DRIVE-AB
DRIVING RE-INVESTMENT IN R&D AND RESPONSIBLE ANTIBIOTIC USE

Innovative Medicines Initiative (IMI): IMI is a joint undertaking between the European Union and the European pharmaceutical industry association EFPIA

Public partners	Private partners
University of Geneva, Switzerland	AstraZeneca
Radboud University Medical Center, The Netherlands	GSK
Tel Aviv Sourasky Medical Center, Israel	Roche
Norwegian Institute of Public Health	Cubist
Center for Anti-Infective Agents, Austria	Astellas
British Society of Antimicrobial Chemotherapy, United Kingdom	Sanofi-Aventis
University Hospital Rijeka, Croatia	Pfizer
University of Lorraine, France	
University of Antwerp, Belgium	
University of Strathclyde, United Kingdom	
Uppsala University, Sweden	
Universitätsklinikum Tübingen, Germany	
Wageningen University, The Netherlands	
Heidelberg University, Germany	
London School of Economics, United Kingdom	
Chatham House, United Kingdom	

Abstract

Antimicrobial resistance (AMR) is widespread. Its global human and economic burden is tremendous and increasing annually. Yet today only four among scores of pharmaceutical companies retain active antibacterial drug discovery programmes; a mere two of these have a novel antibiotic in phase 2 development. While the elaboration of antibiotics with novel mechanisms of action is scientifically complex, the chief challenge is diminishing incentives. Pre-market regulatory requirements and increased control on post-market access, use, and pricing of new antibiotics are strong deterrents to drug development. Meanwhile, healthcare payers are not currently prepared to reimburse antibiotics at prices that would support the cost of development.

Applied to antibiotics, a simple sales-based economic model contradicts the public health mandate to reduce their consumption in order to preserve their efficacy. Alternative models that can create incentives for the discovery of novel antibiotics and yet reconcile these incentives with responsible antibiotic use are long overdue.

The multidisciplinary and multi-stakeholder DRIVE-AB consortium, composed of 16 public and 7 private partners from 12 countries, will produce such models in a stepwise yet interconnected process. First, we will develop an evidence-based, consensus definition for “responsible antibiotic use,” which, with its standardised quality and quantity indicators, will provide the framework for all later steps. Next, data from surveillance systems, antibiotic prescription databases, and published literature will inform estimations of the present burden of antibiotic resistance from both clinical and economic perspectives across varying socioeconomic backdrops. Simulation models informed by these data as well as data from past and ongoing epidemics will estimate future public health needs and impact related to AMR, again in diverse socioeconomic settings.

Together these constructs will allow for valuation models that will estimate the true value of new and existing antibiotics from the perspectives of patients, physicians, payers, and society as a whole. These, in turn, will inform the creation of alternative economic strategies and reward models that will promote and sustain the development of new antibiotics while simultaneously bolstering appropriate consumption of existing antibiotics. The most promising schemes will be presented to policymakers and other stakeholders with attendant implementation and risk-management strategies.

This ambitious project will not succeed if it is developed and championed merely by one sector of society, be it academia, “big pharma,” or public health. The robustness and applicability of the proposed alternative models will only be proportional to their level of input from all involved players. All work from beginning to end will be performed in close collaboration with the consortium’s stakeholder partners, which run the gamut from patients and clinical societies to small- and medium-sized enterprises, large pharmaceutical companies, healthcare payers, public health officials, and government officials. The DRIVE-AB consortium will dedicate considerable resources to this collaboration and to the final dissemination of information to policymakers and the wider public.

Academic Consortium

Coordinator: Stephan Harbarth (University of Geneva)

WP1A: Define "responsible" use of antibiotics
Inge C. Gyssens, Radboud University Medical Center, The Netherlands

Partners: M. Hulscher, J. Schouten, Bart-Jan Kullberg (Radboud University Medical Center), V. Vlahović- Palčevski (University Hospital Rijeka), C. Pulcini (University of Lorraine), H. Goossens, N. Adriaenssens (University of Antwerp), S. Harbarth and B. Huttner (University of Geneva), N. Brown, L. Piddock (British Society of Antimicrobial Chemotherapy)

1. Compile and assess all definitions and metrics of responsible use across diverse socioeconomic, geographic and clinical settings
2. Systematically review the variation in antibiotic use, analysing barriers to and enablers of responsible use
3. Develop a conceptual framework for a standard of responsible use

WP1B: Set, communicate and revise public health priorities
Yehuda Carmeli, Tel Aviv Sourasky Medical Center, Israel

Partners: E. Tacconelli (Universitätsklinikum Tübingen, Germany)

