# Designing Effective Pull Incentives

Prof. Kevin Outterson
Boston University

4th AMR Conference, Berlin
August 25, 2020

# Disclaimer

*These are my academic views, not necessarily the views of CARB-X or any CARB-X funder*

# Pull incentive

Value given after regulatory approval
to reward successful innovation
and promote future R&D investment

# Designing effective pull incentives: targets

**Set clear, objective standards, understandable to preclinical drug developers**

- Goal is to unleash private investment in clinical and preclinical development, with high confidence of payout if targets are hit
  - E.g.: species, indication, route of administration, chemical class, mechanism of action, development of resistance, tox, therapeutic window, dosing, target population[1]
- Stable for 15-year R&D time horizon[2] (grandfathered if changes)
- Agency discretion increases risk for drug developers
- Beware of gaming, which could destroy the program's reputation


**Aim high**

- With limited funds, focus on drugs likely to be clinically differentiated, meeting substantial clinical needs projected many years from now
- Not everyone should be a winner

1. Rex & Outterson, LID 2016;16(4):500-505.
2. See backup slide on R&D time horizons

# Designing effective pull incentives: payouts

**Avoid "uncertainty discount" by private investors: make the risk of discretionary nonpayment as low as possible**

- A $3B subscription agreement after FDA/EMA approval will incentivize R&D, but less so if investors discount the payout for counterparty (sovereign) risk
- Tools: Enduring, bipartisan commitment; Antibiotic Trust Fund; gov't bond financing; designation at IND; limited agency discretion

**Variable payouts:** higher quality receives higher rewards

**Fair share:** no free riding by any G20 country, can scale globally

**Billions, not millions:** must achieve objectives, with transparency

**Delinked:** pay for clinical & social value (current & future), not volume

# 5 Examples

- NHS England Antibiotic Subscription Pilot
- Swedish Access Pilot
- US DISARM Act (proposed)
  - Carves hospital antibiotics out of the DRG bundled payment
  - Bipartisan support has not yet translated into legislative approval
- US PASTEUR Act (proposed) Senators Bennet & Young
  - Antibiotic subscription for all US government payers (Medicare, Medicaid, VA)
  - Not yet introduced
- BARDA Post-approval Contract
  - $285M to Paratek December 18, 2019

# 1. NHS England Antibiotic Subscription

**Target**

- Review based on published standards (in process)
- Relatively few drugs will qualify

**Payout**

- Health Technology Assessment (HTA) with £10M cap & initial 3-year pilot
- Variable payout based on HTA, but may cluster near cap (good result?)
- £100M subscription (assuming full £10M per year over 10 years) is in the range of England's fair share;[1] pilot must become permanent
- Fully delinked (prepaid) subscription for all of the drug that NHS England needs during the subscription period

1. Rex & Outterson. UK Antibiotic Subscription Pilot Implies Pull Incentive of up to $4b Across the G20. AMR Solutions blog (Mar. 29, 2020).

