FIU Robert Stempel College of Public Health & Social Work

PAHO Pan American Health Organization World Health Organization Americas

FIU Global Health Consortium

World Antimicrobial Awareness Week
WAAW Special Webinar Series

AMR in Latin America and the Caribbean: innovations and challenges

Report

Day 1: Wednesday, Nov. 18th

New developments and innovations to address AMR.

Addressing the crisis in antimicrobials research and development.

Agenda

Time	Topic
09:30 am 09:45 am	Opening remarks » Dr. Pilar Ramon-Pardo, AMR Special Program, PAHO » Dr. José Luis Castro, Medicines and Health Technologies, PAHO » Dr. Carlos Espinal, Global Health Consortium, Florida International University (FIU)
	Session 1: Initiatives to develop new molecules and diagnostic procedures: Economic and financial challenges
09:45 am 10:00 am	Setting the scene – AMR development and innovation challenges » Dr. Jorge Mestre-Ferrandiz, Associate Professor, Carlos III University, Madrid
10:10 am 11:30 am	Panel discussion Moderator: Dr. Jorge Mestre-Ferrandiz, Associate Professor, Carlos III University, Madrid Facilitating sustainable access to new antibiotics » Dr. Fernando Pascual Martínez, Global Antibiotic Research and Development Partnership (GARDP) Manufacturers perspective » Dr. Alvaro Quintana, Pfizer » Dr. Holland R. Silas, Merck » Mr. Thomas B. Cueni, International Federation of Pharmaceutical Manufacturers & Associations (IFPMA) Innovations in diagnostic » Dr. Jonathan Hoffmann, Mérieux Foundation
11:30 am 12:15 pm	Discussion Moderator: Dr. Kalai Mathee, Herbert Wertheim College of Medicine Florida International University
12:15 pm 12:20 pm	Closing remarks » Dr. José Luis Castro, Medicines and Health Technologies, PAHO » Dr. Carlos Espinal, Global Health Consortium, Florida International University (FIU)

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Introduction

The world is losing its most powerful tool in healthcare: antimicrobials (AM), and the reason is rapidly rising antibiotic-resistant infections, also called antimicrobial resistance (AMR). Superbugs resistant to antibiotics (AB) not only threaten lives, but they also undermine every aspect of modern medicine. We urgently need new AB, but there are few in the pipeline because of a paradox: despite the huge societal costs of AMR, there is no viable market for new AB. New AB are used sparingly to preserve effectiveness, so in recent years several antibiotic-focused biotech companies have declared bankruptcy or exited this space due to the lack of commercial sustainability, leading to the loss of valuable expertise and resources. The result is a huge public health need for new AB, but a lack of funding for antibiotic research and development (R&D), particularly the later stages of clinical research.

Chaired by Dr. Pilar Ramón-Pardo, Team Lead, Antimicrobial Resistance Special Program Communicable Diseases and Environmental Determinants of Health

Pan American Health Organization/World Health Organization (PAHO/WHO), Dr. José Luis Castro, Advisor, Medicines and Health Technologies at PAHO and Dr. Carlos Espinal, Director of the Global Health Consortium (GHC) and Interim Chair for the Department of Health Policy & Management at the Robert Stempel College of Public Health & Social Work at Florida International University FIU, this seminar addressed this crisis and fostered a discussion with key experts in the field, about the new developments and innovative approaches to face it.

Panelists and Moderators

Dr. Jorge Mestre Ferrándiz is a Doctor in Economics from the Autonomous University of Barcelona. He currently works as an independent economic consultant, is Associate Professor at the Carlos III University, and Co-Editor of the Blog “Economía y Salud” (published by the Association for Health Economics). Jorge spent almost 15 years at the Office of Health Economics (OHE), beginning as an Industrial Economist and ending as a Consulting Director, in December 2016. A respected and widely cited economist, Jorge has published more than 60 articles on health economics, and he is regularly invited to participate in lectures on diverse topics, including: the economics of the life sciences industry; the economics of innovation and incentives to promote biomedical R&D; new financing models for AB; the economics of biosimilars; the economic returns to medical research; drug pricing and reimbursement systems; and health technology assessment. Jorge is Visiting Fellow of the OHE, member of the Editorial Board of Applied Health Economics and Health Policy, and member of the Advisory Board of

the Weber Foundation and the HiTT Foundation.

