CIDRAP Antimicrobial Stewardship Project (ASP)

Quarterly Policy Update: April 2019

A continuation of our series on current policy issues regarding antimicrobial stewardship and the threat of antimicrobial resistance (AMR), this update provides a broad overview of recent policy changes, initiatives, and new findings that have impact on policy decisions. We welcome your feedback on any of the issues addressed in this series. If you have comments or suggestions, please share your thoughts with CIDRAP's ASP project team via Twitter at @CIDRAP_ASP or email at asp-cidrap@umn.edu.

UK aims to cut antibiotics 15% in 5-year AMR plan

In January, the UK government released a new 5- year plan (2019 – 2024) to tackle AMR in three key ways: reduce drug-resistant infections, cut human and animal antibiotic use, and provide incentives to pharmaceutical companies for developing new antibiotics.

The national plan calls for a 10% reduction in the number of antibiotic-resistant infections in people by 2025, a 15% decrease in human antibiotic use by 2024, and a 25% decrease in the use of antibiotics in food-producing animals by 2020. To encourage development of new antibiotics, the government will test a new payment model that will reimburse pharmaceutical companies based on how valuable their drugs are to the National Health Service (NHS), rather than on the quantity of antibiotics sold.

The plan aims to build on the success of the previous UK 5-year AMR strategy, which was launched in 2013 with the aim of improving knowledge and understanding of AMR, conserving antibiotics, and stimulating development of new treatments for drug-resistant infections. Since 2013, sales of veterinary antibiotics in the United Kingdom have fallen by 40%, with sales of medically important antibiotics falling by 52%. In addition, human antibiotic use fell by more than 7% from 2014 to 2017.

The newest AMR strategy builds upon a 20-year vision for AMR, in which resistance is effectively contained and controlled using a "One-Health" approach.

10 threats to global health

In January, the World Health Organization (WHO) released its 10 threats to global health in 2019. AMR was included as one of the threats, specifically resistance to tuberculosis drugs and the overuse of antimicrobials in animal agriculture.

Letter urges congressional action to stimulate antibiotic development

In February, a coalition of drug makers, infectious disease experts, and public health advocates called on US lawmakers to pass measures that could "jump-start" the development of critically needed antibiotics.

The coalition comprises stakeholders from large and small pharmaceutical companies and organizations, including the Infectious Diseases Society of America (IDSA), the Pew Charitable Trusts, and Trust for America's Health.

The main issue addressed in the letter is the lack of economic incentive for making new antibodies. Currently, only 42 antibiotics are in clinical development, a fraction of the 1,000-plus cancer drugs currently in development. Because the current drug reimbursement system links profits to the volume of drugs sold, drug companies don't get as significant of a return on antibiotics as compared to drugs for chronic conditions. Recently, large drug companies, including AstraZeneca, Sanofi, and Novartis, have abandoned their antibiotic development programs in favor of more lucrative programs.

The letter proposes a new range of economic incentives be enacted to spur antibiotic investment, including "pull" incentives to increase the value of new antibiotics and changes in how pharmaceutical companies are reimbursed for antibiotics.

UN committee publishes AMR recommendations, seeks input

In January, the Ad hoc Interagency Coordination Group (IACG) on AMR published its draft recommendations on AMR. The UN secretary-general convened the IACG in March 2017 to provide practical guidance for approaches needed to ensure sustained effective global action to address AMR.

The draft recommendations identified five broad areas that most urgently require action: (1) Accelerate progress in countries; (2) Innovate to secure the future; (3) Collaborate for more effective action; (4) Invest for a sustainable response; and (5) Strengthen global accountability and governance.

The deadline for submitting feedback on the recommendations was February 19. A summary of the feedback can be read here. The final report will be submitted to the UN secretary-general this month.

First review of pre-clinical pipeline underway

The World Health Organization (WHO) and the Global Antibiotic Research & Development Partnership (GARDP) are undertaking the first global review of the pre-clinical pipeline to target drug-resistant bacteria, with the intent to make details available via an open-source repository, shape research and development investment, and ensure drug affordability and access. Companies, institutions, and individuals were encouraged to submit their data on pre-clinical pipeline products that target the WHO Priority Pathogens, tuberculosis, and *Clostridioides difficile* by March 18.

Novartis shares data from discontinued antibiotics program

The Pew Charitable Trusts announced in January that Novartis has shared data from its discontinued antibiotics development program on Pew's open-access database, known as SPARK (Shared Platform for Antibiotic Research and Knowledge).

Achaogen also committed in October to provide SPARK with data from its own discontinued antibiotic research program. SPARK aims to "help spur basic scientific research to overcome barriers preventing the development of new antibiotics." The free, interactive resource allows scientists around the world to learn from past research and share information. Novartis shared data on discontinued antibacterial programs that explored new ways to attack gram-negative bacteria.

Progress in Antimicrobial Stewardship

Study evaluates stewardship uptake, antimicrobial usage in England

Researchers with Public Health England (PHE) report that a survey of England's NHS hospitals found that the vast majority have made progress in establishing antimicrobial stewardship programs (ASPs), but many lack senior leadership and dedicated funding, and there was no significant correlation between stewardship scores and antimicrobial usage.

