

Fostering investment in the development of new antibacterial treatments

World Investment Forum, 23 October 2018, Palais des Nations, Geneva





Report

An event on *fostering investment in the development of new antibacterial treatments* was held on 23 October 2018 at the Palais des Nations, Geneva during the World Investment Forum (WIF). Organised by the United Nations Conference on Trade and Development (UNCTAD) and the World Health Organization (WHO), the event sought to identify the means for global collaboration to upsurge investment to address antimicrobial resistance (AMR). It involved current global funding mechanisms and investors on AMR; representatives of biotechnology and biopharmaceutical industry; civil society and government entities with global outreach on AMR issues. The meeting responds to the major global initiatives on AMR, such as the 2016 Davos Declaration, the WHO Global Action Plan on Antimicrobial Resistance, the G20 Leaders' commitment to action on AMR, including, *inter alia*, a new Global R&D Collaboration Hub, and the 2016 UN High-Level Political Declaration on Antimicrobial Resistance. The event built on UNCTAD's *ad hoc* Expert Group Meeting on this issue organized in collaboration with WHO on 5 October 2017. The event was attended by over one hundred participants from private sector, governments and civil society.



Opening and introduction

Acting as moderator of the event, Professor Laura Piddock, who is the Head of Scientific Affairs at the Global Antibiotic Research and Development Partnership (GARDP), introduced the event programme and speakers. Ms. Isabelle Durant, Deputy Secretary-General of UNCTAD, opened the event with welcome remarks. Emphasising on the challenges posed by AMR and its health and economic implications, Ms. Durant stated that antimicrobial research and development (R&D) is mainly carried out by biotech-oriented small and medium-sized enterprises (SMEs) which face difficulties in attracting the needed investment. In her opinion, actions are required at two levels: finding investors, including motivating non-traditional investors, such as hospitals and re-insurers to invest in AMR; and designing the appropriate incentives to reconcile commercial and health objectives. Ms. Durant thanked WHO for its partnership in organizing this event and stated that in addition to facilitating informal discussion during WIF, UNCTAD will be happy to facilitate any follow up in cooperation with UN sister agencies.

Dr. Ranieri Guerra, Assistant Director General for Special Initiatives of WHO, highlighted the dangers of AMR. In addition to intergovernmental initiatives, he also reminded the participants that the pharmaceutical industry signed a Declaration to Combat Antimicrobial Resistance in 2016. At the policy level, Mr. Guerra observed that there has been important progress so far, including the fact that today over 90% of humanity lives in countries with AMR action plans. The WHO plays an important role in developing R&D blueprints for priority pathogens and systematically drafting roadmaps to identify political and research needs. It also helped the launch of the Global Antibiotic Research and Development Partnership (GARDP) that has so far raised over Euro 65 million. Due to the human, animal and environmental dimensions of AMR, WHO is working in partnership with the UN Food and Agriculture Organisation (FAO) and World Organisation for Animal Health (OIE) under a tripartite plan and with the United Nations Environment Programme (UNEP). Mr. Guerra hoped that such kind of coordination can be an example for member states, as they adopt and implement national plans in line with the WHO Global Action Plan.

Two keynote addresses delivered during the event also brought out the scope of the challenge posed by AMR and the urgent need to invest on the development of new antibiotics. Hon. Dr. Alfred Madigele, Minister of Health and Wellness of Botswana stressed that all stakeholders need to address the issues of funding R&D to tackle AMR. Botswana's position is that the unchecked use of antibiotics on animals and humans has triggered this crisis. Botswana is in the process of establishing a national research fund to try and productively address the AMR issue. Botswana is

also working on improving regulation of the healthcare system. In the Minister's view, Botswana has the potential to become a manufacturing and researching hub due to its strategic position.

H.E Venko Filipche, Minister of Health of the Former Yugoslav Republic of Macedonia (FYROM), on his part stated that, as part of a series of measures regulating the rational and optimal use of antimicrobial medicines, today antibiotics can be obtained in his country only via prescription. All reference laboratories operate in accordance with European Committee on Antimicrobial Susceptibility Testing (EUCAST) standards. Due to the measures implemented by the government, the country has experienced an 11% decline in antibiotics consumption. According to the Minister, there is a need to establish a sustainable mechanism for the development of novel antibacterial agents and to promote public-private partnerships. FYROM has skilled labour that can take part in the global initiatives and collaboration for R&D. The Minister has invited investors to his country.

