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July 9, 2018

Haileyesus Getahun, MD, PhD, MPH

Coordinator and Head

UN Interagency Coordination Group on AMR Secretariat

Avenue Appia 20

1211 Geneva 27

Switzerland

Dear Dr. Getahun:

The Infectious Diseases Society of America (IDSAs) greatly appreciates the work of the Interagency Coordination Group (IACG) on Antimicrobial Resistance (AMR) and the opportunity to help inform its efforts. IDSAs represents over 11,000 physicians and scientists. Our members care for patients with or at risk of infectious caused by multidrug resistant organisms; lead antimicrobial stewardship programs and infection prevention and control programs; conduct basic, translational and clinical research on AMR and on the development of new vaccines, diagnostics and therapeutics; and drive public health interventions to prevent, detect and track resistance.

IDSAs strongly supports international efforts to advance comprehensive solutions to AMR, including stimulating research and development for urgently needed new antibiotics and diagnostics, implementing infection prevention and stewardship programs, and strengthening surveillance. IDSAs has been sounding the alarm on AMR for well over a decade and has helped inform, advance and secure federal funding for the US National Action Plan on Combating Antibiotic Resistant Bacteria. We continue working to advance antibiotic research and development (R&D) incentives in the US Congress. IDSAs is eager to assist the IACG, World Health Organization (WHO) or other global partners on any aspect of global AMR efforts. Below please find responses to questions posed by the IACG.

Research & Development

How could R&D funding be better channeled?

It is important to direct limited resources to the areas of greatest unmet medical need—serious or life-threatening infections with few or no existing treatments. The WHO Priority Pathogen List provides a good set of targets for R&D. New agents with activity against these pathogens would be tremendously beneficial for patients. Well-defined, predictable targets are essential to encourage private investment in antibiotic R&D.

What will it take to increase and sustain donor and private funding of R&D in AMR?

There is currently little to no opportunity for industry and investors to earn a return on investment for antibiotic R&D. Traditional models reliant on high sales volume of a new drug are not feasible for an antibiotic, as public health realities demand that antibiotics be used judiciously. A “pull” incentive that provides a predictable return on investment that is de-linked from antibiotic sales and use is necessary to spur R&D.

While many conversations about incentives are focused on antibiotics, it is also important to spur the development and appropriate use of rapid diagnostics. Diagnostic tests are essential for guiding appropriate antibiotic use, but diagnostic developers face a host of challenges in developing tests (including securing specimens and expert laboratories for validation as well as regulatory burdens). Once a diagnostic is approved, much more work is needed to ensure its clinical uptake.

Which incentives and de-linkage mechanisms could best address each of the challenges and barriers identified?

Push and pull incentives are needed to support early discovery and the full spectrum of clinical development of new antibiotics. Predictability is a priority, and multi-year funding arrangements can be powerful push incentives. Efforts such as CARB-X are very important push incentives, and more resources should be invested into these approaches.

However, it will remain challenging to draw more pharmaceutical company and venture capital resources to antibiotic R&D without a strong pull incentive. IDSA and others have proposed a market entry reward that would be paid out over a period of years to an antibiotic developer. In return, the developer would need to commit to antibiotic stewardship and access for those who truly need the drug.

Research and modeling conducted by DRIVE-AB—a project of the European Union’s Innovative Medicines Initiative involving multiple countries, academic institutions, and industry— developed the following estimates to demonstrate the likely impact of market entry rewards for new antibiotics that target a WHO priority pathogen.

Post-Approval Payments	Total New Antibiotics for Unmet Needs Over 30 Years	First in Class New Antibiotics*for Unmet Needs Over 30 Years
\$0	23	4
\$400 million	27	6
\$600 million	46	11
\$1 billion	74	19

*First-in-class, new antimicrobials are especially sought as they are the most likely to have durable efficacy against multidrug resistant organisms

How should the design of incentive mechanisms be coordinated at global, regional and national levels?

At a global level, it would be useful to build agreement upon the same or similar target pathogens. As discussed above, the WHO Priority Pathogen List is an appropriate start. This agreement will provide clarity and predictability for developers and ensure that incentives are targeted to the areas of greatest unmet medical need.

There are other opportunities for international collaboration that should be further explored. For example, clinical trial networks across multiple country sites may facilitate studies of new drugs with more speed and less cost. To maximize the potential of such an approach it would be important to streamline administrative processes for each site. It would also be useful to provide further opportunities for cross-approval of antibiotics by different regulatory bodies (e.g. the U.S. Food and Drug Administration and the European Medicines Agency) using data from multi-country studies to approve drugs more rapidly. Current attempts to do so are hindered for many indications by different regulatory agencies' guidance documents for the appropriate trial endpoints.