Dr. Fernando Pascual Martinez is a specialist in access to medicines and quality assurance of pharmaceuticals in developing countries. He joined the Global Antibiotic Research and Development Partnership (GARDP) in July 2020. After working in "Doctors without Borders" (DWB) from 2001 to 2012 Fernando became an independent public health consultant to several global organizations. As a consultant, Fernando has strived to increase access to medicines in the field of HIV and Hepatitis C virus, assessing regulatory pathways and regulatory issues for new products and contributing to WHO reports on access to Hepatitis C drugs.

Dr Alvaro Quintana is a scientific expert in anti-infectives in emerging markets. Alvaro started in the Academia as Aggregate Professor of the Department of Bacteriology and Biology in the Universidad de la República de Uruguay. His work focused on bacterial AMR and infection control and he led and run the first multi-institutional hospital infection control system in Uruguay. He then joined Pfizer in 1995 as part of the Latin America & Canada region and became medical lead member of the anti-infective global medical group at Pfizer headquarters in 2001. Alvaro has had country, regional and global medical positions with increasing responsibilities in medical affairs, safety, and regulatory and drug development, until becoming the Global Medical Director. He then spent five years at Johnson& Johnson Pharmaceuticals as Global Medical Affairs Leader and returned to Pfizer in 2010 as Medical Lead in Anti-Infectives. Since 2014 he is the Vaccines Global Medical Lead. Alvaro has published over 50 papers related to AMR, antibiotic development and safety, infection control and hospital infections. He holds a Medical degree in Microbiology and postgraduate degrees in Bacteriology and Biology.

Dr. Silas Holland is Director of Policy and Government Relations at Merck where he is responsible for Global Health policy issues and infectious diseases primarily focusing on AB and antifungals. He is also Head of Communications of the AMR Action Fund. Over the past 15 years he has worked on programs at both the community and global level to expand access to medicines. As Officer of the Global Drug Facility Portfolio, he has managed a portfolio of grants aimed at contributing to the development of anti-tuberculosis medicines and diagnostics to 31 countries/programs in the Americas, Southeast Asia, and Europe. Silas then joined the Global Fund as a Specialist for AMFm Operations and Coordination, managing relationships with key donors and partners to accelerate the end of AIDS, tuberculosis, and malaria as epidemics. He earned a BSc in Biology from Duke University, and his postgraduate degrees in education and public health.

Mr. Thomas B. Cueni is Director General of the International Federation of Pharmaceutical Manufacturers (IFPMA), the global association of research-based pharmaceutical companies and associations. Based in Geneva, IFPMA has official relations with the United Nations and contributes industry expertise to help the global health community find solutions that improve global health. Mr. Cueni is Secretary of the Biopharmaceutical CEO Roundtable (BCR), a policy forum of the global CEOs of IFPMA member companies. He is also Chair of the Business at OECD Health Committee and serves on the Board of Directors of the City Cancer Challenge, an initiative aiming to improve cancer care in major cities in low- and middle-income countries. In addition, Mr. Cueni serves as Industry Co-Chair of the APEC Biopharmaceutical Working Group on Ethics and Chair of the Board of the cross-sectoral AMR Industry Alliance, a group comprising more than 100 companies and associations representing pharma, generics, biotech, and diagnostics committed to tackling the threat of AMR. Prior to joining IFPMA he was Secretary General of Interpharma, the association of pharmaceutical research companies in Switzerland, and for many years he was a member of the Board and Chair of a key committee of the European Federation of Pharmaceutical Industries and Associations. Prior to his appointment with Interpharma, Mr. Cueni had a career as a journalist, inter alia as London correspondent for the “Basler Zeitung” and “Der Bund”, and he served as a Swiss career diplomat with postings in Paris (OECD) and Vienna (IAEA, UNIDO). Mr. Cueni studied economics and politics from University of Basle, the London School of Economics, and the Geneva Graduate Institute for International Studies.