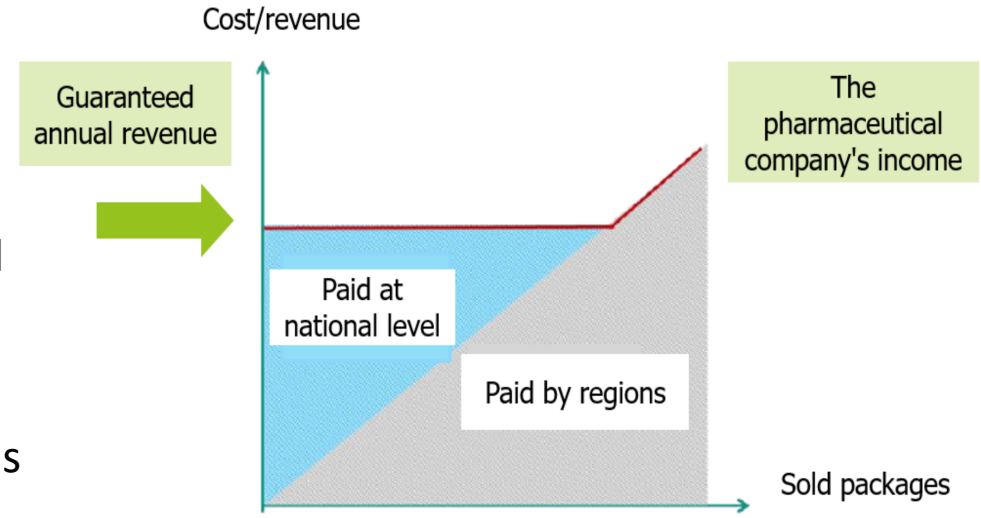
# 2. Swedish Access Pilot

**Target**

- Approved antibiotics, to maintain registration and availability in Sweden

**Payout**

- Many contracts could be issued (4-5 underway now, perhaps for 2 years)
- Pull incentive to support access in Sweden for approved antibiotics
- Not explicitly designed to support global innovation, but funding could be scaled up to achieve that goal
- Partially delinked: national guarantee @ 50% over forecasted sales, offset by sales in regions




Rex. Sweden to Test An Access-Focused Model for New Antibiotics: Contracting for Availability. AMR Solutions blog (Mar. 16, 2020).

# 3. DISARM DRG Carve-Out

**Target**

- Qualified Infectious Disease Products
- Everyone qualifies (almost)

**Payout (Revenues)**

- Lower sovereign risk once enacted in statute (greater risk if by administrative action only)
- Revenues are variable and entirely market-based, with clinician choice (w/ marketing)
- Difficult to predict value, but Needham analyst Alan Carr supports it[1]
- Not delinked – entirely dependent on sales at Average Sales Price

1. Rex. Alan Carr's Sep 2019 Antibacterial –Antifungal Update. AMR Solutions blog (Sept. 6, 2019).

# 4. US Subscription (PASTEUR)

**Target**

- Standards set by public administrative process, to provide certainty and targets that developers know they can work towards
- Relatively few will qualify

**Payout**

- Statutory, with payouts estimated at IND, if standards are achieved
- Variable payout ($750M – 3B) based on which standards are achieved
- Subscriptions in this range will incentivize innovation
- Fully delinked (prepaid) for all US gov't uses; private US markets not included

# 5. BARDA Post-Approval Contract

**Target**

- BioShield (bioterrorism) pathogen; no sig. impact on stock prices of other antibiotic companies (high "uncertainty discount")
- Unknown number will qualify (annual appropriations, BARDA discretion)

**Payout**

- Discretionary agency action; decision public, but not all process
- Variable payout based on conditions in the award (Phase 4 studies, deliveries to Strategic National Stockpile (SNS), onshoring)
- $285M to Paratek requires additional studies; does not repay prior R&D investments
- Fully delinked (deliveries to SNS, but not dependent on use)

# Can be an effective pull incentive if:

**NHE Subscription**

(1) made permanent; (2) HTA standards match social value and are understandable to drug developers; (3) subscriptions remain ~£100M per drug; and (4) other G20 countries join

**Swedish Pilot**

(1) made permanent at a higher level of funding to support R&D at Sweden's "fair share"; (2) standards are understandable to drug developers; and (3) others join

**DISARM DRG Carve-Out**

(1) sales substantially increase w/o harming stewardship; and (2) clinician demand can be predicted by drug developers

**PASTEUR Subscription**

(1) standard setting process accurately predicts clinical differentiation & need; and (2) subscription is automatic if targets are achieved

**BARDA Post-Approval Contract**

(1) a "push with pull" incentive: funding for Phase IV studies & antibiotics in the SNS; and (2) key lifeline to keep companies moving towards profitability & drugs on the market

