institute and the MRC National Institute for Medical Research.

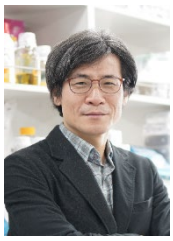
Grace Kaul (Invited Speaker –Session 5) obtained her B.Sc. degree from Dr Ram Manohar Lohia Avadh University, Ayodhya in 2013. In 2015, she obtained her M.Sc. degree in Biotechnology from Dr Ram Manohar Lohia Avadh University, Faizabad. She is the recipient of national DST-INSPIRE fellowship awarded to top scorers of their respective M.Sc. programs and currently working as a Senior Research Fellow in the Division of Microbiology, Central Drug Research Institute, Lucknow with Dr Sidharth Chopra. She is following a rational drug design approach to screening for preclinical evaluation of potent compounds with antimicrobial activity against multi-drug resistant bacterial infections.

Professor Anil Koul (Invited Speaker – Session 3) is Professor of Translational Discovery at London School of Hygiene and Medicine (LSHTM) UK. Anil also serves as VP, discovery research at Global Public Health unit of Janssen pharmaceuticals (J&J) leading a multidisciplinary team of scientists. He served till recently as Director of CSIR-Institute of Microbial Technology, one of India's premier biomedical laboratory. Anil has more than 20 years of experience in drug discovery and has been a key member in discovery of Bedaquiline – a novel drug for treatment of multidrug-resistant tuberculosis. Anil received his Ph.D. from the Max Planck Institute for Biochemistry, Germany and IGIB, Delhi University. Anil has several publications in leading journal and holds more than 20 patents to his credit. In 2020, he was awarded by American Chemical Society for discovery of Bedaquiline. He currently serves on Scientific Advisory Board of Council of Scientific and Industrial Research (CSIR), Government of India.

Morten Kjos (Invited Speaker –Session 4) is the coordinator of the JPIAMR project

"DISRUPT – Fighting antimicrobial resistant infections by high-throughput discovery of biofilm- disrupting agents and mechanisms. Morten is also an Associate Professor in microbiology at the Norwegian University of Life Sciences, Norway. In my research team, we are interested in understanding molecular mechanisms important for antibiotic resistance and development of new antibacterial strategies towards Staphylococcus aureus and other Gram-positive pathogens. In particular, we are interested in mechanisms that are essential for biofilm formation and cell division, as well as in developing novel genetic tools.

Kyeong Kyu Kim (Moderator- Session 6) obtained his Ph.D. (1994) in Chemistry from



Seoul National University, Korea and received postdoctoral training at the University of California, Berkeley, USA. He started his independent research as an assistant professor in 1998 at Gyeongsang National University, Jinju, Korea. He soon moved to Sungkyunkwan University School of Medicine, Korea in 2000, and became a full professor in 2008. He served as the president of the Korean Biophysical Society (2015-2017) and also worked as the chairman of the Biological Chemistry division of the Korean Chemical Society (KCS) from 2017 to 2018. He has been working on the structural and functional studies of key biological macromolecules, such as bacterial two component systems and their modulation. Currently, his main research interest is in developing new antimicrobial therapeutics to overcome the issue of drug resistance. He currently is the director of the Institute of Antimicrobial Resistance Research and Therapeutics (IAMRT) at Sungkyunkwan University, and also is one of the management board members in JPIAMR, representing the Republic of Korea.

Jessica Lee (Invited Speaker – Session 2a) is a Senior Programme Manager in the

Syndicates team at Medicines Discovery Catapult; an independent not-for-profit organisation funded by Innovate UK, which is enabling the community to reshape medicines discovery in the UK. Syndicates test a new model for delivering patient- focused drug discovery, working closely with medical research charities. Jess has extensive experience in the development of collaborative research consortia, bringing together expertise from different sectors to shape research agendas and drive focussed research efforts to address unmet needs. The Cystic Fibrosis (CF) Syndicate in Antimicrobial Resistance is a key example of this, where a critical mass of expertise in CF and pulmonary infection has been convened to accelerate the translation of antimicrobials to the clinic, to bring new treatments to people with CF, faster.

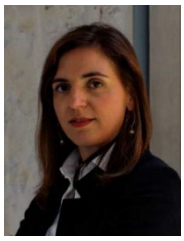
Marc Lemonnier (Workshop Chair) is the founding CEO of Antabio, a private European

biopharmaceutical company developing novel antibacterials targeting drug-resistant infections caused by WHO's critical priority pathogens. He is a molecular and cellular microbiologist with over 25 years' experience in academia and biotech. Prior to founding Antabio, Marc held different research positions at various institutions globally such as CNRS and Inserm (France), CSIC (Spain) and Emory University (USA),

authoring over 25 peer-reviewed articles and patents in the field of bacterial pathogenesis and antibiotic resistance. Under Marc's leadership, Antabio has raised double-digit million funding and received numerous awards including a CARB-X award (2017) and two Seeding Drug Discovery Awards from the Wellcome Trust (2013 and 2015). Marc is also a member of the Board of the BEAM Alliance (European Alliance of Biopharmaceutical companies combating Anti-Microbial resistance), and a member of the Scientific Advisory Board of JPIAMR.