Dr. Jonathan Hoffman is the Tuberculosis Research Manager within the medical and scientific direction of the Mérieux Foundation in Lyon, France. Currently leading a multi-country clinical evaluation and validation of tuberculosis diagnostics for monitoring treatment outcome in five countries of the GABRIEL international network in Madagascar, Bangladesh, Georgia, Lebanon, and Paraguay. Jonathan is also coordinating an operational research project funded by Expertise France and Foundation Mérieux aiming at improving detection and management of latent tuberculosis infection in high-risk groups in Madagascar and Cameroon. He obtained a PhD degree in Infectious Diseases from the School of Lyon and he is also MSc in Molecular Diagnosis.

Prof. Kalai Mathee has been an academician since 1999. As a graduate student formed the first International Graduate Student Association at the University of Tennessee-Memphis. In Florida International Univ (FIU), she was the first founding faculty of Herbert Wertheim College of Medicine, Founding Chair of the Department of Molecular Microbiology and Infectious Diseases, the Founding Director

of the Global Health Consortium, Founder and Founding Chair of the annual Global Health Conference and Founder of Rev Dr. Martin Luther King Jr @ The Frost yearly exhibit. She also has established and helped to develop several endowments at FIU, has successfully organized international conferences and hosted them in Kuala Lumpur while living in the USA — 7th (2009) and 15th (2017) Biennial Asian Conference on Transcription, and 17th Biennial International Pseudomonas Conference (2019). She serves on the International Advisory Board or External Assessor for several Asian institutions. All these were done while maintaining a high research profile with 110+ publications and mentoring over 150 individuals at all levels. FIU recognized Kalai's efforts and bestowed Mentor of the Year Award, the highest FIU accolade, Professor of the year in 2011. The 2014 inaugural Inspiration in Science Award by New England Biolabs only topped the honor. She selected to serve as the Editor-in-Chief for the Journal of Medical Microbiology based in London, United Kingdom. She is the first international editor of this journal's 40-year history. Kalai has worked closely with individuals from large Pharmaceutical Industries, national, and international agencies. She is passionate about inspiring others and extracting high standards from her trainees. She says of herself that she is committed to making a difference in the lives of people.

Session 1 - Initiatives to Develop New Molecules and Diagnostic Procedures: Economic and Financial Challenges

Setting the Scene: AMR Development and Innovation Challenges

Dr. Jorge Mestre Ferrándiz

Associate Professor, Carlos III University, Madrid

Dr. Ferrándiz set the context of the seminar, focusing on the specific issue around developments and innovation in AMR: AM R&D, and diagnostic procedures.

The success rates in clinical development are relatively low in general, but for AB it is even worse. There are difficulties in the design of clinical trials, since superiority of molecules is difficult to prove and there is limited information or evidence about the actual role of the new AB obtained before launching. On the economic side, the current payment/reimbursement system does not offer adequate returns. Although prices can be high, the sales volume will be small so the return will be small as well. AM stewardship programs (ASP) limit the use of AB. To mitigate the risk, incentives for new AM development work around three models: 1) "Push" funding model, to promote R&D providing funding prior to or independently from the results of the research; 2) "Pull" funding model, offering a reward once the results or the research are known and 3) Hybrid models with milestone payments, or a mix of push and pull. Funding initiatives should be coordinated, and new financing models should be developed. Some interesting pilot programs in certain countries should be escalated at a global level.

Panel discussion

Moderator: *Dr. Jorge Mestre Ferrándiz*

Facilitating sustainable access to new antibiotics
Dr. Fernando Pascual Martinez
Global Antibiotic Research and Development Partnership (GARDP)

Manufacturers perspective
Mr. Thomas B. Cueni
Director General
International Federation of Pharmaceutical Manufacturers (IFPMA)

Dr. Silas Holland
Director of Policy and Government Relations
Merck
Dr. Álvaro Quintana
Vaccines Global Medical Lead
Pfizer

Innovations in diagnostic
Dr. Jonathan Hoffmann
Tuberculosis Research Manager
Mérieux Foundation

How is your organization engaging to combat AMR and what are some of the challenges, particularly in Latin America and the Caribbean?