1. Develop mathematical prediction models of multidrug-resistant pathogen spread from first detection to established endemicity
2. Determine the clinical impact of emerging MDR pathogens and AMR and to generalize the impact across various settings
3. Expand the agent-based predictive mathematical model developed in Aim 1 to predict the impact of propagation of MDROs in order to estimate the need for new antibiotics
4. Engage with stakeholders to communicate the models' results

W1C: Develop antibiotic valuation models
Ramanan Laxminarayan, University of Strathclyde, United Kingdom

Partners: J. Wesseler, Dusan Drabik (Wageningen University), T. Göschl (Heidelberg University), Roger Cooke, Alec Morton, Tim Bedford (University of Strathclyde)

1. Quantify the economic consequences of AMR from the perspectives of patient, health care providers and society as a starting point for valuing new antibiotics
2. Develop novel valuation models that will quantify the value of new antibiotics from the perspectives of patients, physicians, payers and society as a whole
3. Evaluate the sensitivity of valuations to alternative models of new antibiotic incentives models and drug development
4. Implement the models developed in Aim 2 to provide broad estimates of economic value of effective antibiotics by categories of antibiotics to develop four valuation cases based on hypothetical new antibiotics
5. Conduct extensive sensitivity analyses to test robustness of new antibiotics valuation to changes in regulatory and market environment

WP2: Create, test and validate new economic models

John-Arne Røttingen, Norwegian Institute of Public Health, Norway
Francesco Ciabuschi, Uppsala University, Sweden

Partners: E. Mossialos (London School of Economics), C. Morel, S. Edwards (University of Geneva), E. Baraldi, S. McKeever (Uppsala University), F. Ciabuschi (Uppsala University), D. Gouglas, C. Årdal and S. Hoffman (Norwegian Institute of Public Health), O. Cars, A. Zorzet (ReAct)

1. Bring stakeholders on board at the outset and use their critical insights to help shape the project
2. Assess the specific bottlenecks and risk perceptions affecting the development of antibiotics
3. Evaluate reward and business models in other industries that also support stewardship and conservation or address key challenges similar to antibiotics
4. Develop, exhaustively analyse, validate, and explore in detail the implementation of the most promising reward models (those that deliver the greatest public health benefit with an acceptable net present value [NPV]), including funding sources, that will increase and sustain investment in antibiotic R&D while encouraging stewardship and conservation
5. Further validate the most promising reward models against a set of public health policy recommendations focused on antibiotics stewardship, including measures to support appropriate use
6. Gain buy-in from all stakeholders on our recommendations and receive endorsement from policymakers regarding our implementation plan

WP3A: Coordinate and manage the project

Stephan Harbarth, University of Geneva, Switzerland

1. Establish governance structure for the DRIVE-AB network
2. Coordinate the work packages and their collaboration, supporting the implementation of any changes in activities or the network
3. Ensure and assist in day-to-day operational management, providing administrative and logistic support to the work packages and Steering Committee
4. Ensure adherence to the project agreement, monitoring the effective execution of tasks and timely achievement of project deliverables and milestones
5. Provide financial management of the network, with oversight of resource usage and payment
6. Protect and monitor intellectual property

WP3B: Stakeholder platform and external communication

Ursula Theuretzbacher, Center for Anti-Infective Agents, Austria

Partners: British Society of Antimicrobial Chemotherapy, C. Clift and D. Heymann (Chatham House, London)

1. Identify and engage stakeholders through the development of a broad multidisciplinary stakeholder platform
2. Develop and implement a comprehensive communication/engagement strategy that will involve and engage all stakeholders
3. Establish effective relationships via meetings with and between decision makers central to the implementation of a new business model by engaging them early and throughout the project
4. Communicate effectively the project's findings and advances to the public
5. Establish effective communication internally to ensure the communication flow between all WPs and stakeholders via WP3B

Associate Partners

- International institutions:
  World Health Organisation (WHO)
- WHO Collaborating Centre for Pharmaceutical Pricing and Reimbursement Policies, Austria
- World Bank
- The Global Health Investment Fund (GHIF)
- Swedish Ministry of Health
- European Centre of Disease Prevention and Control (ECDC)
- European Medicines Agency (EMA)
- Center for Disease Dynamics, Economics & Policy (CDDEP)
- Clinical societies:
  European Society of Clinical Microbiology and Infectious Diseases (ESCMID),
  International Society for Chemotherapy (ISC),
  International Society of Infectious Diseases (ISID)
- Alliance for the Prudent Use of Antibiotics (APUA)
- Universities:
  The Boston University School of Law (Kevin Outersson),
  Harvard School of Public Health (Rifat Atun),
  University of South Australia (Allan Evans)