Cara Leopore (Invited Speaker – Session 2a) is a Senior Associate at the Pew Charitable Trusts in Washington, DC. She works on the Antibiotic Resistance Project, focusing on research and public policy to support the innovation of urgently needed new antibiotics, and leads Pew's antibiotic pipeline assessments. Prior to joining Pew, Lepore worked in federal vaccine development at the U.S. Food and Drug Administration and Walter Reed Army Institute of Research. She holds a Master of Science in biotechnology from Johns Hopkins University.

Laura Marin (Panel Member- Session 1) heads the Secretariat of the Joint Programming Initiative on Antimicrobial Resistance hosted by the Swedish Research Council. Previously she was responsible for Science Policy and Member Relations at the European Science Foundation. Earlier on she was also team leader of the European Science Open Forum in 2008 in Barcelona (ESOF2008) and Director of Operations at the Catalan Foundation for Research and Innovation. She has several years of experience in Brussels and Germany managing research and innovation projects and facilitating numerous fora on science policy and governance issues. She holds a MSc on Political Science by the Universitat Autonoma de Barcelona and a M.Litt in Management, Economics and International Relations by St. Andrews University.



Alessandra Martini (Panel Member- Session 1) works at the European Commission as policy officer in the Unit Combatting Diseases for the People Directorate within the DG for Research and Innovation. She has been involved in designing research policies and has been responsible for portfolio management on infectious diseases, mainly for HIV/AIDS, vaccines development and vaccine hesitancy. During the past year she has taken over policies on AMR in response to the European One Health AMR actions. She has been at the European Commission since 2005, initially working on eHealth. Prior to joining the European Commission, she worked for the US medical technology company BD - Becton Dickinson. Alessandra studied Biomedical Sciences and holds a PhD in Molecular Genetics.

James Mason (Invited Speaker – Session 5) is Head of the Drug Discovery Group (18 Pis)

at King's College London. His research focus combines biophysical methods with systems biology approaches (NMR metabolomics coupled with next generation sequencing) to understand how events at biological membranes influence biological outcomes. This is applied to understanding how antibiotics function, how bacteria respond to these and other environmental challenges and the functional consequences of alterations in lung, gut or vaginal microbiomes. Having completed his D.Phil at Oxford University in late 2001, Dr Mason spent six years abroad, in Germany and then France, before returning to the UK. Ajay Mistry (Invited Speaker – Session 6) is the co-founder of Oppilotech Ltd – a drug-discovery company using system biology and ML to model cellular processes in order to identify drug targets. Ajay completed his PhD in Gene Therapy at Imperial College. He then undertook a postdoctoral research fellowship at Institute of Ophthalmology/Moorfields Eye Hospital and Institute of Child Health/Great Ormond Street Children's Hospital where he was part of the team that developed gene therapy treatments for various forms of blindness and also worked on hematopoietic stem cell gene therapies. Ajay went onto work in the life sciences Venture Capital industry. He then worked in business development roles for biotechnology companies where he has executed multiple deals with Pharmaceutical and Biotechnology companies before founding Oppilotech.

Joseph Meletiadis (Invited Speaker –Session 6) is Assistant Professor of Microbiology in

Medical School of National and Kapodistrian University of Athens, Greece, Head of the Mycology Unit of the Clinical Microbiology Laboratory at Attikon University General Hospital, Athens, Greece and Visiting Scientist at the Department of Medical Microbiology and Infectious Diseases, Erasmus Medical Center, Rotterdam, The Netherlands. He is a member of the EUCAST steering committee as PK/PD expert and as the Clinical Data Coordinator in the EUCAST steering subcommittee for antifungal drugs. He is editor of the Journal of Antimicrobial Chemotherapy and editorial board member of the journals Antimicrobial Agents and Chemotherapy and Infectious Diseases and Therapy. His main interests are in vitro antimicrobial susceptibility testing, preclinical models of bacterial and fungal infections, pharmacokinetics and pharmacodynamics of antimicrobial drugs and combination therapy.