Dr. Fernando Martínez

"Thank you very much and I take the opportunity to thank also PAHO and FIU for inviting us to this online seminar and before saying how my organization is engaging, I would just say two words about the organization. The Global Antibiotic Research and Development Partnership (GARDP) is a public-private partnership non-for-profit organization that was launched in 2016 by WHO and the Drugs for Neglected Diseases Initiative (DNDI) and then became independent, in 2019. I think that in his presentation Jorge covered most of the challenges related to market, for instance the fact that there are low volumes, or the problems linked specifically to the antibiotic market so I will just mention that in the access world we are a little bit formatted by more traditional products like for instance HIV drugs. In GARDP we very soon realized that the solutions that for instance I used for in my past with DWB would not work in the in the field of AB, and this realization is especially important. You mentioned something that is very interesting, about the evidence that we generate in our drug development programs sometimes not yet responding to the huge needs of public health, and one of the of the gaps that was less discussed are the research gaps, not in phase three but in the post development phase, as well as research on repurposing the old AB, the work needed to position and to understand which is the role of these AB. Regarding market access, research is critically important because now more than ever with the pandemic we see that AB are an essential tool to the response. How do we contribute? Our core activity is the development of new AB and antibiotic treatments. I will mention three of the main programs we are currently working on. One is a program on sexually transmitted infections, we are developing solid fluorescence which is currently in phase tree, it's a new antibiotic with a new mode of action for the treatment of gonorrhea resistant to cephalosporin, and that is a clear example of a product which will become probably very important but in a near future because now -and hope it will continue for many years- the currently used ABs work, so as I say, this is "a moving target". The other product I will mention is for serious bacterial infections, we are working on a new beta-lactamase inhibitor called vaborbactam, combined with a fourth-

generation cephalosporin, addressed for hospital acquired infections and active against some of the priority pathogens, so this is a very promising program that we are working, specifically in children. The other program which is remarkably interesting is addressing neonatal sepsis, and for this program GARDP is taking a slightly different approach: we are basically working on repurposing and finding new indications for existing AB. We are exploring three combinations. Our work does not stop in research or in preparing a registration ready package, it goes beyond, we try to work on generating the evidence needed to allow for the optimal use of these AB and their access."

Dr. Álvaro Quintana

"Thank you, Jorge, and let me also thank Pilar and Carlos for the invitation to this event. Since the development of penicillin Pfizer had been committed to fighting infectious diseases and we are really driven by the compromise to protect public health at the time that we try to fulfill the unmanned medical needs of patients that are suffering by infectious diseases, particularly those with infections due to multi-resistant microorganisms. So, I would like to focus on four pillars which we think are critical to fight AMR. One is of course our main aim, which is to bring new drugs. We are always exploring new opportunities also in the development of innovative vaccines that have been shown that are a key factor to prevent the emergency of AMR. We also have a strong pipeline and we have been exploring different innovative ways to develop these drugs. Some of the new combinations have been using new translational analysis to really show the effectiveness over infections which are rare but represent a significant threat for the community. Fernando mentioned the impact of the COVID-19 pandemic, we are seeing that a lot of the specific molecules that are being used to try to manage this new disease are really used based on the real-world evidence that is being generated, so thinking on this perspective, COVID has changed our mind to some extent and may be leading us to explore new ways of drug development. The other point that we focus on is generating the information that is needed to guide the proper AM election at the bedside at the public health level and in the institutional decision. As it was already commented, it is important to know how difficult it is to make decisions when new molecules come along and sometimes patients cannot have access because of facts not at all related with effectiveness but more

on registration, and for not having accurate pharmacoeconomic data. We are really supporting the development of real-world evidence, but at the same time we are investing very strongly in surveillance programs which are a big problem as well. From our perspective we see that not everybody has access to understand which is the epidemiology of resistance at their hospital or institution, so we have been putting together a big surveillance program with open access. The proper use of AB is our pillar, so definitely we are supporting areas of development in ASP and along with the generation of the epidemiology data and, from the patient perspective, also to generate information needed to make the bedside decision for the appropriate treatment of these patients. We know that sometimes the institution may have a good laboratory but there is no proper communication, and the information does not get to the bedside, so we are trying to support some independent initiatives through a very extensive grant program. Then there is also the proper use of the promotional strategies on behalf of the pharmaceutical companies, and the other important aspect is to have a comprehensive environmental risk management strategy that includes manufacturing plants with focus on AB and that third-party suppliers to control the dissemination of residuals in the environment from these plants and make sure that we are not impacting the environment. In terms of the key gaps that we have seen in Latin America, an amazing progress has been done in terms of understanding AB resistance and developing control strategies. However, in a recent survey, specialists in the region shared their concern in terms of the disparity that they find regarding access to this information. There are institutions, particularly at the big cities that have the same resources than any other center in the world, but at the same time there are other centers that for several reasons do not have the necessary resources to acquire this information and thus fail in the proper selection of AB to control AMR. We have been supporting some pilots in Brazil to try to create quality improvement networks that really provide access to technology for molecular epidemiology and rapid diagnostic for the identification of multi-resistant infections."

