CUGH

New Business Models for Antibiotics

Prof. Kevin Outterson
NATIONAL SUMMARY DATA

Estimated minimum number of illnesses and deaths caused by antibiotic resistance*:
At least 🕳️ 2,049,442 illnesses, 👹 23,000 deaths

*bacteria and fungus included in this report

Estimated minimum number of illnesses and death due to *Clostridium difficile* (C. difficile), a unique bacterial infection that, although not significantly resistant to the drugs used to treat it, is directly related to antibiotic use and resistance:
At least 🕳️ 250,000 illnesses, 👹 14,000 deaths

WHERE DO INFECTIONS HAPPEN?
Antibiotic-resistant infections can happen anywhere. Data show that most happen in the general community; however, most deaths related to antibiotic resistance happen in healthcare settings, such as hospitals and nursing homes.
A Serious Problem

US Deaths from various causes, 2011

Peak antibiotics

**EXHIBIT 2**

**US Antibiotic Sales For Human Use, In 2013 Constant Dollars, By Mode Of Administration, 1998–2013**

_SOURCES_ IMS Health (US manufacturer US dollar sales at ex-manufacturer prices), and St. Louis Federal Gross Domestic Product deflator (2013 = 100).
NIH AMR funding

EXHIBIT 3

National Institutes Of Health Research Spending On Antimicrobial Resistance Research, United States, Fiscal Years 2010–15

Millions of dollars

<table>
<thead>
<tr>
<th>Year</th>
<th>Spending</th>
</tr>
</thead>
<tbody>
<tr>
<td>FY 2010</td>
<td>ARRRA</td>
</tr>
<tr>
<td>FY 2011</td>
<td>300</td>
</tr>
<tr>
<td>FY 2012</td>
<td>350</td>
</tr>
<tr>
<td>FY 2013</td>
<td>330</td>
</tr>
<tr>
<td>FY 2014*</td>
<td>320</td>
</tr>
<tr>
<td>FY 2015*</td>
<td>310</td>
</tr>
</tbody>
</table>

Table 1: Antibiotic Approvals (1983-Present)

<table>
<thead>
<tr>
<th>Period</th>
<th>Total # New Antibacterial Agents</th>
</tr>
</thead>
<tbody>
<tr>
<td>'83-'87</td>
<td>16</td>
</tr>
<tr>
<td>'88-'92</td>
<td>14</td>
</tr>
<tr>
<td>'93-'97</td>
<td>10</td>
</tr>
<tr>
<td>'98-'02</td>
<td>9</td>
</tr>
<tr>
<td>'03-'07</td>
<td>6</td>
</tr>
<tr>
<td>'08-'12</td>
<td>1</td>
</tr>
</tbody>
</table>

Source: IDSA’s 2004 Bad Bugs, No Drugs report (modified)

Source: Adapted from Outterson K et al, JLME 2013; * As of September 15, 2014; additional market discontinuations since 2009 not calculated.
Ex. 4
New Systemic Antiinfectives Not Withdrawn in the U.S. as of August 1, 2013, by Decade of FDA Approval, 1980-2009

Outterson, Powers, Seoane-Vazquez, Rodriguez-Monguio, Kesselheim
JLME 2013
ceftaroline fosamil (Oct. 29, 2010)
fidaxomicin (May 27, 2011)
dalbavancin (May 23, 2014)
tedizolid (June 20, 2014)
oritavancin (Aug. 5, 2014)
ceftolozane/tazobactam (Dec. 2014)
AND NOW FOR SOMETHING COMPLETELY DIFFERENT
EntraTympanic’s In-Office Treatment of Middle Ear Infections Eliminates Antibiotics

Drains fluid with instant pain relief.
Eliminates the use of systemic antibiotics.
Mitigates resistance & microbiome disruption.

Disposable with collected fluid sample for culture/analysis.
Map patient and population antibiotic resistance profile.

Potential to eliminate >50% of all pediatric antibiotics!