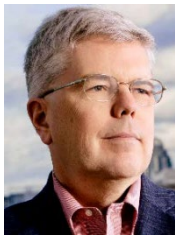
Stefano Messori (Panel Member- Session 1) works at the World Organisation for Animal

Health (OIE), where he is in charge of activities related to research coordination and collaboration. In this framework, he serves for the Scientific Secretariat for the STAR-IDAZ IRC, a major international collaboration initiative that aims to increase research coordination on animal health at global level. In this framework, he runs an international group of experts aiming to identify research gaps and deliver research roadmaps for the development of alternatives to antibiotics for animal use. A veterinarian by training, he holds a PhD in animal science, and have participated in several global initiatives aiming to better coordinate and enhance research and

development on antimicrobial resistance (AMR) across the One Health spectrum, including the Interagency Coordination Group on Antimicrobial Resistance (IACG) and the Global AMR R&D Hub. Twitter handle: @StarIdaz; @OIEAnimalHealth

Ajay Mistry (Invited Speaker –Session 6) is the co-founder of Oppilotech Ltd – a drug-discovery company using system biology and ML to model cellular processes in order to identify drug targets. Ajay completed his PhD in Gene Therapy at Imperial College. He then undertook a postdoctoral research fellowship at Institute of Ophthalmology/Moorfields Eye Hospital and Institute of Child Health/Great Ormond Street Children's Hospital where he was part of the team that developed gene therapy treatments for various forms of blindness and also worked on hematopoietic stem cell gene therapies. Ajay went onto work in the life sciences Venture Capital industry. He then worked in business development roles for biotechnology companies where he has executed multiple deals with Pharmaceutical and Biotechnology companies before founding Oppilotech.

Mirfin Mpundu (Moderator - Session 3 and Invited Speaker- Session 8) is the Director of ReAct Africa and the Partnership & Engagement Lead for the International Centre for Antimicrobial Resistance Solutions (ICARS). He provides countries with technical assistance on AMR National Action Plans development, prioritization and implementation and works closely with the Tripartite plus (WHO, OIE, FAO & UNEP) and Regional Economic Communities (RECs) such as the Southern African Development Community (SADC) on regional AMR strategies and policies. His expertise of over 30 years includes pharmaceutical supply chain management, pooled procurement, infectious diseases and antimicrobial resistance (AMR), global health security, One Health, international health policy and diplomacy. He sits on several boards including Wellcome Trust's- Surveillance and Epidemiology of Drug-Resistant Infections Consortium (SEDRIC), he is a Co-chair of the External Advisory Board of the Newton AMR Drug Discovery Programme and an honorary fellow at the University of KwaZulu Natal in South Africa among others.



Kevin Outterson (Panel Member- Session 2) teaches health care law at Boston University, where he co-directs the Health Law Program. He serves as the founding Executive Director and Principal Investigator for CARB-X, a $480M international public- private partnership to accelerate global antibacterial innovation. Key partners in CARB-X include the US Government (BARDA & NIAID), the Wellcome Trust, the German Federal Ministry of Education and Research (BMBF), the UK Government (GAMRIF), and the Bill & Melinda Gates Foundation. Professor Outterson's research work focuses on the law and economics of antimicrobial resistance (available at Google Scholar). He served as a senior author on many key research reports on antibiotic innovation, including Chatham House, ERG, DRIVE-AB, and the Lancet Commission. Professor Outterson was given the 2015 Leadership Award by the Alliance for the Prudent Use of Antibiotics for his research and advocacy work. He has testified before Congress, Parliamentary working groups, WHO, and state legislatures. Since

August 2016, he leads CARB-X, the world's largest and most innovative antibiotic accelerator.

Vipul Panchal (Invited Speaker – Session 4) Vipul studied the pathogenesis of Mycobacterium tuberculosis, the causative agent of tuberculosis, between 2012 and 2018 at the Institute of Genomics and Integrative Biology, India, and received a PhD degree in 2018. He then joined Brenk lab in 2019 at the University of Bergen, Norway to explore novel targets as antibacterial agents. With Prof. Ruth Brenk, he is currently exploring the therapeutic potential of riboswitch element(s) as an antibacterial target by developing the riboswitch specific high throughput and virtual screening techniques together with conventional structure biology approach. They aim to develop lead like antibacterial compounds.

Jean-Marie Pages (Invited Speaker – Session 6) is Emeritus Research Director INSERM (Institut National de la Santé et de la Recherche Médicale) is member of the research Unit "Membranes and Therapeutic targets", Pharmacy Faculty Aix-Marseille University, Marseille France. He previously chaired, 2008-2017, the UMR-MD1 "membrane Transporters, Chemoresistance and Drug Design" (Aix-Marseille Univ- Health Dept French Army). He studies the bacterial envelope permeability, from genetic regulation, biological activities to clinical aspects including the role of outer membrane porins and drug efflux pumps in bacterial adaptation. Recently, with IMI-Translocation he developed new methods to dissect the drug translocation across membranes of gram-negative bacteria and proposed new concepts to understand the molecular bases of antibiotic resistance. He has published over 300 papers, patents and abstracts in various international journals (EMBO J., Clin Microbiol Rev, Nat Microbiol, Nat Rev Microbiol, PNAS, etc) and has presented several talks during top International meetings (GRC, Nature Conferences, Microbes, ECCMID, etc.).