Panel Discussions

Following the opening and the keynote addresses, discussions were organised under three panels. The first panel for investors and funding facilities; the second panel for biotech companies and researchers and the third panel for civil society and the public sector. The panel discussions were conducted with presentations from key global leaders followed by questions by the moderator, Ms. Laura Piddock, and the audience.

Panel 1: The scopes and experience of funding and investment mechanisms

The first panel brought together Richard Lawson, a Senior Project Manager at Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator (CARB-X), Christopher Egerton-Warburton, currently a Founding Partner and co-CEO of Lion's Head Global Partners (a London-based bank) and previously the Chair of the United Kingdom Advisory Committee on the Global AMR Innovation Fund (UK-GAMRIF) and Tomotaka Goji, the Managing Partner of the University of Tokyo Edge Capital (UTEK) and the Managing Director of Japan Venture Capital Association.

CARB-X accepts applications from around the world for diagnostics, vaccines and therapeutics in line with the WHO list of priority pathogens. It does not invest in basic research. It maintains an alliance of funding institutions, such as the United States government, the Wellcome Trust fund, the UK government and the Bill and Melinda Gates Foundation, and a network of project accelerators. The success behind CARB-X's model, according to Mr. Lawson, rests on its strategic decision-making process through a pre-award assessment by scientist and technical experts from around the world and forming a support team, once investment is made, to help the development of the products. CARB-X has so far funded over 40 projects from all over the world and it expects

to expand. As a testimony to its success, Mr. Lawson stated that CARB-X is receiving more applications and that the R&D pipeline in AMR is expanding. Although CARB-X does not claim a direct causal relationship, companies receiving investment from CARB-X seem to be able to attract private investment. For every \$1 invested by CARB-X in companies with AMR R&D projects, \$9 are invested by private sector.

CARB-X has received £20 million from the UK GAMRIF, which was matched by the Bill & Melinda Gates Foundation (BMGF). Mr. Egerton-Warburton recalled his role as Chair of the UK-GAMRIF. According to him AMR is a moving train, despite the hostile and arid environment. The harder you make the problem the more scientists will flock to the problem. GAMRIF had £50 million, which is a small capital, so needed to give more support to established entities. The fund excluded TB, since the UK has already invested in it through several channels. The investment on CARB-X was to diversify R&D to vaccines and other preventives. £10 million went to bilateral project with China with a focus on harnessing the potentials of Chinese traditional medicines. Recalling artemisinin, Mr. Egerton-Warburton stated that there are more traditional Chinese and Indian medicines which need to be brought into the pharmaceutical innovation sphere. Another £5 million was allocated for a joint project with Argentina that will focus on environmental impact. £5 million is invested in the Foundation for Innovative New Diagnostics (FIND) targeting connectivity of diagnostic tests and data. £1 million went to GARDP. Mr. Egerton-Warburton believes that:

- As drugs will not solve the problem alone, strengthening health systems becomes essential;
- Clinical trial regulations need to consider the specific nature of AMR. The focus should be on efficacy. His remark was also supported by Mr. Lawson who stated that CARB-X has developed a good interaction with the regulators and managed to shift their approaches to AMR over the last 5 years
- There is a need for new pull mechanisms¹ to ensure that there is a market for the drugs to be developed.

The University of Tokyo Edge Capital Japan Fund (UTEC) has invested in BUGWORKS which is a company that aims to discover novel pharmaceutical assets for addressing AMR and had also

¹ Pull mechanisms are rewards for R&D of new products. Some of these mechanisms are monetary in nature. Two examples are market entry rewards that are paid to the developers of novel products at a certain milestone, or at early stages and advance market commitments, which allow developers of new products to sell a defined volume of their products to funders at a pre-specified price. Other mechanisms are non-monetary. Examples are fast-tracking medicines regulatory reviews and transferable priority review vouchers that provide a developer the possibility of either transferring the voucher to other products in its portfolio or selling it to another company. See further Inter-Agency Coordination Group (IACG), [Antimicrobial resistance: Invest in innovation and research, and boost R&D and access IACG. Discussion paper. Inter-agency Coordination Group](#), June 2018, Geneva.

successfully received support from CARB-X. UTEC's managing partner, Mr. Goji, recalled that Japan has a long history of investing in antibiotics, including Colistin that had been considered the last line of antibiotic defence. However, he noted that resistance to Colistin was witnessed in the United States.

