Written responses to open questions of the webinar 'The challenges and opportunities for antimicrobial R&D in low- and middle-income countries – India case study' by Anand Anandkumar and Kamini Walia, originally broadcast on 9 July 2020. See webinar recording here: https://revive.gardp.org/the-challenges-and-opportunities-for-antimicrobial-rd-in-low-and-middle-income-countries-india-case-study/

Question asked	Response from the speakers
How do you see the use of narrow-spectrum anti-infectives?	Encouraging narrow-spectrum use is important to prevent misuse of broad-spectrum anti-infectives. The use of narrow-spectrum anti-infectives is limited due to no availability of timely diagnosis. Narrow spectrum antibiotic will be a more rational way of addressing AMR provided it accompanies with companion diagnostic which detects pathogen of particular infection very rapidly. However, in most of the hospital-associated infection in a critical care setting, the infection will be of polymicrobial in nature and there is an urgency of saving the patient's life and that is why the physician chooses the broad-spectrum antibiotic.
How are diagnostics done in hospitals?	Except for tertiary care hospitals, there is limited capacity to carry out diagnostics in hospitals. The diagnostics are usually outsourced to labs in absence of inhouse capacity.
My question to Anand is that though we are all aware of the completeness of antibiotic doses for any disease control but many of peoples of our country are not seriously maintain that instructions by which antimicrobial resistance happen… so what would be your advice or suggestion regarding this step?	AMR in society operates due to multiple reasons. Incomplete treatment, lower dosage, wrong antibiotics and most importantly overuse of antibiotics. In addition to natures reaction by the various genetic method. In such a multifactorial operation there is no simple easy solution. Governments must make this a priority area and bring all stakeholders together!
How to establish antimicrobial stewardship in India with limited resources health facility and what is your opinion?	ICMR has initiated AMSP in tertiary care hospitals. Govt of India has pledged to establish infectious disease blocks in District hospitals. These would need to be supported with suitable by ID physicians and other resources.

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My question is for Anand - the focus of BugWorks' research is on broad-spectrum drugs. Will that not face the same fate as an antibiotic are facing today? Is there merit in focussing on narrow-spectrum drugs specifically for the bugs that we are facing major resistance within India and around the world, i.e. *Klebsiella, Enterococcus, Pseudomonas* etc.?	Bugworks believes in its scientific innovation in addressing AMR with broad-spectrum antibacterial as it uses highly differentiated strategy in discovering antibiotic which are optimized with iso-potent dual-targeting mechanism combined with bacterial efflux avoidance. This led to the identification of broad-spectrum antibacterial series which is completely devoid emergence of resistance in the lab setting against Gram-negative species and effective against all known mechanism of drug-resistant bacterial species. Every antibiotic will become resistant to certain pathogens; however when you have a novel class and its dual target action, then there is a good chance that such an antibiotic will be around for many decades before being totally taken out by bacteria. Also, in most hospital settings, the infection will be of polymicrobial in nature and there is an urgency of saving the patient's life and little time left for diagnosis. In such a scenario, Bugworks strongly believes that broad-spectrum antibiotic will be most suited and that is why our product TPP is focused on hospital/ventilated associated infections. Yes, there are merits in focussing truly narrow-spectrum antibiotic as it is a more rational way of addressing AMR provided it accompanies with companion diagnostic which detects pathogen of particular infection very rapidly. However, in many cases, a highly spoken narrow-spectrum antibiotic may also cover the sub-mic concentrations of some bacterial species which are not responsible for the infection thus leading to trigger the emergence of resistance.
What is ICMR's viewpoint on developing phage therapy as an antimicrobial?	Phage therapy is still in experimental phase.
For Anand; How do you recruit patients for a clinical trial based on indication or bacterial strains?	It will be based on Indication as ours is a broad-spectrum antibiotic. Initially, we are thinking of serious hospital infections, pneumonia (HAP/VAP)

