How to stimulate and incentivize the development of needed, new Antibiotics

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Estimated minimum number of illnesses and deaths caused annually by antibiotic resistance*:

At least 2,049,442 illnesses, 23,000 deaths

*bacteria and fungus included in this report
Pipelines are inappropriate

Discrepancy between antibiotic R&D pipelines and public health needs

Scientific challenges  Economic model
Bottlenecks to antibiotic innovation

- Profitability
  - Competing with highly profitable fields
  - Many generic antibiotics are still highly effective
  - Generic antibiotics are cheap
  - Demonstrating superiority through clinical trials is difficult
  - Stewardship
    - Markets for each of the different drugs is fragmented

- Human capital

- Scientific challenges
Consumption of generic antibiotics

Consumption of select key retail antibiotics in 2010, by year of market introduction and price

Bubble sizes correspond to the estimated quantity of standard units per capita dispensed in the retail sector in 2010
Antibiotic use per capita by income in selected countries, 2010

Antibiotic use

Extended-spectrum macrolide use is highly prevalent in the United States, and increasing in developing countries.
Antibiotic use

Per capita total carbapenem use, retail sector, 2005-2010

Per capita total carbapenem use, hospital sector, 2005-2010

Source: Based on data obtained under license from IMS Health MIDAS™ (January 2005-December 2010); IMS Health Incorporated. All Rights Reserved.
Consumption of systemic antibacterials, 2014

Community

Map showing the consumption of antibiotic DDD per 1000 inhabitants and per day in different regions across Europe.

- Blue: 0
- Green: 10.57 to < 15.27
- Light Green: 15.27 to < 19.96
- Yellow: 19.96 to < 24.65
- Orange: 24.65 to < 29.34
- Red: 29.34 to 34.04

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Existing health R&D financing mechanisms

- Financed through development aid
- Focus on stimulating national/regional research with no agreed priority-setting and no linkages to responsible use and access
  - The Generating Antibiotics Incentives Now (GAIN) Act, added exclusivity for antibiotics, Priority Review
  - Pathogen-focused antibacterial drug development pathway
  - House DISARM Act: add-on Medicare payments to DRG, incentivise hospitals to use new high prized antibiotics
WHO – Global Action Plan AMR

- Improve awareness and understanding
- Strengthen knowledge through surveillance and research
- Reduce incidence of infection
- Optimize the use of antimicrobial medicines
- Ensure sustainable investment in R&D
GOAL 4. Accelerate Basic and Applied Research and Development for New Antibiotics, Other Therapeutics, and Vaccines

- Fundamental Research
- Clinical Trials with New Antibiotics
- Significantly Increase Economic Incentives for Developing Urgently Needed Antibiotics
BARDA Accelerator

- Public private partnership
- Proof-of-concept stage through pre-clinical development
- Non-equity accelerator that provides non-dilutive funding, retain full ownership and control of their company
- BARDA will provide direct funding and NIAID will provide in-kind services (e.g. preclinical services, technical expertise) to the Accelerator that will manage a portfolio of investments of early stage antimicrobial product candidates
Antibiotic resistance is highest priority

- G7 Summit, May, Japan
- World Health Assembly, May, Geneva
- G-20 Summit, September, China
- G7 Health Ministers’ Meeting, September, Japan
- UN General Assembly Meeting, September, New York
R&D financing and incentive mechanisms

Delinkage / Push mechanisms

- Open knowledge innovation
- Milestone and end prizes
- PDP financing
- Grants
- Subsidies
- Tax breaks

Pull mechanisms

- Advance Market Commitment (AMC)
- Debt / loans
- Equity / bonds
- Government-backed volume guarantees

John-Arne Rottingen 2015, DRIVE-AB
Convergence of principles

- Better use of existing antibiotics
- Prevention, infection control
- Surveillance
- Education, training
- Stimulate R&D of new antibiotics: innovation + sustainable use and equitable access provisions
- Global collaboration and coordination
New economic models

Innovation

Prioritisation

www.drive-ab.eu

Access

Small markets LMIC

Conservation

Sustainable use

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

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All incentives to stimulate innovation will be paired with

- Sustainable use policies, conservation measures
- Equitable access provisions
## Where is innovation coming from?