In Mr. Goji's view, involving the private sectors in funding mechanisms is a key to increasing their investment to address AMR in a sustainable manner. Since innovative approaches are needed to solve the AMR problems fundamentally, venture capital investors with scientific expertise could be invited to participate at the earliest stage of the process for setting up the funding mechanism. Over the past several years, the AMR sector has become an investment opportunity with dozens of start-ups, among which several were acquired or established alliances with global pharmaceutical companies. The private investment landscape can go hand in hand with public sector initiatives to implement a whole package of policies to ensure a more conducive environment for venture capitalist and to scale up investment. However, it is not enough for each country to take their own measures, hence, Mr. Goji called upon the United Nations to play the role of coordination.

Following questions from the moderator and participants, Mr. Lawson stated that access in low- and middle-income countries and stewardship are part of the conditions of investment for certain projects. Mr. Goji, supported by other panellists, stated that there have not been enough new drugs in the last half century, and investment for new antibiotics is urgently needed. He also stressed the need to increase successful examples of R&D projects to increase the engagement of private investors. The moderator, Ms. Laura Piddock, remarked that healthcare providers take quite a long time to change to new protocols. She also referred to the difficulty of compliance with many guidelines.

According to Mr. Egerton-Warburton, there is a need to be careful in linking intellectual property/TRIPS flexibilities on access to medicines with AMR. Every company is willing to expand access to antibiotics; the bigger challenge is how to reduce unnecessary usage. The drugs the companies are trying to develop and produce now are the ones that health officials do not want everyone to use. WHO has consequently stressed the considerable importance of stewardship.

Panel 2: Capacity and challenges of researchers and bio-pharmaceutical industry

The second panel was organized to assist researchers and industry to present their challenges and views on current financial and investment mechanisms and to suggest proposals they may have for the future. The Panel discussion involved Marc Gitzinger, the CEO and founder of BioVersys AG and the Vice President of the Board of the Biotech companies in Europe combating AntiMicrobial Resistance (BEAM) Alliance; Anand Anandkumar, the co-founder and CEO of Bugworks; Yoshinori Yamano, the Chief Scientific Officer for Infectious Diseases at Pharmaceutical

Research Division of Shionogi Co., Ltd and Jean-Pierre Paccaud, the Incubation Business Development & Strategy Director of GARDP. All the panellists underscored that so far significant funds were allocated as a ‘push’ incentive, though a major funding gap exists in terms of pull mechanisms to support clinical trials and to bring the product into the market.

BEAM alliance has brought together more than 50 European SMEs. Considering the shortfall, Mr. Gitzinger and BEAM alliance believe there is a potential for a larger AMR impact fund in the context of a ‘one health’ approach, something that BEAM has been actively discussing with WHO and UNCTAD. Although, the pharmaceutical sector returns have a very high margin in general, the suggested impact fund would provide only 3-5% return, which is slightly above the inflation rate of several western countries. Such additional fund is needed because the world remains dependent on AMR treatments essentially developed in the 1980s. The proposed impact fund would involve an envelope of at least one billion USD including from new investors, such as re-insurance companies. It would target:

1. 20% for diagnostics, 65% for new drugs and the remaining for ICT and medical technologies;
2. The fund should target seven distinct intervention points of AMR, involving product and process innovation and targeting prevention, rapid diagnostics, cure, avoiding treatment failure, fighting infection damages, preventing contagion and avoiding relapse.

Talking about BioVersys, Mr. Gitzinger said that his company is focused on new products, including transcription regulator inhibitory compounds (TRIC) which enable the company to screen, identify and develop molecules that switch off bacterial resistance mechanisms. Emphasizing the importance of R&D in both diagnostics and pharmaceuticals, the company has prioritized tuberculosis.

Bugworks is a global biotech start up currently targeting the development of next generation antibiotics that can tackle a broad spectrum of superbugs. It has received funding from CARB-X and investment from UTEC. Mr. Anandkumar remarked that antibiotics are the single biggest invention of modern medicine that have had the most profound impact on raising average human age – they are the very edifice on which surgery, chemotherapy etc are built. That edifice has begun crumbling. He described that outlook as the perfect storm for all of us to come together like we have never done before. He thanked CARB-X, UTEC and its South African investor, Aquipharma.

The current funding facilities do not have backing to pull the R&D pipelines into the market. Mr. Anankumar believes that a funding mechanism with 70% public and 30% private investment is a practical solution. In the process of innovation, he is particularly convinced that countries like

India and South Africa have become important part of the solution because of the speed and cost efficiencies of generating clinical trial data and their manufacturing capacity. Gone are the days where a billion dollars were required to have a drug developed. AMR is a space dominated by SMEs, including in developing countries. He expressed the view that a new antibiotic can be brought into the market with USD 100-120 million. Major changes are required on part of medicines regulatory agencies, including introducing global collaboration; using data from markets like India and Africa as precedent for multi-site Phase III trials and for pushing products into the market. Innovation is to come also in how we undertake clinical trials. Lack of business capacity, clinical behaviour and inadequate market entry rewards are the challenges. For the price countries pay for four fighter jets, they can fund the development of more than ten antibiotics and buy the world another century of protection. It could probably take the G20 countries and the top 5 insurance companies of high-income countries plus public-private partnerships to create a consortium enough to provide all the investment needed against AMR.