Dr. Silas Holland

"Thanks a lot, I really appreciate the opportunity of speaking here today. I will not repeat the challenges and the commitments Fernando and Alvaro have already mentioned, I think for MSD

it is very much he same, we see our first responsibility as bringing these new vaccines and treatments to the market. There are less and less companies like MSD that are continuing on this track, I am proud to say that we have brought quite a few AB over the last five years but I think the responsibility of the industry goes way beyond that, and as we have started to see in AMR, to be a credible partner and player in Infectious Diseases you have to also be a responsible player and what that means in practice is that companies have to be actively promoting the responsible use of the products that they develop. Companies in the anti-infective market need to be active in surveillance and I am proud today to announce that MSD, as part of our WAAW, has relaunched the smart AMR surveillance interface which will allow a much better access to these data with researchers. This is probably one of the longest running largest collections of AMR surveillance data in the world and includes dozens of sites across Latin America. Finally, I think companies need to be active on access. We know that there are huge gaps in access to AB, in particular novel AB within countries between the public sector and the private sector as well as across countries and as a global community we need to figure out how to address this problem. Despite acknowledging that access is a challenge and that there are places in many low- and middle-income countries (LMIC) where resistance is a huge issue, there are few solutions or even really guidance on how to expand access to novel AB in weaker health systems. So, through the AMR industry alliance and in partnership with GARDP we are trying to look at ways to potentially address these issues. The role of the industry and of MSD as part of that really in AMR goes far beyond just the development of new treatments and vaccines."

In the AMR space, can we say that the industry is more trusted than in other areas?

Mr. Thomas Cueni

"Thank you very much Jorge. First a few reflections from my position as Chair of the AMR Industry Alliance already referred to by Silas. AMR needs to be approached in a holistic way, in a "one health" way which means we need to talk about appropriate use, we need to talk about environmental discharge, we need to talk about access, and we need to talk about R&D. In terms of the environment, we all know that AB are probably a drop in the ocean and not the biggest issue, yet one of the proudest achievements in the AMR industry

alliance is the work our manufacturing working group did, they were really the first ones to establish manufacturing discharge targets and are now moving beyond towards a cleaner production. A second element which I would like to refer to in the context of PAHO and Latin America is that we need to look at the one-health approach, where I believe Latin America has still a long way to go even if there is progress on appropriate use of AM. We have heard from Pfizer and MSD about their efforts regarding incentives to their sales representatives not for selling maximum amounts of AB but really for educating physicians on how to use them appropriately, which is great. Right now, the market for new AB is broken, it is simply not functional. I do not believe that you can create the sustainable environment for new antibiotic research with the NDI model. This model may work for schistosomiasis and many other neglected diseases, but AMR is not a neglected disease, it is prevalent in all our countries. I must admit in terms of what are you doing, Silas and others, now I think my biggest contribution in my whole industry career has been to convince leaders from the industry that we should not wait for governments to initiate market reforms If we really want a serious debate about incentives to break out of the impasse, we as industry need to be leading the debate and leading the debate also means investing. And that is why as we all know right now there are about half a dozen big pharma companies still seriously investing in AB. We really need a collective industry action and therefore I was extremely pleased that earlier this year in July we were able to announce a consortium of 23 pharma companies willing to invest a billion dollars in the setting up of an AMR action fund. This is important also in the context of the public health discussion, because early on when we discussed the architecture of the funds, the mission, the objectives, we committed to looking into WHO or CDC priority list of pathogens and we worked very closely with the Welcome Trust, an organization that has done a lot in terms of AMR. We also involved the European Investment Bank, so this unique partnership which we were able to create is not about making money from AB, I had a challenging time convincing industry leader that they need to sign big checks for something that all of them know is unlikely to have an immediate return, even in the medium term. But we had tremendous political response, which was a major surprise in the middle of the COVID-19 pandemic that nobody saw coming. The