While it is important to aim for global coordination to ensure that priorities are accurately reflective of global needs and to leverage resources and strengths wherever possible, we must also recognize that some nations may be able to act more quickly than others or may need to utilize different financing mechanisms. We should not allow the push for multi-national coordination to slow or stymie progress

Access

Are there other mechanisms that should be considered to expand access to AMR-related health technologies and address the challenges identified?

Access for new and existing technologies, including vaccines, diagnostics and antibiotics, is an essential component of the broader strategy to combat AMR. Access to antimicrobial drugs in particular poses some unique challenges due to the need for stewardship. Currently, over the counter availability of antibiotics in some countries is leading to significant misuse and overuse of these precious drugs. Efforts to expand access to antimicrobial drugs must be coupled with efforts to ensure a stable workforce of healthcare providers in all countries who are trained on appropriate antibiotic use.

R&D and Access

How should the guiding principles (global public benefit, equity, gaps in response, value for money) be operationalized?

As discussed above, it is important to focus new incentives for antibiotic R&D on the WHO Priority Pathogen List to ensure that funding is aimed toward the most serious gaps and toward products that will provide the greatest public benefit. Wherever feasible, incentives should be de-linked from sales volume or use, to ensure that developers have the opportunity for ROI without compromising appropriate use or access. IDSA also recommends that developers receiving

incentives should be required to make commitments regarding stewardship and appropriate access.

One Health Approach in the Context of R&D and Access

How and which organization(s) could take the lead to ensure that the next generation of scientists is trained in the One Health approach and that sufficient resources are allocated to attract researchers?

WHO should take the lead given its expertise and ongoing efforts in the global AMR response. Without WHO's leadership, continued progress would likely be at risk. Collaborative centers that include multiple institutions across multiple countries may be a cost-efficient way to provide sustained paths for AMR researchers.

IDSA is dedicated to ensuring the next generation of scientists to address infectious diseases threats, including AMR. We routinely lobby the US Congress to increase funding for biomedical research to attract new scientists. We host an annual meeting with the National Institutes of Health for medical students, residents and fellows interested in pursuing an ID research career to provide them with opportunities to engage with senior researchers and to learn about career development. We also provide mentorship opportunities at **IDWeek**, our annual scientific meeting, and provide research funding to support young investigators. We would welcome the opportunity to explore more global engagement on supporting the next generation of scientists and attracting more AMR researchers.

National Action Plans

What support do Member States need to build AMR-specific and AMR-sensitive activities into national strategies for public health, animal health, plant health, food security and sustainable economic development?

Stakeholders in member states need support to bring AMR to their national agendas. While health ministers in many countries are already engaged, the World Organization for Animal Health (OIE) and the Food and Animal Organization of the United Nations (FAO) should help bring additional relevant ministers to the table.

Member States also need help to make a compelling economic case for animal and environmental health and AMR. More data is needed to demonstrate the economic reasons for investments in combating AMR, including how investments can be made in an affordable and feasible manner and the economic costs of inaction. These data should be communicated in a clear manner that is compelling to the public. Increasing public pressure on individual governments will be an important tool to advance AMR solutions.

WHO, OIE and FAO should provide additional opportunities for stakeholders within various countries to discuss common challenges and share lessons learned. IDSA conducted successful advocacy campaigns in the US to advance several AMR activities on the national agenda, and we would welcome the opportunity to share our insights and learn from others.

What forces maintain national responses to AMR in silos, and how can we overcome them?

The political silos at country level make national responses to AMR fragmented. FAO and OIE, as well as UN environment (which should significantly increase its response and involvement in the global AMR agenda) have a significant role to play in bringing relevant ministers to the AMR table with ministries of health. Economic cases will also assist in breaking down political silos at country level.

How can AMR be integrated into the plans and budgets of governments and, where appropriate, development partners?

AMR is a cross-cutting issue that spans multiple sectors as well as multiple Sustainable Development Goals (SDGs). Failure to successfully address AMR will have devastating impacts for health systems, public health, food supply and even entire economies. Leveraging the SDGs and SDG agendas can get help secure additional funding for AMR activities across different sectors.

What is the role of the international community in supporting international public goods such as AMR surveillance data?

Global AMR surveillance data is absolutely essential for the international community, especially within the Global Health Security Agenda. Without these data, we cannot effectively target interventions or evaluate their impact. Increased investments in infrastructure and training for public health practitioners and other implementers at the country level are needed to support good quality national surveillance data that spans the human, animal and environmental sectors.