Source and developing companies for antibiotics in Phase 2 or 3 clinical development:

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Source</th>
<th>Developing companies</th>
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<tbody>
<tr>
<td>Eravacycline</td>
<td>Harvard Univ</td>
<td>Tetraphase</td>
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<tr>
<td>Plazomicin</td>
<td>Isis</td>
<td>Achaogen</td>
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<tr>
<td>Brilacidin</td>
<td>Univ of Pennsylvania</td>
<td>Polymedix Cellceutix</td>
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<td>Debio 1450</td>
<td>Univ of Toronto</td>
<td>Affinium Debiopharm</td>
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<td>Solithromycin</td>
<td>Optimer</td>
<td>Cempra</td>
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<tr>
<td>Delafloxacin</td>
<td>Wakunaga Abbott</td>
<td>Wakunaga Rib-X=Melinta</td>
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<tr>
<td>Omadacycline</td>
<td>Paratek Paratek/Bayer</td>
<td>Paratek/Merck Paratek/Novartis Paratek</td>
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<td>Nemonoxacin</td>
<td>TaiGen Procter&amp;Gamble</td>
<td>Warner Chilc TaiGen</td>
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<td>Radezolid</td>
<td>Yale University Rib-X=Melinta</td>
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<td>Lefamulin</td>
<td>Sandoz/Novartis Nabriva Forest/Actavis* Nabriva</td>
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<tr>
<td>Acorafloxacin</td>
<td>J&amp;J (Janssen) Furiex Forest/Actavis*</td>
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<td>POL7080</td>
<td>Univ Zürich Polyphor Roche Polyphor</td>
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<tr>
<td>Carbavance (+Meropenem)</td>
<td>Rempex</td>
<td>The Med Comp</td>
</tr>
</tbody>
</table>

*Allergan

University/Small company
Mid-sized company (>500 employees)
Global pharmaceutical corporation
New economic models

- Stimulate innovation + sustainable use + equitable access

- Models researched
  - Grants
    - Determines research at universities, non-dilutive capital for companies
  - Product Development Partnerships
    - Non-profit entity (the PDP) and private sector industry to develop drugs on a not-for-profit basis. Innovation?
  - Post-approval payments (aka lump sum payments)
    - Structure of payments, source of funding, how much?
  - Payer licenses
    - Annual license fee and still charge unit costs, how much?
Testing a new economic model

- Will it stimulate action? By whom? Cost/benefit?
- How to pair with responsible use and availability?
- How can it be implemented?
- Validation
UK AMR Report

TACKLING ANTIMICROBIAL RESISTANCE ON TEN FRONTS

- Public awareness
- Sanitation and hygiene
- Antibiotics in agriculture and the environment
- Vaccines and alternatives
- Surveillance
- Rapid diagnostics
- Human capital
- Drugs
- Global Innovation Fund
- International coalition for action

The Review’s proposals to incentivise antibiotic development

- A global innovation fund to support early stage research - more money, spent in a more coordinated and strategic way

- Lump sum ‘market entry rewards’ - of as much as $1-1.5bn - for successful developers of the products we most need - including a new TB treatment regimen

- $16bn over a decade could support a pipeline of around 15 new antibiotics

We will need reliable, sustainable ways to fund this

Compared to the costs of inaction, this is money well spent, and governments of the G20 can easily afford it. But other mechanisms for raising ‘new money’ exist that reduce political risk of long-term funding commitments:

- Given the systemic risk to the pharmaceutical industry, the sector could contribute to supporting market entry rewards - on a ‘pay or play’ basis

- International financial institutions

- Taxation options - particularly on the agricultural use of antibiotics
Develop new economic models to stimulate antibiotic R&D