

Declaration by the Pharmaceutical, Biotechnology and Diagnostics Industries on Combating Antimicrobial Resistance

January 2016

Antimicrobials, and specifically antibiotics, play a crucial role in modern medicine. These precious medicines are often taken for granted and are not only necessary to treat life-threatening infections, but are also vital to underpin most common surgical procedures and many chronic treatments such as chemotherapy and HIV and transplant medicines. They also play a crucial role in the health of animals.

The increase in bacterial resistance to antibiotics has been dramatic, and combating this growth is a top priority for global policy and public health. There is a particular concern that antibiotics are losing effectiveness faster than they are being replaced by new, innovative drugs, including both antibiotics and alternative non-antibiotic approaches to treating and preventing infections.

This innovation gap has been examined extensively and is widely acknowledged to be the result of a combination of scientific as well as commercial barriers that have impeded antibiotic development over a number of years. The scientific difficulties are formidable and traditional R&D approaches have largely failed: companies, private and public funders have invested billions of dollars over the last 20 years to discover new antibacterials, yet no new class of antibiotic for Gram-negative infections has reached approval in over 40 years.

This situation poses a unique set of challenges. We will always need a supply of innovative new antibiotics; all antibiotics need to be used cautiously to conserve their effects; and, in many countries, we still need to improve access to existing antibiotics.

We welcome the economic analysis of Jim O'Neill's Review on Antimicrobial Resistance (AMR), which quantifies both the costs and investments needed. The challenges are clearly substantial and call for transformational changes from many stakeholders. The pharmaceutical, biotechnology, and diagnostics industries have an important role to play, and we are committed to doing our part. Leadership from other sectors is also required, and we welcome the initiative of the Review on AMR, as well as the attention of governments and politicians world-wide (including the recent G7 Berlin declaration), and the leadership of key international organisations (WHO, OIE, FAO, ECDC, US CDC), public funding bodies (NIH, BARDA, the European Commission, and IMI), and charitable foundations (Wellcome Trust, BMGF, and Pew Charitable Trusts)*, amongst others.

We similarly welcome those steps already taken by key regulatory authorities around the world, such as the US Food and Drug Administration (FDA) and European Medicines Agency (EMA), to enable antibiotic development in advance of widespread resistance, and we support a continuation of these efforts to ensure greater harmonisation of regulatory processes internationally.

Taking collective action

We support the increasing recognition that the value assigned to antibiotics and diagnostics often does not reflect the benefits they bring to society, nor the investment required for their creation. Therefore, we call on governments to commit to allocating the funds needed to create a sustainable

* WHO – World Health Organization; OIE – World Organisation for Animal Health; FAO – Food and Agriculture Organisation of the United Nations; ECDC – European Centre for Disease Control; US CDC – United States Centers for Disease Control; NIH – US National Institutes of Health; BARDA – US Biomedical Advanced Research and Development Authority; IMI – European Innovative Medicines Initiative; BMGF – Bill & Melinda Gates Foundation.

and predictable market for these technologies while also implementing the measures needed to safeguard the effectiveness of antibiotics. Specifically:

- **Creating a sustainable and predictable market.** We call for governments to commit funding and support the development and implementation of transformational commercial models that (a) enhance conservation of new and existing antibiotics, while (b) improving financial and access-related predictability for both industry and health systems.
 - **Enhancing conservation.** We support measures for the prevention of infection along with conservation and appropriate use of all antibiotics, including:
 - Implementation of the WHO's Global Action Plan calling for comprehensive stewardship programmes and activities that enhance health system capability to use antibiotics appropriately.
 - Enhanced integration of fast and accurate point-of-care and laboratory diagnostics with antibiotics to ensure appropriate use of antibiotics for the patients who need them. To enable this, we call for improved reimbursement and use of advanced diagnostics.
 - Furthermore, we call for governments, insurers, healthcare providers and other health system stewards to remove financial incentives for individuals (such as doctors, veterinarians and pharmacists) or institutions that reward the prescribing of antibiotics in greater volumes.
 - **Improving financial and access-related predictability** for both Industry and health systems is required to ensure sustainable investment in new antibiotics and diagnostics. To this end, we welcome appropriate incentives, coupled with safeguards to sustain the effectiveness of new and existing antibiotics. We believe two fundamental approaches are needed to accomplish these goals:
 - We welcome proposals that (a) support reduction in the link between financial revenues for new antibiotics and the amount they get used while (b) mitigating the financial risk for both developers and health systems. As different jurisdictions may require different solutions, a range of approaches to creating such delinkage will likely need to be utilised. Possible approaches include the system of lump sum Market Entry Rewards proposed by the Review on AMR, insurance-like purchase models, and novel intellectual property-based approaches with appropriate safeguards. An integral part of these models is a reduced need for promotional activity from companies.
 - We also support the principle that in developed markets, prompt reimbursement decisions at prices that reflect value should be provided for new drugs and diagnostics to reflect the benefits they bring (with measures for stewardship to prevent misuse) – as also acknowledged in the work of the Review on AMR. This calls for funding to be allocated and for payers to appropriately assess and value innovative antibiotics and diagnostics, in line with the good progress that has been made by regulatory authorities.
 - **Global coordination, local action.** We call for a global commitment to coordinated action on stewardship, conservation, hygiene, and the creation and use of new commercial models for antibiotics and diagnostics. As noted above, we recognise different models may be appropriate for different countries, health systems, and