Katherine Payne (Moderator – Session 7) is an academic health economist with 26-years applied and methodological research experience in the economic evaluation (using RCT and decision-analytic models) and valuation (using discrete choice experiments and contingent valuation) of health care interventions and specifically precision medicine. She has over 135 peer-reviewed publications and had a key role in multi- disciplinary research programmes and projects that, in the last three years, generated a total of over £15.5m for The University of Manchester. She has a particular interest in the use of economic evidence to inform decision- making in practice and was a member of a NICE Technology Appraisal Committee between October 2003 and 2012. She is a member of a NIHR PGFAR review panel and has been a member of numerous national funding review panels appraising projects on the economics of precision medicine (Canada, UK, The Netherlands, France, Switzerland, Singapore, Luxembourg). (ORCID: 0000-0002-3938-4350)

Camilla Petrycer Hansen (Panel Member- Session 2) joined Novo Seeds in June of 2018.

Camilla brings 10 years of business development experience from early academic start-up to industry. Most recently, Camilla was responsible for scouting and building new growth platforms for Novozymes A/S. Prior to that, Camilla held a business development position at Statens Serum Institute (SSI) where she was commercializing preclinical and clinical life science products and projects, in addition to being instrumental in divesting the Vaccine Production business from SSI. From 2009 to 2012 she worked in technology transfer at Wake Forest University Health Sciences in the US where she was involved in out licensing and commercializing early and mid-stage assets, including company creation. Camilla has a PhD in Medicinal Chemistry and a Master of Pharmacy degree from Copenhagen University.

Laura Plant (Invited Speaker- Session 8) has a PhD in Microbiology from the University

of New South Wales in Australia. She has a research background in the field of bacterial pathogenesis and immunity from the Nestlé Research Centre, University of Melbourne, and Karolinska Institute. Since 2013, Laura has worked in research administration with specialisation in research funding as a Grants Specialist at Karolinska Institute and as a Senior Research Officer at the secretariat of the Joint Programming Initiative on Antimicrobial Resistance at the Swedish Research Council. Laura is engaged in management of projects funded by the European Commission, is a national Programme Committee Expert for Widening and ERA in the Horizon Europe framework programme and is the Swedish delegate in the Global AMR R&D Hub.

Laura Piddock (Panel Member- Session 2) is the Scientific Director of the Global

Antibiotic Research & Development Partnership (GARDP). Laura is also Professor of Microbiology at the University of Birmingham, UK. researching clinically relevant mechanisms and using this information as a basis for drug discovery. Prof. Piddock has published over 200 original research articles in international peer reviewed journals and given over 200 presentations at international conferences. In 2001, Prof. Piddock was made a Fellow of the American Academy of Microbiology. In 2017, she was appointed as a founding Fellow of the European Society of Clinical Microbiology and Infectious Diseases. Until 30 September 2017, Prof. Piddock was the British Society for Antimicrobial Chemotherapy Chair in Public Engagement, and she was the Chair of the EU Joint Programming Initiative on Antimicrobial Resistance Scientific Advisory Committee until December 2018.

John H. Rex, MD, FACP (Moderator and Keynote Speaker- Session 2) is a physician and

drug developer with more than 30 years of development and policy experience focused on antimicrobial agents. He is currently CMO for F2G, Ltd. (an antifungal biotech), is an operating partner with a venture capital group (Advent Life Sciences) and was a voting member on the US Presidential Advisory Council on Combating Antibiotic Resistant Bacteria (PACCARB). He also blogs regularly at http://amr.solutions/blog.html. His experience includes moving

compounds from early preclinical development through all development phases via academic positions (NIH, Bethesda, MD; Univ. of Texas Medical School-Houston) and VP-level roles at a multinational pharmaceutical firm (AstraZeneca). Other past activities include advancing novel regulatory paradigms for antibacterial agents, publications on novel reimbursement models for antibiotics, co-founding of a public-private partnership (CARB-X), co-founding of the New Drugs for Bad Bugs (ND4BB) program of Europe's Innovative Medicines Initiative (IMI), and a 4-year term as Industry Representative on the FDA Anti-Infective Drugs Advisory Committee (AIDAC, 2007–2011). Twitter: JohnRex_NewAbx Website: https://amr.solutions/

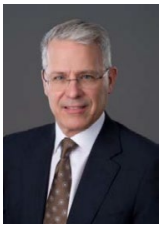
Modesto Jesus Remuiñán-Blanco (Invited Speaker – Session 3) received his Ph.D. in

organic chemistry in 1997 from Universidad de Alcala (Madrid). In that year, he moved to UK for postdoctoral research at Nottingham University. In 2001, he began his professional career as a Medicinal chemist at pharmaceutical industry (Pharmamar, Ely Lilly and GSK). In 2005 he joined GSK as Project Leader of both lead generation and lead optimization programs in Tuberculosis. Dr Remuiñán has authored more than 20 research publications and 15 international patents in tuberculosis.