industry is willing to commit to investing in novel AB with a good public health purpose, and therefore tackling the pandemic which is already on us and which is already killing more than 700 thousand people around the world. I was extremely proud about how our industry reacted to the AMR pandemic amid the current pandemic, and because the industry is really working 24/7 to find new treatments to find vaccines which will end the pandemic and provide us light at the end of the tunnel."

Dr. Jonathan Hoffman

"I am pleased to attend this panel discussion, thank you very much for inviting me. I work for Mérieux Foundation, which is a family foundation dedicated to the fight against Infectious Diseases in LMIC. We aim at promoting diagnostics and research capacities to improve the screening and management of populations and communities affected by tuberculosis (TB) and AMR in LMIC. Beyond strengthening TB reference laboratories and access to diagnostics for remote communities, we promote initiatives including the development and coordination of multi-country operational clinical research programs supporting national TB control programs. I would say that we are fighting AMR by building diagnostics and research capacities of different laboratories worldwide to improve access to innovative and standardized diagnostics and improving screening and management of vulnerable populations. To develop these actions and research projects we rely on the Global Approach to Biological Research, Infectious Diseases and Epidemics (GABRIEL) international library network, which is a non-profit network bringing together1 9 research laboratories from academic and private institutions. We have developed several collaborative research programs in this network, on acute respiratory infections, AMR, TB, and AMR as a major challenge for TB treatment. TB treatment remains a challenge for patients and clinicians, especially in individuals with multi-drug resistant TB, for whom adherence to treatment is complicated, partly due to the to the long duration of treatment, which is often associated with adverse events leading patients to prematurely stop medications. Poor adherence to treatment favors the emergence and circulation of multi-drug resistant TB, so it is therefore important to identify and evaluate laboratory tools to help the clinician to monitor treatment efficacy, especially in the early phase of the treatment. To date only clinical and culture-based sputum analysis are used

to know the effectiveness of the treatment, but these tools have several limitations, so we need to have a diagnostic tool that is sensitive, specific, inexpensive, easy to process, rapid and that can be used at various levels of the healthcare system with of course a good diagnostic and a good prognosis value. I have been coordinating a multi-country evaluation of TB diagnostics tools in five different countries of the GABRIEL network including Paraguay. We evaluated different diagnostic tools and we built research capacities. The tools that have been tested can really help fight AMR and TB in this country. I believe it is necessary to strengthen collaboration between research and health actors and companies to obtain funding, to promote technology transfer, and to give access to innovative TB diagnostics tools."

How can we create the environment for ongoing investment?

Dr. Jonathan Hoffmann

"It is a very tough question. I think we can create an environment that supports investment in AMR innovation by creating a multi-country evaluation that aims at answering a precise public health question, by bringing together scientists, clinicians, community agents, diagnostic companies, and political actors such as members of the national TB control program. I think we need to think about an integrated approach."

Thomas, you said you had tremendous political response after announcing the AMR action fund so I mean I do not want to open all your strategy, but how come we get the discussion to the next stage? how can we get governments to talk about business models now? How do you think we can get more countries to try these pilots?

"Actually, in my view we have to go beyond pilots. On the positive side I see a realization. Before we set up the AMR industry fund, we had many discussions with leading experts, what for me was interesting was that all of them firmly agreed we need the private sector, because tackling and successfully developing new AB it is not just a question of money, it is a question of the critical industry knowledge. Now on the positive side, I guess that later this week on Friday I expect the announcement from Dr. Ted Ross and his colleagues from FAO and the Organization for Animal Health about the global leadership group which should flagship leaders to make sure that AMR is not forgotten. I do expect that the private sector will be prominently included in this