products. All parties should commit to allocating funding and finding paths that work for their situation. We are ready to work stepwise with countries to implement such models.

Commitments by signatory companies

The under-signed companies are already actively engaged in combating AMR as appropriate to their business. We stand ready to work in partnership with leading countries to deliver sustainable solutions to meet this global challenge. We invite other companies to join this Declaration and comments from all other stakeholders are welcome. We will review and update the Declaration every 2 years, to reflect progress and changing priorities.

We commit to:

Work to reduce the development of antimicrobial resistance

- We are committed to antibiotics only being used in patients who need them, we support continued education for clinical professionals on appropriate use, and we welcome the WHO Global Action Plan's focus on improved stewardship.
- We encourage infection control via improved hygiene, vaccination, and preventive treatments to help reduce the number of infections needing antibiotic treatment.
- We support measures to reduce environmental pollution from antibiotics, along with a 'one health' approach towards prudent and responsible use, including a global reduction of unnecessary antibiotic use in livestock, and we applaud moves from major food groups to work towards this goal.

Invest in R&D to meet public health needs with new innovative diagnostics & treatments

- We are investing in a range of innovative antibiotics, vaccines, alternative technologies, and diagnostics for resistant infections. We are advancing our pipelines, but more work and investment into multiple approaches is needed to overcome the significant scientific difficulties of antibiotic discovery.
- We will continue to support research in academia and SMEs on new and re-purposed antibiotics. We welcome proposals to increase investment via coordinated global routes in efforts to develop useful diagnostics, antibiotics, vaccines, and alternative technologies.
- We support new ways of working such as open collaborations between industry and public researchers to overcome the scientific challenges of creating new antibiotics and diagnostics. Collaborative public-private projects already demonstrate what we can achieve together, but more can be done: several companies co-established the New Drugs for Bad Bugs (ND4BB) programme as part of IMI with the European Commission and others are actively engaging in collaborations funded in the US by BARDA and the NIH.
- As acknowledged, the value assigned to antibiotics and diagnostics often does not reflect the investment required for their creation or the benefits they bring to society, and we stand ready to work with payers and policymakers on new valuation mechanisms and commercial models that specifically address the unique challenges of this market.

Improve access to high-quality antibiotics and ensuring that new ones are available to all

- As part of the WHO Global Action Plan's proposal for a comprehensive program of sanitation, hygiene, vaccination, infection control, education, and stewardship, we support mechanisms to ensure affordable access to new and existing antibiotics to the patients who need them, in all parts of the world and at all levels of income.
- We recognise the success of programmes to improve global access to drugs in HIV, TB, and malaria and call for a similar collaborative effort to address issues of access to antibiotics.