Tahira Riaz (Invited Speaker – Session 5) is a postdoctoral research fellow in

tuberculosis (TB) drug discovery at the University of Oslo, Norway. Her PhD in immunology and microbiology with emphasis on proteomics studies aimed to understand cellular functions in infection biology. Riaz has a unique background with a combination of theoretical studies, biostatistics and practical experience in molecular biology experimentation with emphasis on mass spectrometry (MS)-based proteomics. She employs a broad spectrum of molecular biology and bioinformatics tools in a multidisciplinary setting. Thereby, she merges different fields of bioscience into a broad unifying approach to understand macromolecular dynamics in infection biology. With a strong background in advanced MS-based molecular medicine and clinically relevant TB and other infectious diseases, her research spans from basic science to clinical medicine in a translational manner.

Pierre Sabourin (Invited Introducer – Session 8) was appointed Assistant Deputy



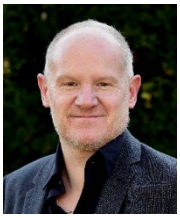
Minister of the Health Products and Food Branch at Health Canada in October 2016. As the regulatory authority for health products and food, Health Canada evaluates and monitors the safety, quality and efficacy of human and animal health products including drugs, medical devices, biologic and genetic therapies, and natural health products; develops and implements nutrition and food policies and standards; helps Canadians make informed decisions about their well-being; and anticipates and responds to public health issues associated with human and animal health products, food and nutrition. Mr. Sabourin was previously the Senior Vice-President, Corporate Services at Canada Mortgage and Housing Corporation, and has served in senior roles at the Canada Border Services Agency and the former Department of Foreign Affairs and International Trade, as well as being a part-time professor with 15 years of experience at the University of Ottawa's Telfer School of Management.

Javier Sancho (Invited Speaker – Session 4) is a protein scientist working on protein folding, target- oriented drug discovery and development, and biocomputation. He pioneered the application in Spain of HTP screening methods for the identification of small molecules targeting proteins. Among the hits found in his laboratory, there are aggregation inhibitors for Parkinson Disease, pharmacological chaperones for Phenylketonuria and antimicrobials for Helicobacter pylori infection. These antimicrobials target flavodoxin, an essential Hp protein not present in humans. Some of them, uncombined, have been able to eradicated Hp from up to 50% infected mice upon a very naïve and perfectible administration protocol. These flavodoxin inhibitors, which are being developed within the FLAV4AMR project, may provide new, effective and more microbiota-friendly alternatives to current triple/quadruple therapies for Hp eradication (particularly of CLA-resistant Hp strains) whose efficacy keeps declining.

Hatim Sati (Panel Member- Session 1) is a member of the International Research Coordination (IRC) Team at the Department of Global Coordination on Antimicrobial Resistance (AMR) within the WHO AMR Division. Since joining the WHO Headquarters, he has worked primarily on antimicrobial R&D priority setting, including the annual analysis of the clinical and preclinical antibacterial pipelines. Hatim is a medical doctor with training in primary care and public health. Prior to joining WHO Headquarters, he worked at the AMR Special Program in the WHO Regional Office of the Americas (PAHO/WHO) supporting countries in developing and implementing their multi-sectoral national action plans on AMR. Hatim's experience includes healthcare provision as a primary care physician, healthcare policy in the Ministry of Health of Sudan, and healthcare administration with Johns Hopkins Medical International in the United States.

Rada Savic (Invited Speaker – Session 3) is the Associate Director of the UCSF Center for TB and a Professor in the Department of Bioengineering and Therapeutic Sciences and the Division of Pulmonary and Critical Care Medicine in the Schools of Pharmacy and Medicine at the University of California San Francisco. Her research focuses on applications of Pharmacokinetic/Biomarker/Pharmacodynamic and Pharmacogenetic modeling to problems in drug development and routine drug therapy in infectious diseases including special populations such as children and pregnant women. Dr Savic is recognized as a world leader on tuberculosis drug regimen and dosing pharmacokinetics and was named the 2021 LeonI. Goldberg Early Investigator Award recipient, which recognizes and honors young scientists for outstanding accomplishments in the field of clinical pharmacology achieved early in their career.

