Political processes for the global need for effective antibiotics: Moving towards concerted action

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We are facing a public health threat

Antibiotic Resistance

Drug Development

Morbidity

Mortality

Costs
An international network to improve the management of antibiotic resistance

“Our vision is that current and future generations will have access to effective prevention and treatment of bacterial infection as part of their right to health.”

www.reactgroup.org
Main areas of action

• Increasing the visibility of antibiotic resistance in the global health dialogue

• Promoting evidence generation on the burden of antibiotic resistance

• Catalyzing action towards national coordinated strategies against antibiotic resistance

• Promoting the development of new antibiotics to meet global needs to manage antibiotic resistance
Antibacterials in the Pipeline

New Molecular Entities Publicly Disclosed in R&D Programs of the World’s 15 Largest Pharmaceutical Companies

90.2% Rest of the Pipeline
1.6% Antibacterials
8.2% Other Anti-Infectives

Adapted from Spellberg, 2004
Some causes for lack of antibiotic innovation

• Return of Investment is much safer from medicines for treatment of chronic diseases
  - antibiotics given in short courses
  - size of market must be reduced
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- ......plus one cause that is often underestimated: **Major scientific challenges**
1990s genomics approach: ‘gene to drug’.

From David J Payne, GlaxoSmithKline, Collegeville, PA, USA with permission
Pipeline of 'HTS to drug' for antibacterials is not delivering

**Number of milestones needed for 1 Launch (AB compared with industry average)**

<table>
<thead>
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<th></th>
<th>HTS</th>
<th>Leads</th>
<th>Development Candidates</th>
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<th>Ph2 starts</th>
<th>Phase 3 starts</th>
<th>Files</th>
<th>Launch</th>
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<tr>
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Why is this so difficult?

• Bacteria have been around for billion years, have huge population sizes and are experts of adaptation and survival

• Compound libraries biased towards attributes suited for mammalian targets

• Antibacterial targets need different types of chemical diversity drug molecules need to enter bacteria and avoid efflux

• Lack of standardized methods that reliably predict the probability of occurrence of resistance mutations, and their probability for persistence (fitness cost/compensation)
There have been numerous initiatives to promote action to stimulate R&D for novel antibacterial drugs.

In the US.....

A PUBLIC HEALTH ACTION PLAN TO COMBAT ANTIMICROBIAL RESISTANCE

Interagency Task Force on Antimicrobial Resistance

Co-Chairs:

Centers for Disease Control and Prevention
Food and Drug Administration
National Institutes of Health
In the EU.....
Innovative Incentives for Effective Antibacterials

A conference during the Swedish Presidency of the EU 2009 focusing on the need to reinvigorate research and development of new antibiotics

Governments
Academia
Pharmaceutical and biotech industry
Civil society
COUNCIL OF THE EUROPEAN UNION

Council Conclusions on innovative incentive for effective antibiotics

2006th EMPLOYMENT, SOCIAL POLICY, HEALTH AND CONSUMER AFFAIRS Council Meeting

Brussels, 1 December 2009

The Council adopted the following conclusions:

2. RECALLS the Council Recommendation of 15 December 2001 on the prudent use of antimicrobial agents in human medicine.
3. RECALLS the Council Conclusions on antimicrobial resistance of 10 June 2008.
4. RECALLS the Council Recommendation of 9 June 2009 on patient safety, including the prevention and control of healthcare-associated infections.

PRES

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ReAct and Uppsala University hosted the conference “The Global Need for Effective Antibiotics” in 2010.
Urgent need for new antibiotics

But we cannot keep (mis)using them the way we have for the last 70 years!

Marketing and use needs to be restricted

→ less incomes from sales

We need a new business logic!
Urgent need for new antibiotics

The overall innovative capacity is low

There are major scientific challenges

Who is going to do the work?
Big Pharma? Small pharma? Academia?

New collaborative models needed
Urgent need for new antibiotics

Market failure

Impending health crisis

High health and economic burden from resistance

Justifies intervention from the public sector
A new business model must be built on the global needs and secure access and affordability as well as rational use.
Illegal OTC antibiotic sale in the EU

Athens, Greece 2008 (174 pharmacies)

2008:

- 100% of all visited pharmacies sold Amoxicillin/clavulanate acid OTC
- 53% sold Ciprofloxacin OTC, despite extra restrictions for fluoroquinolone prescriptions

Plachouras et al. Euro Surveill. 2010
Some parts of the world are already running out of effective antibiotics

Muhimbili hospital, Dar es Salaam Tanzania

The mortality rate from Gram-negative bloodstream infection in children (43.5%) was more than double that of malaria.

Blomberg et al. BMC Infect Dis. 2007
Lead Identification

Crossing the "Valley of Death"

Discovery

Pre-Clinical

Clinical

Development

Post-marketing

Medicinal Chemistry

Regulatory Approval

Access and Rational Use
Towards a new business logic for R&D of novel antibiotics

- Needs driven - based on analysis of pipeline vs resistance and its burden

- Prioritization, target product profiles

- Solving the scientific challenges

- Incentives that reward priority antibiotics
  - Special regulatory designation
  - Pricing and reimbursement
  - Push and pull incentives

- De-linking return of investment from sales

- Controlled use and distribution

- Equitable global access and affordability
Sharing resources

• Explore ways to reduce the scientific challenges sharing resources/knowledge within and between public and private sectors

• Addressing the brain drain and the low capacity for "antibiotic biology"
Sharing risks

Facilitating a rapid preclinical and clinical testing of lead compounds by:

- providing research infrastructure
- financial contributions (push/pull)
- special regulatory designation for priority antibiotics (based on a continuous "gap" analysis)
Sharing the R&D risks

**Pull**
- Advance Purchase Commitment,
- Prizes,
- Patent buyouts,
- Patent extensions

**Push**
- Public funding for R&D
- Tax incentives
- Product development partnership (PDP)
Sharing rewards

• A low return of investment from sales is compensated for by public investment in the early development process and/or by e.g. advance market commitments.

• Equitable access and affordability

• Controlled distribution and rational use
The solution... collaboration

New antibiotics

Pharm. industry

National governments

Academia

DG Enterprise
DG Research
DG SANCO

WHO

EU Agencies (EMA, ECDC)

Civil Society

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