Signatories – as at April 1, 2016

Pharmaceutical and biotechnology companies

ABAC Therapeutics, Spain
Abgentis Ltd., United Kingdom
Absynth Biologics Limited, United Kingdom
Achaogen Inc., United States
Actelion Ltd., Switzerland
Aequor Inc., United States
AiCuris Anti-infective Cures GmbH, Germany
Alaxia Pharma, France
Allecrea Therapeutics, Germany
Antabio, France
AntibioTx ApS, Denmark
Arsanis, Austria
AstraZeneca plc, United Kingdom
Auspherix Limited, United Kingdom
BioFilm Control, France
BioVersys AG, Switzerland
Biovertis AG, Austria
Blueberry Therapeutics Ltd., United Kingdom
Cantab Anti-infectives Ltd., United Kingdom
Cardeas Pharma, United States
Cempra Inc., United States
Chemical Biology Ventures Ltd., United Kingdom
Cipla Ltd., India
Contrafect, United States
Da Volterra, France
Deinobiotics, France
Destiny Pharma Ltd., United Kingdom
Dipexium Pharmaceuticals, United States
Discuva Ltd., United Kingdom
DSM Sinochem Pharmaceuticals, Netherlands
Eligo Bioscience, France
Entasis Therapeutics, United States
Evotec, Germany
F. Hoffmann-La Roche AG., Switzerland
Fedora Pharmaceuticals Inc., Canada
GlaxoSmithKline plc, United Kingdom
Helperby Therapeutics plc, United Kingdom
IMMT, Slovenia
iNtRON Biotechnology, Inc., Korea
Johnson & Johnson, United States
Laboratorios Cinfa, Spain
Lamellar Biomedical Ltd., United Kingdom
MaaT Pharma, France
Macrolide Pharmaceuticals Inc., United States
Meiji Seika Pharma Co., Ltd., Japan
Melinta Therapeutics, Inc., United States
Merck & Co., Inc., Kenilworth, New Jersey, U.S.A
Merck, Germany
MGB Biopharma Ltd., United Kingdom
Microbion Corporation, United States
MicuRx Pharmaceuticals Inc., China and United States
Motif Bio, United States
Mutabilis, France
Nabriva Therapeutics AG, Austria
NAICONS, Italy
Nexgen Bio, United States
Northern Antibiotics Ltd., Finland
Nosopharm, France
NovaBiotics, United Kingdom
NovaDigm Therapeutics, Inc., United States
Novartis AG, Switzerland
OJBio Ltd., United Kingdom
OLMIX Group, France
Otsuka, Japan
Pfizer Inc., United States
PHARMA VAM Ltd., Russia
Pherecydes Pharma, France
Phico Therapeutics Ltd., United Kingdom
Polyphor AG, Switzerland
Redx Pharma plc, United Kingdom
Sanofi S.A., France
SetLance, Italy
SETUBIO S.A., France
Shionogi & Co. Ltd., Japan
Spero Therapeutics, LLC, United States
Synamp Pharmaceuticals B.V., The Netherlands
Synthetic Genomics, United States
TechnoPhage, Portugal
Tetraphase Pharmaceuticals, United States
The Medicines Company, United States
VenatoRx Pharmaceuticals Inc., United States
VibioSphen, France
Vitas Pharma Ltd., India
Wockhardt Ltd., India

Diagnostic companies

Alere Inc., United States
bioMérieux SA, France
BD, United States
Cepheid, United States
Curetis AG, Germany
F. Hoffman-La Roche Ltd., Switzerland
HemoCue AB, Sweden
Hyra Biosciences (Pty) Ltd., South Africa
LabCorp, US
Mobidiag Oy Ltd., Finland
Momentum Bioscience Ltd., United Kingdom
QuantuMDx Ltd., United Kingdom
Spectromics, United Kingdom
Thermo Fisher Scientific, United States

Industry Associations

We support the aims of the Declaration signed by our Member companies and look to work with all stakeholders to help deliver its objectives.

Alliance of Biopharmaceutical companies from Europe innovating in Anti-Microbial resistance research (BEAM Alliance)
Association of the British Pharmaceutical Industry (ABPI)
Antimicrobial Innovation Alliance (AIA)
British Generic Manufacturers Association (BGMA)
The British In Vitro Diagnostics Association (BIVDA)
European Federation of Pharmaceutical Industries and Associations (EFPIA)
European Generic and Biosimilar Medicines Association (EGA)
International Federation of Pharmaceutical Manufacturers Association (IFPMA)
The German Association of Research-Based Pharmaceutical Companies (VFA)
Japan Pharmaceutical Manufacturers Association (JPMA)
The UK BioIndustry Association (BIA)