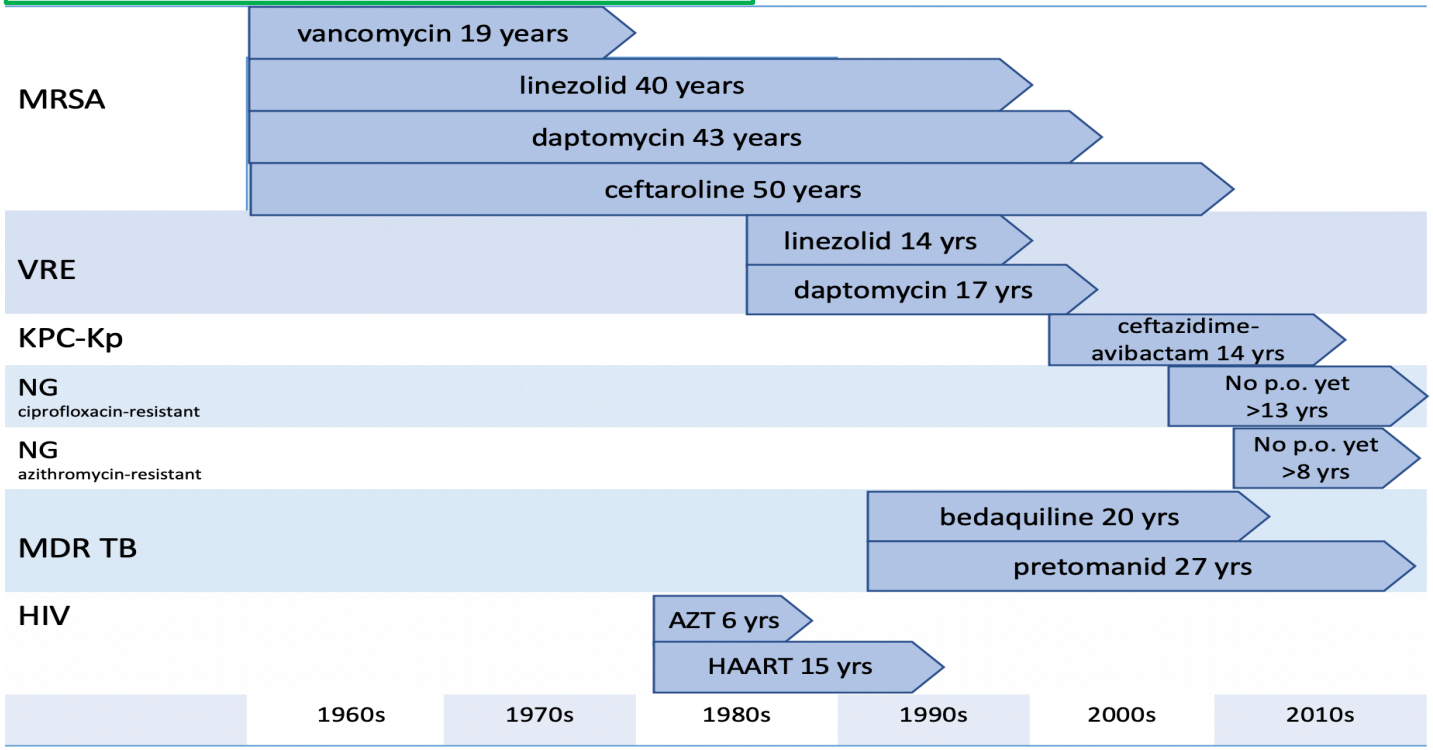
BOSTON UNIVERSITY

Thank you!

Academic papers @ Google Scholar

# Planning horizon for new challenges

**No quick fixes for some resistant infections**
Time from identification until FDA approval of new drug




Identifications: CDC AR Threats 2019, at 35; MRSA 1960 (Jevons MP 1961. BMJ); VRE 1986 (Uttley AHC, et al. Lancet 1988); KPC-Kp 2001 (Yigit H, et al. AAC 2001); NG-CR 2007 (CDC, MMWR 2007); NG-AR 2012 (Soge OO, et al, STD 2012); MDR-TB 1992 (Vallarino ME, et al., Pub H Rep 1992); HIV 1981 (initial ID, not emergence of resistance). Drug approvals: Vancomycin approved 1958, but US usage did not grow until 1979 (Kirst HA 1998. AAC). Other approvals from Drugs@FDA.gov. For emergence of MRSA resistant to ceftaroline prior to its FDA approval, see Kelley WL et al., AAC 2015.