

Economic models to stimulate antibiotic development

Kevin Outterson

All Party Parliamentary Group on Antibiotics
Portcullis House, Westminster
30 November 2016

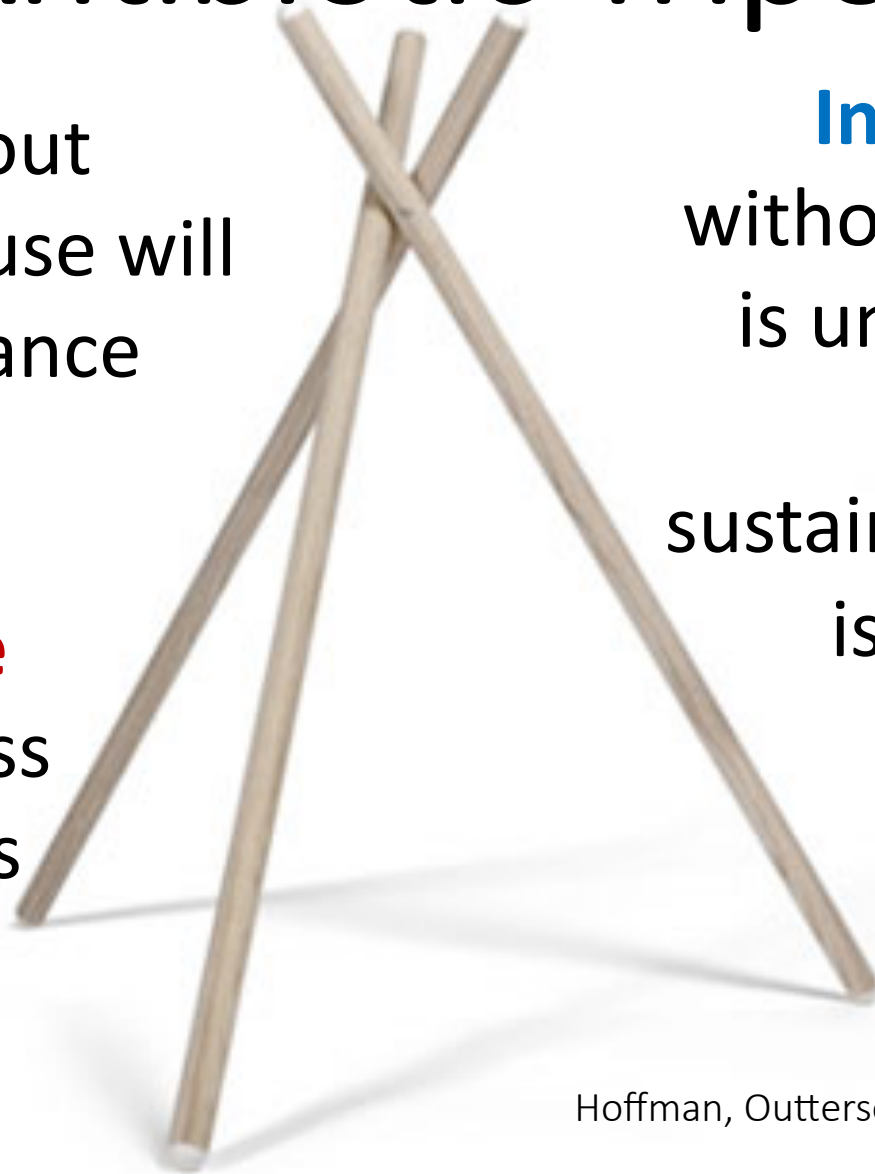


The Antibiotic Tripod

Access without
sustainable use will
speed resistance

Sustainable use
constrains access
and undermines
innovation

Innovation
without access
is unjust, and
without
sustainable use
is wasteful



The Antibiotic Tripod

Human

Environmental

Agricultural



Hoffman, Outterson et al. JLME 2015

The players

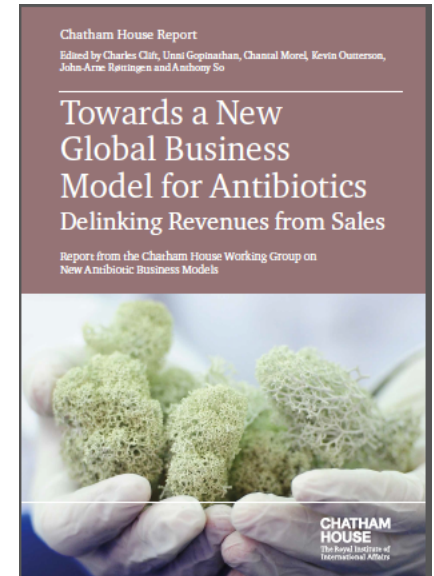
		Pre-Clin	P1/2	P2/3	Market
US BARDA	Funding & resources	+++	+++	+++	
US NIAID		+++	+++	++	
EC (JPIAMR, IMI, FP6, FP7, H2020)		+++	+++	+++	
Wellcome Trust (UK)		+++	++		
Other Governments (e.g., UK AMRC, UK-China Fund)		+	+		
FDA	Updated Guidance		+++	+++	
EMA			+++	+++	
PMDA			+	+	
SE (2H09 EU Presidency)					+++
Chatham House (2014-15)					+++
WHO Global Action Plan (2014+)					+
US PCAST, CARB, & PACCARB (2014+)					++
DRIVE-AB (IMI, 2014-17)					+++
UK (O'Neill AMR Review, 2014-16)					+++
Duke-Margolis (2016+)					+++
NE (1H16 EU Presidency)					+++
DE (2017 G20 run-up)					++

+++ : Strongly engaged; ++ : Visibly engaged; + Early engagement &/or limited details`