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As very few new antibiotics are being discovered, are there any initiatives from ICMR or BugWorks to invest in antibiotic discovery?	ICMR is focussing on creating clinical trial capacity in the country. All agencies like ICMR DBT CSIR are focussing on new drug discovery.
Thanks, Kamini for your great talk. Do you think Covid19 has an effect on AMR?	In the absence of no availability of specific COVID treatment, antibiotics are being used in both mild and sick COVID patients. There is a need to emphasise antibiotic use only in cases with positive bacterial or fungal cultures.
Wonder how much ICMR has achieved in changing the mindsets of clinicians in antibiotics prescriptions and overuses! Can a realistic view be alluded to??	We have trained more than 600 hospital professionals on Antimicrobial Stewardship. The effect will be visible in due course of time. There is need to spread this initiative to lower levels of health care.
I have a question for Anand. I would like to know if a traditional solution to address the problem of the small size of the market, like pooled procurement (grouping orders and making demand more visible to allow risk mitigation for manufacturers) is possible in India, in particular in the private sector. Also, if he thinks this could be enough or if in addition to that some kind of incentives would be needed.	The Indian market for a true broad-spectrum antibiotic is not to be ignored. It may make it to $50 to $100M type revenues within 5+ years of launch. BUT It won't be an easy route forward. Indian government must support innovation by allowing for pooled purchase (thereby guaranteeing certain volumes). We keep our costs low by doing local trials and using local CMC, but also need some sort of subscription or pull incentives from the Indian government. else not many players will look at the India market!
What's your take on enmetazobactam discovered in India?	Not being used in India currently. Enmetazobactam is extended-spectrum -lactamase (ESBL) inhibitor works against KPc, OXa-40 and CTX-M, currently being tried in combination with cefepime and has potential to treat infections caused by enterobacteria and Pseudomonas. It has to compete with already approved Avycaz, Zerbaxa and Vabomere products. However, the cefepime-enmetazobactam combination will have an oral advantage.

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What is India doing to establish and enact regulation to stop the unabated release of antibiotic residues into its water bodies?	The central pollution control board is developing standards for releasing antibiotic effluents in water bodies.
Real-time surveillance would be very helpful so that can be shared with health care providers. Are there any initiatives in this regard by the ICMR?	ICMR shares annual AMR surveillance data on ICMR website. This data is from tertiary care hospitals. ICMR has recently started an initiative to collect community data.
which antibiotics may be used in Covid19 cases?	Most common conditions in COVID patients are HAP, CAP, VAP and sepsis. Depending upon the local incidence of pathogens antibiograms of community or hospital, antibiotics should be used.
How can medical students help in reducing AMR? Especially pharmacists.	A medical student like a doctor and pharmacist can play a major role in creating awareness on AMR and rational use of antibiotic. Doctors and pharmacist are front-line works as far as health is concerned and they play an important role in advocating antibiotic stewardship.

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Where would you like to be in a year or two with Bugworks?	I hope we will be in phase 2 or early phase 3 pneumonia indication in 3 years time and already helping hard to treat DR cases
Does this cover education and focus on the environment (climate) favorizing spread? Does surveillance provide data on the online way to understand the mechanism of resistance? Does it covers also microbiome data collection given link with the composition of microbiome and immunity especially in young? Does your plan incorporate phages use? we were trying to give a hand with Dilip Mathai and Ravi Kumar (Bangalore) to expand resistance as you comment expanding to antiviral, antifungals, antiparasitic (malarial) and collection of microbiome data and storage of genomes apart a collection of data in cooperation with Apollo hospital and Pasteur Paris.	Yes, ICMR surveillance data provides information on mechanisms of resistance. Currently, there are no efforts on microbiome and immunity.
Clean water and environment, sanitation and increasing temperature favorizing proliferation of vector and vector born diseases as you mentioned - dengue, malaria. France developed with Australia strategy targeting also vector - Wolbachia. are you taking part in it?	Yes, the malaria team of ICMR is working on Wolbachia project
Antivirals (viruses but not only) are in a close relationship with cancer - long list of examples. Are you involved to access to medications and in-depth study of immunity and links virus (pathogens) and cancer and vaccines development (microbiome-derived or others)?	Sorry not able to respond to this query, but sounds like an interesting space worth looking into
Taking the example of COVID 19 apart serum institute there is strong and experience platform for vaccine and treatment and dg development and quality of laboratories are top (referring to Bangalore for example) Affordable innovation is maybe also to look in Ayurveda herbals and diaspora of India business leaders are heavily working in this path for various therapeutic areas	These can be looked into once ready.