What are the highest priorities for training in Member States with respect to NAP implementation?

Stewardship in human and animal health and surveillance are high priorities for training. These activities are essential in all countries to effectively identify and track AMR and to promote appropriate use of antibiotics. Within human health, it is distressing that antibiotics are still available over the counter in some countries. In order to remedy this substantial challenge, efforts to ensure the availability of health care providers trained in appropriate antibiotic use will be essential. Even in countries with large numbers of healthcare providers, many still lack stewardship training.

In the US, IDSA is launching a new curriculum to train all infectious diseases fellows on stewardship. Some of our members are utilizing telemedicine or other means to provide stewardship training to providers in other countries. We would welcome the opportunity to connect with additional providers in other countries to provide support wherever it may be useful.

What platforms would be most useful for sharing success stories, examples of best practice and lessons from experience in NAP development and implementation?

Online platforms such as the community of practice for National Action Plan development hosted by WHO is a very useful example. Such communities should be made available to individuals involved in the animal health sector of NAP development. Additional topics that can be explored include securing national funding to support NAP implementation, and breaking silos in AMR response on the national level.

Surveillance

What are the opportunities for, and obstacles to, integrating data analyses within and across sectors?

Obstacles include the diverse backgrounds and varying levels of expertise in different countries. This difference is very pronounced in the animal and agricultural sector where very little surveillance is done globally. Lack of agreement on antibiotic consumption indicators is another challenge for appropriate monitoring.

What further support do countries that are establishing surveillance systems need (in addition to existing tools) to implement a national surveillance system for AMR and AMU?

Through the Global Health Security Agenda, the US and other countries and partners are providing resources to help low- and middle-income countries establish surveillance systems for AMR and other emerging infectious disease threats. US funding for the GHSA is scheduled to end in 2019 unless the US government acts to extend it. IDSA is advocating for continued investment, and urges other partners to continue investing as well.

What more can be done to facilitate the surveillance of falsified and substandard medicines in the human, animal and plant sectors and leverage the resulting data?

Further training and increased laboratory capacities in all sectors to identify counterfeit, falsified and substandard meds is essential. Regional cooperation can be leveraged for an improved surveillance platform.

What support do Member States need to strengthen national surveillance systems and improve the quality, collection and submission of their data to global surveillance databases?

Additional financial resources are needed to support these activities. For example: in the US the National Action Plan sets a goal for the vast majority of hospitals to report antibiotic use and resistance data to the Centers for Disease Control and Prevention National Healthcare Safety Network by 2020. Unfortunately, progress on this metric has been very slow. This program at CDC has not received the increased funding necessary to provide the technical support that healthcare facilities need to begin reporting. IDSA continues to advocate for these resources.

What more can be done to harmonize collection of data on AMR and AMU among sectors and levels?

Multinational agreement on antimicrobial use measures and a global antimicrobial use index would allow for comparison across countries and sectors (human, animal, environmental). Such measures would also allow for targets to be set and progress to be measured. As data collection and reporting hopefully drive all countries to reduce inappropriate use, we must also be cautious to ensure that appropriate access to antibiotics is not impeded.

What additional work is needed on methods for testing antimicrobial susceptibility or to include new technologies in existing systems (e.g. WGS)?

Currently there may be a significant gap between when a new antibiotic is approved and when antimicrobial susceptibility testing guidelines are made available to clinical microbiology laboratories. Pharmaceutical companies and test developers must be supported in their efforts to work together to coordinate development. Regulatory barriers to susceptibility test device development must be addressed. Incentives should be provided to susceptibility test developers to begin test development earlier in the process in order to address the higher level of risk assumed by beginning to develop a test before the antibiotic has received regulatory approval.

What tools are required to address the investment required for surveillance of AMR and AMU?

We need to develop and publicize a strong economic case in support of AMR surveillance in order to drive increased interest in investment by additional countries and non-government donors. Better economic arguments can also help sustain investment in the Global Health Security Agenda, which is supporting the establishment of surveillance systems.

What support do countries require to develop and report accurate national data and share them on global surveillance systems?

Many countries require training for health providers and public health practitioners to learn how to conduct surveillance. Additional investments in sustainable surveillance platforms is also needed.

Once again, IDSA thanks all members of the IACG for your commitment to advancing robust global efforts to address AMR. We look forward to additional opportunities to assist with this important work.

Sincerely,

A handwritten signature in black ink, appearing to read "Paul G. Auwaerter". The signature is fluid and cursive, with a long horizontal stroke at the end.

Paul G. Auwaerter, MD, MBA, FIDSA
President, IDSA