Mark Sculpher (Invited Speaker – Session 7) is Professor of Health Economics at the Centre for Health Economics, University of York, UK where he leads the Centre's Programme on Economic Evaluation and Health Technology Assessment. He is also Co- Director of the Policy Research Unit in Economic Evaluation of Health and Care Interventions, a programme of research for the UK Department of Health and Social Care funded by the National Institute for Health Research (NIHR). He has over 270 peer-reviewed publications and is a co-author of two major textbooks in the area: Methods for the Economic Evaluation of Health Care Programmes (OUP, 2015 with Drummond, Claxton, Torrance and Stoddart) and Decision Modelling for Health Economic Evaluation (OUP, 2006 with Briggs and Claxton). Mark is an emeritus member of the UK NIHR College of Senior Investigators. He has also been a member of the National Institute for Health and Care Excellence (NICE) Technology Appraisal Committee, the NICE Public Health Interventions Advisory Committee and NICE's Diagnostics Advisory Committee. He has also been involved in advising NICE on methods over many years. Mark has also advised the UK House of Commons Health and Social Care Select Committee, as well as health systems internationally on health technology assessment methods including those in France, Ireland, Japan, Singapore, Germany, Portugal, Taiwan and New Zealand. He is currently undertaking research for the National Institute of Health and Care Excellence (NICE) and NHS England on a novel value assessment approach for new antimicrobials as part of the UK government's new funding arrangements for such products.



Florence Séjourné (Panel Member- Session 1) is the Chief Executive Officer of Da Volterra, a late- stage French biopharmaceutical company developing innovative products to protect patients with cancer from consequences of intestinal microbiome dysbiosis induced by antibiotics. The company's lead product-candidate, DAV132, is entering a Phase 3 clinical trial in patients with hematological malignancies to demonstrate multiple benefits of microbiome protection, including prevention of severe infections and dissemination of resistance to antibiotics. In addition to her activities at Da Volterra, Florence has been the founder and President of the BEAM Alliance from 2016, which represents 70 European biotech companies involved in developing innovative products to tackle AMR, in order to speak with one voice in front of stakeholders in charge of policy changes required to support AMR innovation. Prior to joining Da Volterra in 2008, Florence co-founded another French biotech GENFIT (GNFT), and holds degrees from Mines Paritech and from the University of Illinois, Chicago.

Vinayak Singh (Invited Speaker – Session 3) a molecular mycobacteriologist focussing on tuberculosis (TB) drug-discovery, leads a TB biology team at the Drug Discovery and Development Centre (H3D), University of Cape Town (UCT), South Africa. His research focuses on screening diverse compound libraries, deconvoluting the mechanism of action of potential lead compounds, and mycobacterial metabolism - to fulfil a broad and acute interest in the discovery of new innovative drugs. Vinayak's exceptional skills as a microbiologist with high-level expertise in antimicrobial drug discovery and development began from his experience at the CSIR-Central Drug Research Institute in

Lucknow, India, where he completed a Ph.D. degree in Biochemistry (2010). Next, he joined the UCT where he completed a very successful postdoctoral fellowship (2011-2016) with Prof. Valerie Mizrahi. He has identified and validated >10 novel TB drug targets which have attracted significant interest in the global TB research community.

Jean-Claude Sirard (Invited Speaker – Session 4) studied pathogenesis of Bacillus anthracis, the causative agent of anthrax between 1991 and 1998 at the Pasteur Institute, and he received his PhD degree in 1995. As a postdoctoral fellow (1998 and 2003) at the Swiss Experimental Research Center on Cancer in Lausanne, Switzerland, he studied the interaction of intestinal epithelial cells with Salmonella enterica and he identified flagellin as a major bacterial component that triggers pro-inflammatory responses. In 2003, he joined the Institut Pasteur de Lille to develop research on epithelial innate immunity. His investigations are now focused on the host immune defenses during respiratory infections by pathogenic bacteria, especially antibiotic-resistant Streptococcus pneumoniae and Klebsiella pneumoniae. The team aims at developing new adjuvants to trigger respiratory innate immunity in prophylaxis and therapeutic settings.

Graham Somers (Panel Member- Session 1) has a PhD in drug metabolism from the University of Manchester, and 35 years of experience in the pharmaceutical industry. Industrial roles originated in DMPK but have also included a number of different line management roles across the Pharma business. These include extensive input into early research and development of new molecules to full development of small molecules, several of which are now successfully marketed products in different disease areas. More recent experience has included matrix management of science innovation teams with external partners as an alliance manager, and most recently as portfolio director and leadership of the IMI group at GSK.