Canadian resistance surveillance shows progress, remaining challenges

The Public Health Agency of Canada released the 2016 Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS) Annual Report, which found that while the overall quantity of antimicrobials intended for use in animals had decreased, the number of *Salmonella* isolates resistant to five or more antimicrobial classes continued to rise.

New dashboard provides overview of investment in antimicrobial resistance research

The Joint Programming Initiative on AMR (JPIAMR) has published a Research Funding Dashboard, which allows users to explore data on grants by agency, country, and research area, and includes funding data for the year 2017 from 22 JPIAMR member countries, the European Comission, and the Wellcome Trust.

WHO publishes proceedings from meeting on antibiotic shortages

The WHO published a report summarizing a meeting last year in Oslo regarding antibiotic shortages and their magnitude, causes, and possible solutions. Antibiotic shortages can have an adverse impact on stewardship due to the creation of treatment guidelines based upon which antibiotics are available in a country.

Pooled data show pharmacists' input helpful in stewardship programs

A meta-analysis of 15 studies in the *Journal of Antimicrobial Chemotherapy* concluded that ASPs involving pharmacists are effective in decreasing antibiotic prescribing and increasing guideline-adherent antibiotic prescribing by general practitioners.

Review of hospital stewardship programs finds economic impacts

A systematic review of previous research suggests that hospital ASPs help save costs by decreasing length of stay and antibiotic expenditures.

Guidelines

WHO releases methodology for point prevalence surveys on antibiotic use

The WHO released guidance on methodology for conducting point-prevalence surveys on antibiotic use in hospitals.

UK updates antimicrobial prescribing guidance for common infections

The UK National Institute for Health and Care Excellence updated its summary table of antimicrobial prescribing guidance for common infections to reflect recent changes to recommendations for acute cough and bronchitis, influenza, suspected meningococcal disease, *Helicobacter pylori*, chlamydia, *Neisseria gonorrhoeae*, pelvic inflammatory disease, leg ulcer, and dermatophyte infection.

FDA releases guidance on coordinated development of antimicrobial drugs and testing devices

The US Food & Drug Administration (FDA) released finalized guidance on coordinated development of antimicrobial drugs and antimicrobial susceptibility test devices. The draft of the guidance was issued in September 2016.

Guidelines for antibiotic prescribing in Indian ICUs

The Indian Critical Care Medicine Society has released national guidelines for antibiotic use in intensive care units (ICUs) in an effort to minimize the unneccessary use of antibiotics in hospitals.

Policy Commentary

Best practices, policy targets for action on antibiotic resistance in Europe

The Organisation for Economic Co-operation and Development (OECD) posted resources associated with the recent EU Health Ministerial Meeting on best practices for combating antimicrobial resistance, held in Bucharest in collaboration with the European Centre for Disease Prevention and Control, including slides from a keynote presentation given by OECD deputy secretary-general Ulrik Vestergaard Knudsen and a policy brief on avenues for action in Europe.

Antimicrobial resistance addressed at the World Economic Forum

In an article composed as part of the World Economic Forum Annual Meeting, Kristina Lagerstedt, PhD, MSc, discusses the importance of data sharing, technological development, and communication to address the spread of AMR.

Report: Antibiotic resistance, sustainable development are intertwined

A new report from ReAct and the Dag Hammerskjold Foundation calls for antibiotic resistance to be integrated into the sustainable development agenda.

The report, titled, "When the Drugs Don't Work: Antibiotic Resistance as a Global Development Problem," argues that if antibiotics continue to lose their effectiveness, efforts to achieve the United Nations' 2030 Agenda for Sustainable Development could be in jeopardy. Using data from the WHO, World Bank, and other sources, the report focuses on how antibiotic resistance could hinder efforts to eradicate poverty, promote economic growth, reduce inequality, fight hunger, improve public health, and protect the environment.

SIDP president urges action on antimicrobial stewardship and research

The Society of Infectious Diseases Pharmacists (SIDP) posted a full script of comments from SIDP President Kerry LaPlante, PharmD, who spoke to the US Presidential Advisory Council on Combating Antibiotic-Resistant Bacteria (PACCARB) and urged action for prioritizing the development of new antibiotics, protecting existing ones and advocated the inclusion of an infectious diseases pharmacist on PACCARB.

Presidential advisory council on resistance appoints new voting members

PACCARB announced that it has appointed four new voting members to serve on the council.

ReAct: 3 key political actions to combat antimicrobial resistance

ReAct details three political actions seen as necessary to prioritizing AMR as a global health threat during 2019.

5 priorities for antibiotic stewardship

In an article for the Pew Charitable Trusts, Kathryn Talkington, MPA, lists five priorities for improving antibiotic stewardship and development during 2019.

Partnerships

Joint Commission, Pfizer fund grants to boost stewardship in Asia-Pacific

The Joint Commission and drug company Pfizer announced the selection of six quality improvement projects to receive funding as part of a 2-year grant to improve antimicrobial stewardship in the Asia-Pacific region.