Convergence of principles

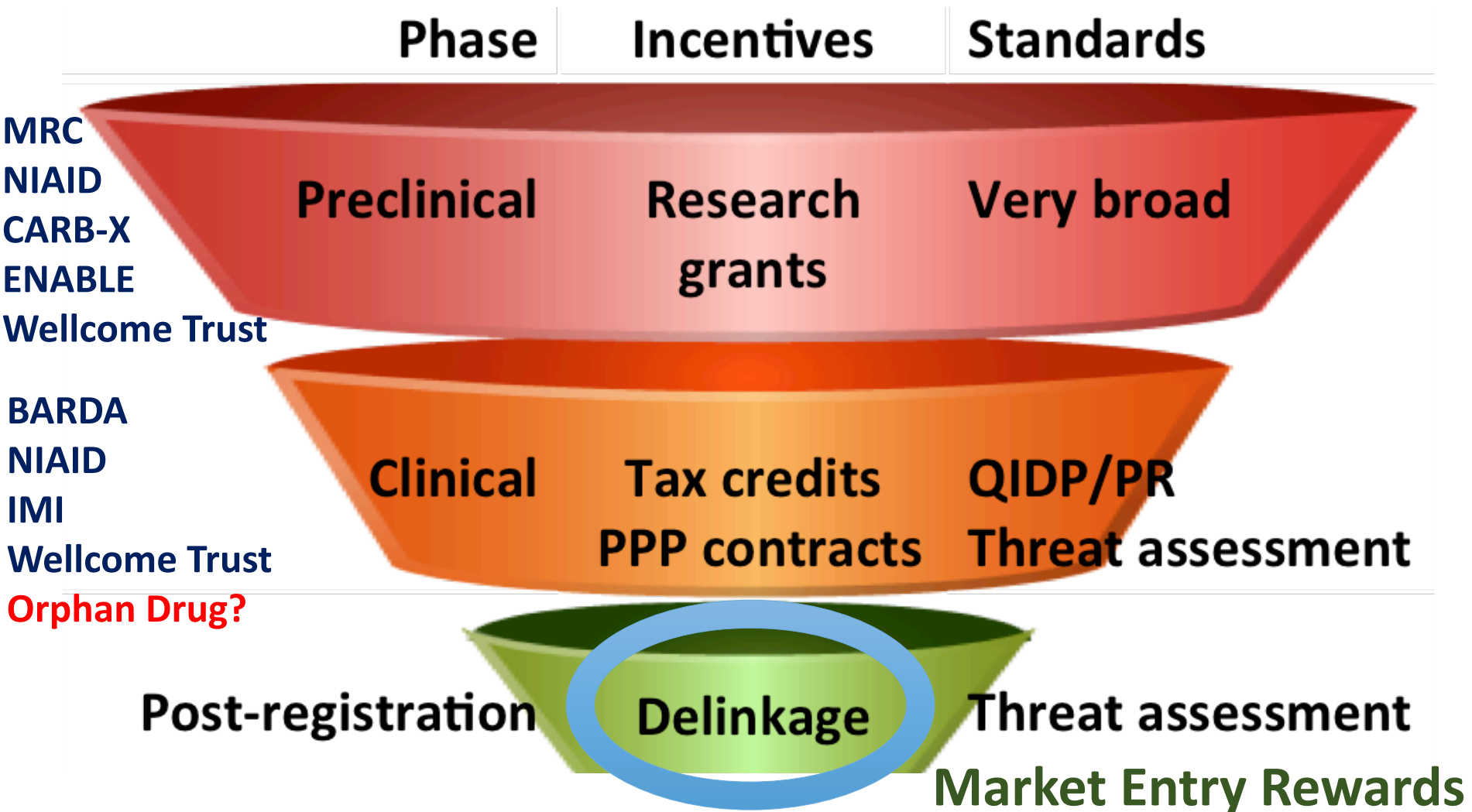


- Need for both “push” and “pull” mechanisms
- Delinkage (i.e., revenues delinked from volumes sold)
- Access and sustainable use are integral
- Global collaboration and financing necessary



June 17, 2016: “Actively engage in initiatives and proposals to implement a new business model to bring new antibiotics to the market, including models in which investment costs or revenues are de-linked from sales volumes.”

Incentives



Market Entry Rewards

1. Structure
2. Magnitude
3. Adjustments
4. Other rules
5. Funding

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Market Entry Rewards



Antibiotic reimbursement in a model delinked from sales: a benchmark-based worldwide approach

John H Rex, Kevin Outterson

Lancet Infect Dis 2016;
16: 500–05

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Waltham, MA, USA, F2G
Pharmaceuticals, Eccles,
Cheshire, UK, and University of
Texas Medical School-Houston,
Houston, TX, USA
(Prof J H Rex MD); and Boston
University School of Law,
Boston, MA, USA, and
Chatham House, London, UK
(Prof K Outterson JD)

Despite the life-saving ability of antibiotics and their importance as a key enabler of all of modern health care, their effectiveness is now threatened by a rising tide of resistance. Unfortunately, the antibiotic pipeline does not match health needs because of challenges in discovery and development, as well as the poor economics of antibiotics. Discovery and development are being addressed by a range of public–private partnerships; however, correcting the poor economics of antibiotics will need an overhaul of the present business model on a worldwide scale. Discussions are now converging on delinking reward from antibiotic sales through prizes, milestone payments, or insurance-like models in which innovation is rewarded with a fixed series of payments of a predictable size. Rewarding all drugs with the same payments could create perverse incentives to produce drugs that provide the least possible innovation. Thus, we propose a payment model using a graded array of benchmarked rewards designed to encourage the development of antibiotics with the greatest societal value, together with appropriate worldwide access to antibiotics to maximise human health.