According to Yoshinori Yamano, Shionogi is a 120-year-old company with a traditional focus on infectious diseases. It has successfully completed a clinical study on Cefiderocol without external “push” funding. However, without the potential for profitability it will be difficult to sustain R&D activities in the AMR space and, hence, new “pull” incentives are decisive to address the commercial challenges of bringing new drugs that address AMR into the market. The challenge has scientific, developmental, regulatory and economic dimensions, including, limited returns and difficulty to predict returns relative to other therapeutic areas, limited use to address stewardship and difficulty to predict demand and investment in manufacturing capacity accordingly. Mr. Yamano found the current funding mechanism dominated by push mechanisms, with a number of promised pull mechanism that have yet to be implemented. Promising pull mechanisms, according to Mr. Yamano, includes market exclusivity voucher that can be used for any other product or sold to other companies and market entry rewards and improving market data to provide for predictability of demand.

Finally, Jean-Pierre Paccaud stated that there is a need to look at public health priorities as a driving force for investment decisions. We need to avoid the same trap, resistance being developed, while choosing and undertaking R&D. We really do not know much about the resistance trends unless we improve global surveillance. It was noted that re-fencing old drugs is more like exploring the full potential of the drugs. Founded by DNDI and the WHO and funded by governments and philanthropic foundations, GARDP has selected a few intervention areas that are perceived as those that will not be of such interest to other organisations This covers four areas: sepsis, gonorrhoea, optimizing current treatments and accelerating development of new antibiotics for children, and recovery & exploratory programme for old antibiotics. In the future it might include other indications. GARDP look beyond R&D in that their investment considers access, stewardship and all other elements from the beginning. Any tools that are developed will be brought to emerging and developing economies.

Interventions by participants supported the proposal for a funding mechanism with 70% public financing and 30% private investment. Based on the experience for non-communicable diseases,

it was noted that it is essential to keep the private sector on board. However, the private sector representatives should also undertake their own outreach to the G-20 leaders' summit, including next year's meeting in Japan.

Panel 3: The need to reconcile innovation, access and stewardship

The third panel brought together civil society, governments and other public entities with programmes on AMR with a global outreach. The panellists were Andreas Sandgren, Policy Adviser at Action on Antibiotic Resistance (ReAct) of the Uppsala University, Sweden; Niresh Bhagwandin, the Executive Manager of Strategic Research Initiatives, Medical Research Council, South Africa (SAMRC); Clemens Martin Auer, Director-General at the Federal Ministry of Labor, Social Affairs, Health and Consumer Protection, Austria and Jenny Hellman, who works at the antibiotic and infection control unit of the Public Health Agency of Sweden.

According to Mr. Sandgren, the first point is that investment in new drugs, diagnostics and vaccines should be driven by global public health needs and follow the broadly adopted principles for R&D to address AMR. Secondly, like climate change, AMR has no boundaries: lack of access to appropriate and effective antibiotics as well as their inappropriate use are problems that should concern all countries. Thirdly, the issue should not only be about financing R&D but also about strengthening health systems in line with the WHO framework. Hence, as stated earlier by Mr. Paccaud, Mr. Sandgren stated that the overall picture surrounding AMR, namely, affordable access to and the appropriate management, distribution and use of new antibiotics needs to be considered throughout the R&D process – not just as an afterthought - to ensure that decisions taken upstream do not undermine efforts downstream. Ensuring investment in WHO's priority pathogen list with a public-private partnerships model can help to achieve all the key issues around AMR.

According to Niresh Bhagwandin, following the adoption of a national AMR strategy, South Africa has established an AMR Ministerial Advisory Committee and National Training Centers; and enacted various guidelines, including on stewardship for health practitioners. SAMRC has established partnerships with local and international organizations to collaborate, including with GARDP and FIND; and participates in the BRICS AMR network and the Joint Programming Initiative on Antimicrobial Resistance (JPIAMR) – an international initiative launched by the European Union. SAMRC recently established the “Centre for the Study of AMR” at the University of Cape Town and is funding several AMR projects under its Strategic Health Innovation Partnership (SHIP) funding model. Mr. Bhagwandin also noted that, although

antibiotics can be purchased only with prescription, there is no clear picture on the extent of the black market in South Africa. In his conclusion, Mr. Bhagwandin stated that there is a need for:

- increased collaboration among key players’;
- implementing universally accepted guiding principles to inform R&D;
- sustainable funding for developing novel drug entities;
- new models for conservation, access and stewardship;
- fast tracking entry into the market of new drugs, and
- a focus on addressing the needs of poor countries.