12–18 Months
Clinical Trial Ready Prototype Device

12–15 Months
Clinical trial, regulatory approval, market launch!
Private NPV

- Private NPV variable across indications
- CABP has the highest private NPV & HABP/VABP the lowest

Figure 3: Estimated Private ENPVs by Indication for a New Antibacterial Drug (in $ Million)

<table>
<thead>
<tr>
<th>Indication</th>
<th>Private ENPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABOM</td>
<td>-$3</td>
</tr>
<tr>
<td>ABSSSI</td>
<td>$27</td>
</tr>
<tr>
<td>CABP</td>
<td>$37</td>
</tr>
<tr>
<td>CIAI</td>
<td>$9</td>
</tr>
<tr>
<td>CUTI</td>
<td>$22</td>
</tr>
<tr>
<td>HABP/VABP</td>
<td>-$4</td>
</tr>
</tbody>
</table>

ERG for DHHS 2014
Annual US private and social ENPV by indication, in millions of US$
Adapted from ERG for DHHS 2014
$144 million 2015-24
$14.4mm/year
Chatham House WG

- Broad ranging discussion leading to a workshop on new business models Oct. 2013
- Reports were prepared in advance for the workshop, covering all known proposals
Chatham House WG

• March 2014: new *functional* approach
• 6 subgroups, with a broad range of Members and Observers
• Iterative process
• Full day workshop in Geneva Oct. 2014
• Editors: Charles Clift, Unni Gopinathan, Chantal Morel, Kevin Outterson, John-Arne Røttingen, Anthony So
Key delinkage elements

• Delink revenues from sales volume (conservation);

• Increase total incentives for antibiotics; and

• Preserve access without regard to ability to pay.

Kesselheim AS Outterson K. Health Affairs 2010; Yale J. Health Policy, Law & Ethics 2011; Chatham House 10.2.13; Outterson. Health Affairs Feb 2015
Functional elements

1) Structuring the reward
2) Product scope
3) Financing
4) IP
5) Rationalizing antibiotic use
6) Geographic scope
Recommendation 1.1

Phase
- Preclinical
- Clinical
- Post-registration

Incentives
- Research grants
- Tax credits
- PPP contracts
- Delinkage

Standards
- Very broad
- QIDP/PR Threat assessment
- Threat assessment
Recommendation 1.2

Create a fully transparent and independent process to evaluate the fairness and effectiveness of all antibiotic development incentives.
Recommendation 2.1

- Global threat assessment
- Data-driven, transparent, and focused on threats posed by resistant pathogens
- Triage list outcome
- Goal is to maximize public health
Recommendation 4.1

• The delinkage business model should guarantee global access to antibiotics together with appropriate use.

• Appropriate responsibilities should be allocated between governments and the innovator when negotiating the terms of the delinkage payments.
Recommendation 5.3

• Ban the use of antibiotics as growth promoters in agriculture, backed by an international health regulation and coherence with global trade rules.

• Alternative ways of preventing infection in agriculture should be researched and implemented.
Recommendation 6.1

• While complete global coverage is the ultimate goal, the geographic scope of participation can vary in the early years.

• Financial participation can begin with a core group of countries.

• Every country should participate through surveillance, hosting clinical research, conservation and public health initiatives.
Recommendation 6.2

A globally harmonized antibiotic approval process, acceptable in particular to countries with weaker national drug regulatory systems, should be established for antibiotics resulting from the new business model.
Recommendation 6.4

Evaluate the Medicines Patent Pool as an entity to hold and coordinate global IP licences for antibiotics.
Trans-Atlantic

USA G7 & WHO EU

- FDA
- BARDA
- IDSA, Brookings & Pew
- CDC Threat Assessment
- ERG 2014
- PCAST & National Strategy
- EMA
- ND4BB/IMI
- ReACT
- Wellcome Trust
- Chatham House
- O’Neill Commission
- DRIVE-AB
Repairing The Broken Market For Antibiotic Innovation

Bold, global action
Based on science
For long-term ecological balance and human health

Outterson K et al. Health Affairs (Feb.2015)
Papers at ssrn.com
Blog: TheIncidentalEconomist.com
Twitter: @koutterson