New European alliance aims to improve diagnosis, prevention and treatment of infectious disease

The European Clinical Research Alliance on Infectious Diseases (ECRAID) posted a presentation from Herman Goossens, MD, and Marc Bonten, MD, PhD, introducing the alliance, which aims to reduce the impact of infectious diseases on individual and population health by efficiently generating rigorous evidence for new or improved diagnosis, prevention, and treatment of infections and to better respond to infectious disease threats.

Fleming Fund selects UK partners for African stewardship program

The Fleming Fund, a UK government aid program to help low- and middle-income countries fight AMR, announced the 12 hospitals and research institutions that will work with partners in four African countries to promote antimicrobial stewardship.

CARB-X adds 6 new organizations to its Global Accelerator Network

The public-private partnership, Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator (CARB-X), announced it has added six new life sciences organizations from around the world, expanding its Global Accelerator Network to 10 groups.

Agriculture

EPA urged to deny proposal for more antibiotic spraying on citrus fields

The proposal would allow citrus growers to spray more than 650,000 lbs of streptomycin on citrus fields to treat the bacteria that cause citrus greening disease. Several groups contend that it does not cure the disease and would be an irresponsible use of an antibiotic that's considered critically important for human health by the WHO.

Use of antibiotics to promote growth in food animals down, OIE report says

The use of antimicrobials for growth promotion in food animals worldwide is down, and more nations are reporting specific data on the use of the drugs in livestock, according to the World Organization for Animal Health's (OIE's) third annual report on antimicrobial agents in animals.

Public-private effort launched to boost animal antimicrobial stewardship

The Foundation for Food and Agriculture Research (FFAR) announced a $15 million investment in the launch of the International Consortium for Antimicrobial Stewardship in Agriculture, a public-private partnership to advance research on antimicrobial stewardship in animal agriculture and improve animal health and welfare.

Commentary: The role of veterinarians in stewardship policy

In *Bovine Veterinarian*, Matthew J. Kuhn, DVM, describes the role that veterinarians can play in putting US policy regarding veterinary oversight of antibiotic sales and use into practice.

International coalition releases declaration for action on AMR in agriculture

The Antibiotic Resistance Coalition released the "Bangkok Declaration on Antimicrobial Resistance, Food Systems and Farming," which describes principles to guide global agricultural stewardship.

Antibiotic Development

IDSA notes antibiotic development progress, concerns for future

In an update to their 2013 antibiotic pipeline status report, experts from IDSA note that the number of new antibiotics approved by the FDA has reversed its previous decline. But they worry that, if the goal of 20 new antibiotics by 2020 (20 x '20) is achieved, it could mark the pinnacle of antibiotic development for years to come, according to their paper in *Clinical Infectious Diseases*.

CARB-X grant focuses on gram-negative superbugs

CARB-X announced an award of $4.4 million to Recida Therapeutics of Menlo Park, Calif., to develop a novel antibiotic targeting gram-negative superbugs.

CARB-X to fund new antibiotic for multidrug-resistant lung infections

CARB-X announced that it's awarding up to $5.7 million in funding to San Diego–based biotechnology company Forge Therapeutics to develop an antibiotic for lung infections caused by *Pseudomonas aeruginosa* and other multidrug-resistant gram-negative bacteria.

CARB-X to fund Polyphor's novel class of gram-negative antibiotics

CARB-X announced that it will award up to $2.6 million in funding to Swiss biopharmaceutical company Polyphor to develop a novel class of antibiotics to treat infections caused by gram-negative ESKAPE pathogens (*Escherichia coli*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *P aeruginosa*, and *Enterobacter* species).

CARB-X provides additional funds for phage lysin to treat Pseudomonas

ContraFect Corporation announced that it has received an additional $2.3 million in funding over the next 2 years from CARB-X for the development of a phage lysin therapy to treat drug-resistant *P aeruginosa* infections.

FDA clears first test for *Mycoplasma genitalium*

The FDA cleared a new test for diagnosing the common sexually transmitted infection, *Mycoplasma genitalium*, a step that could aid antibiotic stewardship efforts.

FDA grants Fast Track status to new *C difficile* antibiotic

The FDA has granted Fast Track designation to a new investigational antibiotic for *C difficile* infection.

FDA grants priority review for new TB drug

The TB Alliance is seeking approval of a drug as part of a regimen for the treatment of drug-resistant tuberculosis.

FDA approves New Drug Applications for Nabriva's pneumonia antibiotic

Nabriva Therapeutics of Dublin announced that the FDA has accepted its New Drug Applications (NDAs) and granted priority review for both the oral and intravenous formulations of lefamulin, a first-in-class, semi-synthetic pleuromutilin antibiotic for treating community-acquired bacterial pneumonia.

FDA to review new treatments for urinary tract infections, pneumonia

Merck announced that the FDA has accepted for priority review a NDA for the combination of relebactam and imipenem/cilastatin and a supplemental NDA for Zerbaxa (ceftolozane and tazobactam).