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Agree 200% that India is a leader in manufacturing, dg, vaccines possibilities but what is spectacular working jointly regionally - Australia, Pakistan science and mds, japan, France (new Caledonia) but also with Africa, South America, Europe. Bugs are old organism and very adaptable hence developing in parallel alternatives like phages, vaccines, taking care of the environment and use in animals, ongoing surveillance and understanding of the mechanism of resistance as you said is essential. this along with immunity - condition with nutrition and clean water/sanitation and education of population going to school and families, e.g. non-medical part of the population	Yes, the introduction of vaccines and WASH strategy can add to reducing unnecessary antimicrobial use in communities.
Gram resistance - and as worked on new treatment where only colistin and tigecycline were effective is already causing 30 % death given NO OPTION, no treatment, no vaccines and in this interconnected world pathogens spreads quickly. It is a GLOBAL serious public health issue worth attention of economic sector, corporate social responsibility, governmental cooperation, clear strategy, preparedness from biosafety standpoint. As an example, cepi was created in 2017 to work on vaccines but preparedness and surveillance against pathogen X. Health and public health issues are prerequisites for economic growth along with living conditions (zoonosis, nutrition, clean water) Hope you agree?	Yes, the problem of AMR has many intertwined socio-economic issues.
In China, bubonic was reported, and other pathogens due to permasol and climate temperature pose a risk to see a resurgence of old pathogens like variola...this worth urgent global and regional tangible plan to be prepared and to learn from COVID lessons. before was SARS, MERS, Ebola. We must do better - private, governments (G20 put healthcare already on agendas and should be part of all economic agendas - public health as a priority of XXI century)	G20 Health and Finance ministers need to meet as soon as COVID-19 settles down, to commit real monies towards AMR marketplace, without which this space will continue to see bankruptcies. I have suggested to the WHO AMR section that they should take the leadership in pulling the G20 together on this cause.

Remaining audience questions from Anand Anandkumar and Kamini Walia's webinar 'The challenges and opportunities for antimicrobial R&D in low- and middle-income countries – India case study', broadcast on 9 July 2020

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Finally, faecal transplantation we experienced in France (before targeted intervention based on the sampling of faecal and adjusting as personalised medicine - see French society nahibu) is another option to decrease carriage of pathogens. But phages are a really good alternative as well and India already evaluated phages in tuberculosis and collaboration with other countries was already established in Europe this is a very promising stream discussed with regulators. DG, treatment (considering microbiome)? VACCINES, phages...all alternatives along with regional and global online surveillance allowing analysis of genomics and PREPAREDNESS for any kind of unprecedented crisis we live today.	Thanks for the comment. This is worth looking into, in India and globally.
Hi there, lovely presentations, when I visited India last year and toured several institutes and companies, I was left with the impression that India has some AMR infection issues which are not so important in the west (yet!) leading to a lack of investment in new global solutions. What are your thoughts?	Yes, there is a general lack of investment for R&D and certainly for AMR. Bugworks was fortunate to get support from DBT via grants and local ecosystem being provided to us (CCAMP), but a long way to go to get this space truly properly funded.
Great presentations, thank you. My question is for Anand. What do you think of Jim O Neil's view that we might have to consider the alternative for a completely publicly owned antibiotic producer?	I actually really appreciate Jim's thought processes in this regards. However, we have very little precedence for public institutions successfully driving drug delivery and hence I don't think this will work. I would rather that the top pharma and top governments of the world fund pull incentives to help SME's cross the line, then markets will take over