because political leaders realize that we need the private sector for the solution. Now the second element is that the value of AB is not properly respected by health care systems. We really need to think about how we can recreate a market for novel AB, where we need to make sure in the interest of appropriate use that companies do not get money from maximum sales of AB but for the value they provide. Hospitals may only need a novel antibiotic which is successful against resistant strains of bacteria half a dozen times per year or maybe a big hospital two dozen times a year, but why isn't it possible to pay a kind of insurance premiums? I believe in the importance of industry sitting down with senior government officials, with academics and think creatively about how we can organize such a system. I give you one example: hip replacements or arthroscopic knee surgery are among the most routine interventions in hospitals and everybody who has that will get a by and large extremely cheap low-cost AB to prevent infections. Now in the odd case you may develop a resistance the question is could not one imagine paying a kind of insurance fee which might help to fund the cost of developing these new AB? Wouldn't it be possible to think about a subscription fee? We really need to think creatively, and I do believe that we need to be willing to listen to others and co-create solutions, that's why we set up this AMR action fund, to trigger the debate."

Silas, in your view, what would be your insights on move to action rather than talking?

"I think that despite the high-level discussions we have had on AMR for years now, the signals that governments and payers are sending to the industry on AB are clear, about their pricing and reimbursement. It is clear they are saying these are not valuable products, these are not needed, these are not things we are willing to pay for, and I think the industry except for some few remaining companies, need to start seeing action, and it looks like it is going to be different in different countries, what the UK will do is going to be very different than the US, or Brazil, or Mexico, so I do not think that we are particularly concerned about what it looks like as long as there are really some changes to hospital reimbursement system. AMR is truly a global threat, governments need to recognize their responsibility towards patients and change the way that these drugs are valued, and then finally I think the AMR action fund is an opportunity to really push for policy progress."

Alvaro, your insights on how can we get things going, how can we support access?

"It's a difficult question. I agree with most of what has been said, and as Pfizer participated in most of the initiatives, I will start saying that in Pfizer we believe that the speed and the scope of R&D that is needed can be achieved through a mix of new R&D initiatives and methodologies, and at the same time a new reimbursement model that really gets the necessary funding to develop the drugs. In Latin America It is still difficult to open the discussion with governments, and the participation of the pharma industry in this kind of panels. It is important to really bring up our ideas and our perspective on how to be innovative."

Fernando, in your view and in your experience, what would your recommendations be to get the action going?

"I think the NDI kind of model may not be perfect for the simple reason that what we are working is needed also in developed countries, and that changes completely the picture. Therefore, partnering with the industry is particularly important. The projects I mentioned before on serial bacterial infections or neonatal sepsis, and others are always done together with the industry. I can take the opportunity to mention an initiative that is now under discussion, it's called a secure initiative, a collaborative initiative to really work on creating a portfolio of essential AB to which countries can subscribe and could cover both new and existing AB."

Open discussion

Moderator: *Prof. Kalai Mathee*

Editor-in-Chief (with N. Fry, Public Health England), J Medical Microbiology (UK)

Professor at Herbert Wertheim College of Medicine Florida International University

We all know AMR levels are increasing. The participants want to know at what rate.

Dr. Alvaro Quintana: "I already mentioned Pfizer efforts to really make public access of the surveillance programs and data that we are generating through the ATLAS program. I think this is a model that can be followed at the different levels and as I

said, it also provides a focus on the quality of the data."

Many of you spoke about the lack of research. Could the industry help smaller entities to advance the research?

Dr. Fernando Martínez: "I can try to answer although I am not Industry, we work in partnership with industry, but I think at least about GARDP we identified that one of the main gaps is that all the evidence needed to adequately use the new products is sometimes missing and that needs to be also adapted to every country. What we try to do in the countries where we are researching is work with the ministries of health and only then define which are the specific needs that could drive a policy change or a stewardship guideline."

How could industry, the governments, intervene to make a difference to ensure the continuity of the programs initiated by the previous government?

Mr. Thomas Cueni: "I have already commented on this and screamed a little bit on the use of AB for growth stimulation. Consumer power can play a key role. There is a serious lack of concerted effort in public education."

How can we raise community awareness and involvement in AMR?

Prof. Kalai Mathee: "In Asia the Welcome Trust funded a project has nine chapters in a quite simple language. This document now has been translated into six languages, but it is all in the Asian region"

Dr. Alvaro Quintana: "From the pharmaceutical industry perspective this is a difficult area where we cannot really collaborate because of obvious conflict of interest that maybe rise up, but I can say that Pfizer is moving towards trying to find ways to collaborate with education for the public."