Fadi Soukarieh (Invited Speaker – Session 4) obtained his degree in Pharmacy and Pharmaceutical Sciences from Damascus University, and his PhD in Medicinal Chemistry and Drug Design from the University of Nottingham. He worked on an anticancer drug discovery project targeting CDK9, and on a multinational project (SENBIOTAR) for the discovery of new PqsR antagonist as novel antipseudomonal and antivirulence agents. He joined the National Biofilms Innovation Centre (NBIC) in January 2019 and is currently focusing on the management and detection of biofilm using Medicinal Chemistry tools and approaches. This includes virtual and in-vitro screening of compound libraries, design and synthesis of small molecules and hybrid and prodrugs with enhanced permeability profiles.

John Patrick Stewart (Moderator – Session 8) is the Director General of the Therapeutic Products Directorate in the Health Products and Food Branch of Health Canada. He is responsible for overseeing the review and approval of drug and medical device submissions seeking authorization to be sold on the Canadian market or in the context of clinical trials, as well as managing the strategic vision, focus and priorities of the directorate and alignment with that of the Government of Canada. Dr Stewart holds a Bachelor's and Master's degree in science as well as a Medical Doctor degree from McMaster University. In addition, he holds a CCFP Emergency Medicine certification. Over the course of his career, he worked for over 20 years as full-time emergency physician. In a former role as an Assistant Professor with the Faculty of Medicine at the University of Ottawa, he was responsible for coordinating undergraduate medical student education in the Emergency Departments in Ottawa and was actively involved in the Department's research program.

Ursula Theuretzebacher (Keynote Presenter- Session 1) is an independent expert for antibacterial drug research, discovery/development strategies and policies based on clinical and public health needs. Her broad area of expertise includes public and philanthropic funding strategies for antibacterial drug R&D and initiatives to recover the global pipeline, evaluation and comparative assessment of antibacterial drugs, and optimization of antibacterial therapy concepts. She was leader or partner in several EU funded international collaborative projects and served as President of the International Society for Anti- Infective Pharmacology, Founding President of the European Society for Clinical Microbiology and Infectious Diseases (ESCMID) PK/PD of Anti- Infectives Study Group, and as Executive Committee member of the International Society for Infectious Diseases (ISID). She was member of the coordinating group of the WHO project Priority Pathogen List for R&D and leading scientist for the Clinical and Preclinical Pipeline analysis, and development of Target Product Profiles at WHO.

Mat Upton (Invited Speaker – Session 5) is co-founder and Chief Scientific Officer at Amprologix and a Professor of Medical Microbiology at the University of Plymouth. Mat discovered the NI01 peptide whilst working at the University of Manchester and has overseen its development into lead pre-clinical candidate at Amprologix. He runs an academic research group focused on antibiotic natural product discovery and infection control. Mat is co-founding Director at Spectromics.

Jordi Vila (Moderator- Session 4) is the Head of the Department of Clinical Microbiology of the Hospital Clinic in Barcelona, Full Professor of the School of Medicine, University of Barcelona, and Research Professor in the Institute for Global Health (ISGlobal) of Barcelona, Spain. In this last institution, he is leading the Initiative of Antimicrobial Resistance. His main field of interest is the development of new drugs against MDR bacteria and molecular tools for rapid diagnosis of infectious disease. Dr Vila was the Programme Director of EECMID from 2009 to 2014 and he is the current president of the Spanish Society of Infectious Diseases and Clinical Microbiology (SEIMC). He has

recently received an Award of the National Plan against Antibiotic Resistance (PRAN) for the Micro-combat card game, in the category of better communication and public awareness initiative on the antibiotic resistance. He has published 462 articles in peer-reviewed journals (H- index 82; 27261 citations). He has patented two molecules.

Margo Warren (Invited Speaker – Session 8) is the Government Engagement & Policy Manager at the Access to Medicine Foundation. She liaises with governments, private foundations and multilateral organisations to share the Foundation's research findings and identify key opportunities for collaboration and change-making. Before taking on her current role, Margo was a researcher for the Access to Medicine Index, with findings published in top global media outlets and journals, including the New York Times, the Financial Times, the Guardian and the Lancet, among others. Margo was featured in the Canadian Society for International Health's 2020 list of Canadian Women in Global Health, which recognizes the achievements of established leaders in global health. Prior to joining the Foundation, Margo worked for the Ministry of Health and Long-Term Care in Ontario, Canada, in strategic health policy. Margo holds both a bachelor's degree and a master's degree in international development with a focus on health policy.

Oliver Williams (Invited Speaker – Session 8) is a Policy Adviser for Wellcome Trust's Drug Resistant Infections Priority Programme, where he leads on aspects of policy and advocacy related to antimicrobial resistance, antibiotic stewardship and access, and diagnostic development and uptake. Before joining Wellcome in 2018, Oliver worked as the Policy & Advocacy Manager at the non-governmental organisation Malaria Consortium, where he led global policy and advocacy across a broad range of infectious diseases and childhood illnesses. He has ten years of experience of working in global health policy and advocacy for not-for-profit and philanthropic organisations and is passionate about equitable access to healthcare and medicines.