Clemens Martin Auer at the outset expressed some pessimism regarding global collaboration on AMR but then developed a more optimistic view. In his view, the AMR challenge affects even high-income countries, as in the case of affordability of hepatitis C treatment. He stated that ministries of health are unaware of the activities of public research grants or ministries of science. According to him the first and big problem is weak coordination among the key actors. There is very little systematic, structured and explicit priority setting going on, and what the WHO is doing is not enough. Secondly, there is a public-private imbalance. The European Commission must understand that grants of money must also require return. Finally, there are a long list of regulatory issues.

Mr. Auer stated that AMR is only highlighting the urgency for action in establishing an international organizational framework for publicly financed R&D in the medical field. It is an obvious policy failure that the widely fragmented public R&D funding mechanisms fall short of effectively coordinating their effort to meet their health objectives. Initial steps to overcome these shortcomings are under way but more leadership is urgently needed. In particular, the fact the G20 leaders stepped in is a good sign. Yet, it is necessary to have a global, strategic approach, instead of the current national patchwork of initiatives.

Jenny Hellman presented that one aspect of the effort of the government of Sweden concerns ensuring availability of antibiotics. Antibiotics are used in a relatively restrictive way in Sweden compared to many other countries. Consequently, some products face such low demand that there is a risk that pharmaceutical companies do not make them available in the Swedish market. Questions on the availability of antibiotics arise when new products are not launched in the Swedish market and when existing products are withdrawn from the Swedish market. Hence, Sweden has developed a pilot programme for 2018-2022 to ensure availability of antibiotics. The model defines, prioritizes and categorizes antibiotics to benefit from a compensation scheme under a pilot project. Ms. Hellman stated that the model would be good for suppliers to have a more predictable revenue stream. A separate commission is undertaking research on an incentive model for investments in new antibiotics, which is expected to be completed and reported on by December 2018.

In his closing remarks, Mr. Christoph Spennemann, Officer-in-Charge of UNCTAD’s Intellectual Unit, emphasized UNCTAD’s intention to provide a continuous forum of exchange on investment-



related AMR policies and to engage in a discussion on how to best ensure follow-up to this event, in particular with WHO.



Annex: Event Program

Welcome: Isabelle Durant, Deputy Secretary-General, UNCTAD

Key note addresses:

Hon. Dr. Alfred Madigele, Minister of Health and Wellness, Botswana

Venko Filipche, Minister of Health, former Yugoslav Republic of Macedonia

Ranieri Guerra, Assistant Director General for Strategic Initiatives, WHO

Moderator: Laura Piddock, Head of Scientific Affairs, Global Antibiotic Research and Development Partnership (GARDP)

1. Funding mechanisms and investors: Scope and experience
 - a. Richard Lawson, Senior Project Manager, Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator (CARB-X)
 - b. Christopher Egerton-Warburton, Expert Advisory Board Chair, UK Global AMR Innovation Fund (UK GAMRIF)
 - c. Tomotaka Goji, Managing Partner, University of Tokyo Edge Capital (UTEC) Japan Fund
2. Researchers and industry: Capacities and challenges
 - a. Marc Gitzinger, CEO, Bioversys, Switzerland
 - b. Anand Anandkumar, CEO, Bugworks Research, India
 - c. Yoshinori Yamano, Chief Scientific Officer for Infectious Diseases, Shionogi, Japan
 - d. Jean-Pierre Paccaud, Director, Business Development & Corporate Strategy, GARDP
3. Civil society, governments and public entities: The need to reconcile innovation, access and stewardship
 - a. Andreas Sandgren, Policy Adviser, ReAct – Action on Antibiotic Resistance, Uppsala University, Sweden
 - b. Niresh Bhagwandin, Executive Manager of Strategic Research Initiatives, Medical Research Council, South Africa
 - c. Virander Paul, Ambassador/Deputy Permanent Representative of India to the UN
 - d. Clemens Martin Auer, Director-General, Federal Ministry of Labor, Social Affairs, Health and Consumer Protection, Austria
 - e. Jenny Hellman, Public Health Agency of Sweden