Structure

- Guaranteed, unambiguous payment upon FDA registration
 - Size of payment varies with TPP
 - Payment spread over 5 years
 - No profits from sales volume
 - Conditions for stewardship & global access

Market Entry Rewards

1. Structure
- 2. Magnitude**
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Magnitude

	Payments from governments	Expected NPV benchmark at commencement of R&D
Sertkaya et al ¹¹	\$919 million (spread over entire R&D process and at registration; USA only)	\$100 million
Sharma and Towse ¹⁸	\$2.5 billion (\$500 per year for 5 years)	\$300 million
Review on Antimicrobial Resistance ¹⁹	\$2–4 billion (paid 3 years after registration)	Not stated

All values are in US\$. R&D=research and development.

Table 1: Nominal and expected net present value (NPV) estimates of the needed size of antibiotic delinkage payments

Taking the smallest estimate, roughly adjusted to 2017 dollars = \$1b total or a base payment of \$200m a year paid for five consecutive years after FDA/EMA registration.

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Model to provoke debate

- Define one base payment as \$200m/yr x 5yr
 - This is the global PROFIT to the developer
 - No other profit permitted; actual sales effectively at cost
- Then this scheme on a global basis...

Requirement	Step earned
FDA & EMA approval, treats a CDC 2013 threat pathogen	1x Base
Treats CDC Urgent pathogen	1x Base
Treats CDC Serious pathogen	0.5x Base
First of a novel class	1x Base
2 nd , 3 rd , or 4 th of a novel class	0.75x, 0.5x, or 0.25x Base

Requirement	Step earned
5 th or later of novel class, but offering safety, efficacy or dosing improvement	0.1x Base
Delivery of pediatric commitment	Cost recovery payment
2 nd , 3 rd , or 4 th defined indication for a given agent	0.25x Base for each
Oral dosage form	0.25x Base





¹Rex & Outtersen. LID 2016. It is possible to earn multiple payments, but CDC pathogen category payments can only be earned once. Payments need not be concurrent. Defined Indications Novel Class are broadly lumped, not finely divided – a consensus rule may be needed. Slide from Rex.


Model to provoke debate

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A spectacular new oral Gram-negative agent would be well rewarded: 3.75 x base in this case

global basis...

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Adjustments

	Annual payment*
Drug approved at US FDA and European Medicines Agency to treat at least one defined infection‡ caused by at least one or more pathogens listed on the CDC 2013 threat assessment as either urgent, serious, or of concern to public health²	Base payment†
Has a clinical spectrum of activity on the label that includes one or more urgent pathogens on the CDC 2013 threat assessment§	Bonus equal to one base payment
Has a clinical spectrum of activity on the label that includes one or more serious pathogens on the CDC 2013 threat assessment§	Bonus equal to 50% of a base payment
Is the first approved drug to act via a given mechanism of action¶	Bonus equal to a base payment
Is the second, third, or fourth agent approved to act via a given mechanism of action	Bonus equal to 75% of a base payment for a second agent, 50% for a third agent, or 25% for a fourth agent
Is the fifth or subsequent agent to act via a specific mechanism of action but offers a medically relevant improvement in safety, efficacy, or ease of dosing	Bonus equal to 10% of a base payment
Delivery of agreed paediatric commitment studies	Payments based on model or separate contract open to tender
Is approved for a second, third, or fourth defined infection‡ for a specific agent	Bonus equal to 25% of a base payment
Approved in oral dosage form	Bonus equal to 25% of a base payment

Also consider a much smaller but long-term “market access” payment to support warm mfg base

Adjustments

- Target Product Profile (previous slides)
- Clawback for federal grants & tax credits
(assumed in ERG)
- Global coordination

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Other Rules

- Payment rules must be guaranteed when R&D decisions are made (i.e., grandfathered for > decade)
- Payments cease if drug withdrawn from market or key conditions violated
- Generics may need special rules

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Funding

1. General taxation
2. Pay or play
3. User fees
4. Transferable exclusivity vouchers (In US only, with guardrails)

Bottom Line

- Globally coordinated
 - Tripod
 - Both push & pull
 - Billions, not millions
- Sustainable, not short-term

Tweeting antibiotics R&D @koutterson

Research papers at Google Scholar & SSRN

Kevin Outterson
Boston University



CARB-X