Annex 3. Workshop Organising Committee

Dr Jessica Boname (MRC-UK), Lead for the Workshop Organising Committee and Member of the JPIAMR MB – see Annex 2

Édith Brochu (CIHR, Canada), Member of the JPIAMR MB. After her Masters in

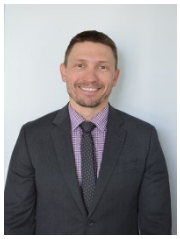
Experimental Medicine at Laval University, Edith engaged in a 12-year clinical research career in the pharma Industry touching a variety of therapeutics research areas within the North America territory. Then, she moved to work for seven years for two non-profits organizations and contributed to the development from ground up of two provincial and a national Networks in clinical research in oncology and personalized medicine as a Director of the Clinical Research and Infrastructure Network. Both these networks are still active to this day. Edith has been with the Institute of Infection and Immunity of the Canadian Institutes of Health Research since January 2017 and now acts as a Project Manager, Strategic Research Initiatives under the scientific direction of Dr. Charu Kaushic. Edith has been actively involved in the international development of the JPIAMR-Virtual Research Institute since early 2017.

Dr Emily Brown (MRC, UK) is the Programme Manager for Parasitology in the Infections

and Immunity Board at the Medical Research Council (MRC). She completed her PhD at the University of Sheffield, researching genes involved in resistance to gut parasites, before moving to Canada to conduct postdocs at the University of McGill, the Université du Québec à Montréal (UQAM) and the Université de Sherbrooke. Before moving to MRC, she was working for a community non-profit organisation in Montreal in the fundraising team.

Dr Rafael Cantón (Ramón y Cajal Institute of Health Research/ Complutense University of Madrid, Spain), Member of the JPIAMR SAB – see Annex 2

Adam Doane (Health Canada) Mr. Adam Doane is the Project Lead for Antimicrobial



Resistance for the Therapeutic Products Directorate in Health Canada's Health Products and Food Branch and is responsible for advancing organizational efforts to combat AMR, including enhancements to antimicrobial stewardship, improving the level of access to therapeutics relevant to AMR, and supporting research and innovation. Mr. Doane holds a Bachelor's and Master's degree in science, and over the last 12 years has worked on several priority files for the Government of Canada. Prior to joining the public service, Mr. Doane worked in regulatory consulting, medical diagnostics, and the pharmaceutical industry.

Dr. Patriq Fagerstedt (Swedish Research Council-VR), Research Officer, Dept of Research Policy, SRC and Programme Manager of the Swedish National Research Programme on Antibiotic Resistance. He is currently involved in the JPIAMR secretariat function and the ERA-Net Cofund JPI-EC-AMR. He has a PhD in systems neuroscience from Karolinska Institute and research experience from both academia and industry. He joined SRC from a Senior Grants Specialist position at Karolinska Institute in 2014.

Dr Sophie Gay (French National Research Agency-ANR), scientific officer for transnational collaborations in the Biology & Health department. After a PhD in molecular oncology (Sorbonne Université, Paris), she moved to Milan (Italy) to pursue her research activity at the IFOM Cancer Research Center. She joined ANR in 2018 to manage national and multilateral programs. She is presently involved in the JPI HDHL as well as in the JPIAMR, for which she will assume the responsibility of the call secretariat for the Therapeutics call that will be launched in 2022.

Dr Richard Gordon (MRC-SA), Member of the JPIAMR MB – see Annex 2.

Dr Carolyn Johnson (MRC, UK) is a Programme Manager for the Infections and Immunity Board at the MRC, covering bacterial disease, fungal disease and antimicrobial resistance. After a PhD in Immunology from King' College London, Carolyn moved to Lincoln, then Oxford to pursue her research career. In the past, Carolyn has worked for several UK based Charities (Alopecia UK and The Daphne Jackson Trust). She joined the MRC in 2020.

Dr Kyeong Kyu Kim (Sungkyunkwan University, Korea), Member of the JPIAMR MB – see Annex 2

Dr Marc Lemonnier (AntiaBio France), Workshop Chair and Member of the JPIAMR SAB – see Annex 2

Dr Mirfin Mpundu (ReAct Africa) – see Annex 2

Dr Katherine Payne (University of Manchester, UK) Member of the JPIAMR SAB – see Annex 2

Dr Jordi Vila, (ISGlobal/ University of Barcelona, Spain) Member of the JPIAMR SAB – see Annex 2