Dr. Silas Holland: "I think the pharmaceutical industry can communicate, I think even governments can communicate, but I think we see the limitations of these approaches. In vaccine confidence for example, where people are still suspicious about messages from the government, what you need is real people and patients who are able to tell their stories, but there is no real patient face in ARM."

Prof. Kalai Mathee: "There is always this distrust of the industry because they are focused on the economy and there is distrust in the government, so academic institutions play an important open neutral role in promoting AMR.

Education must start early, even with a simple microbiology component in schools introducing children to what are microbes and then what are the problems. One of the participants pointed out the existing courses on AMR and workshops are not globally available, there should be efforts to make them free and globally available for people AMR must become a national issue, and it needs to be part of m the countries legislations so that the different governments cannot alter the policy. We need to use the lessons learned from vaccination laws in some countries in Latin America to integrate AMR within the legislation of each country."

Dr. Jorge Mestre Ferrándiz: "Political involvement is needed, we need political champions and leaders who understand this problem and work with scientists, industry and the people."

About the "one-health" approach, how is the industry working on it?

Dr. Silas Holland: "MSD is actually one of the only big companies active in both human and animal health, and from experience I can tell you that it is difficult even within the same company to try to align the perspectives. The products, stake holders, customers, they are all different, it is a different business, so it has taken us a couple of years to align even within the same company, so we can imagine how this could work within governments, where you have the interests of different sectors, it must be complex. When you look at the achievements in the human health side in terms of reducing unnecessary prescriptions, we have not been very nearly as successful as they have in AB in animal health, so I think there is a lot of lessons that can be learned. We need to have evidence-based discussion and policies."

How to prioritize or what are the most critical issues that should be addressed?

Dr. Fernando Martínez: "Stronger partnerships and coordinating projects is essential. Also, diagnostics are really important and as a community probably we also need to make sure that we talk about diagnostics and we develop diagnostics because many of the issues with AMR could be sorted out if we had good diagnostic tools."

Dr. Alvaro Quintana: "Lots of projects are ongoing, we need better coordination to try to be more effective. Forum like this one can foster to address this challenge. Also, from my perspective, I think that generating the necessary information to understand the

situation in a geographical area and at each institution is critical. Also, policy actions are key to address AMR."

Dr. Jonathan Hoffman: "We need a strong partnership also in between academics and companies to improve research on TB diagnostics and improve coordination involving different actors from multidisciplinary sectors."

Dr. Silas Holland: "There is a need a collaboration. The Welcome Trust has just published a report that helps us guide that prioritization, looking and mapping out different interventions ranging from water sanitation to developing of new treatments and access issues. The highest impact really is around infection prevention and control and water and sanitation."

Mr. Thomas Cueni: "Vaccines in terms of AMR prevention can play a truly important role."

Prof. Kalai Matthee: The biggest problem in the hospitals is getting an AMR profile for the infecting pathogen and now with the microbiome we can create a resistance map not knowing where the bacteria are coming from, but just knowing all the AMR genes in that population we can make an informed decision as what AB not to use or use. If such diagnostic is available, we can have a resistance map within 24 hours. I would finally like to comment is that we have a lot of meetings, we listen to extraordinary presentations, we write many reports and even draw action lines, but we lack evaluation about what improvements have been made, how do we measure that we have reached a particular milestone, I think this is a huge lack."

Conclusions

The complexities of AMR discussed in this seminar show its various aspects, the panelists shared information on initiatives with particularly good prospects, and good comments on some results.

It is key to highlight the importance of global initiatives as mobilizers, to promote movements in the countries to develop national plans, as has been going on in Latin America with the support of PAHO / WHO.

In the light of the pandemic, the need of aligned initiatives is clear. Despite all the efforts in AMR, raising awareness remains a need. Awareness generates movement, with transparent mechanisms put in place that favor coordination and innovative ideas between the public and private sectors.

The Chairs thanked all panelists for the incredible amount of information and elevated level of discussion, the magnificent moderation during the three hours seminar, and thanked the over 700 participants for attending this first out of three consecutive online seminars.