CLINICAL INNOVATION: Fair & Effective Incentives for New Uses of Established Drugs

Alternatives Incentives to Patents

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Presenters:

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- **Prof. David Ridley** *Faculty Director, Duke University Health Sector Management Program*
- **Dr Bruce Bloom** *CEO, Cures within Reach*

Panellist:

- **Otto Licks***Licks Legal*

REPURPOSING DRUGS

Constance E. Bagley
Yale University

CEO and Founder
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DISCOVERING NEW USES

- Public-private partnerships
- Open innovation (e.g., IMI)
- Consortia with high through-put and trusted intermediary
- Condition NIH grants on sharing of upstream tools and willingness to participate in testing for secondary uses and/or to license to all comers on non-exclusive basis in exchange for fair royalty.

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A NEW REGULATORY SCHEME FOR SECONDARY USES

- It can be medical malpractice for a physician not to prescribe a drug for an off-label use yet the FDA severely limits the ability of pharma companies to provide truthful information about off-label uses.
- This may well constitute an unconstitutional infringement of the free-speech rights of the pharma companies and their reps.
- It has effect of pushing companies toward me-too indications and delaying gathering and dispersion of data re secondary uses.

PROPOSAL

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- Just as entrepreneurs can offer and sell securities without meeting the onerous SEC registration requirements if they sell only to accredited investors, the FDA could create an exemption for licensed physicians to receive briefings from registered reps on promising off-label uses.
- Create a rep licensing system akin to the Financial Industry Regulatory Authority to register reps and require them to pass a competency and record-keeping exam and be subject to a background check.
- Impose record-keeping requirements.
- Apply clear antifraud rules and require full disclosure of any side effects or conflicts of interest.

SOURCES

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- Constance E. Bagley & Christina D. Tvarnø, "Promoting 'Academic Entrepreneurship' in Europe and the United States: Creating an Intellectual Property Regime to Facilitate the Efficient Transfer of Knowledge from the Lab to the Patient," *Duke Journal of Comparative and International Law*, vol. 26 (2015), pp. 1–77.
- Constance E. Bagley & Christina D. Tvarnø, "Pharmaceutical Public-Private Partnerships: Moving from the Bench to the Bedside," *Harvard Business Law Review*, vol. 4 (2014), pp. 373-401.
- Constance E. Bagley, Joshua Mitts & Richard J. Tinsley, "Snake Oil Salesmen or Purveyors of Knowledge: Off-Label Promotion and the Commercial Speech Doctrine," *Cornell Journal of Law and Public Policy,* vol. 23(2) (2013), pp. 337-393.

Encouraging Investment

David Ridley, PhD

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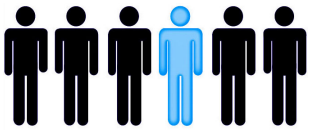
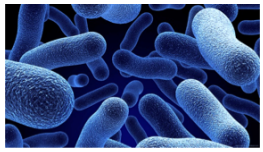
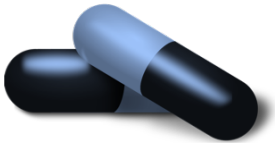
Stimulating R&D

	Rare diseases  ODA, PRV (2012)	Neglected diseases  ODA, PRV (2007)
Medical countermeasures  ODA, Bioshield, PRV (2016)	Antimicrobial resistance 	Secondary uses 

ODA = Orphan Drug Act. PRV = Priority Review Voucher

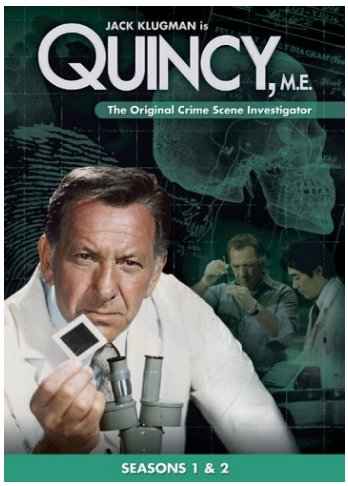
Push: Supply side

National Institutes of Health, Orphan Drug Act

Pull: Demand side

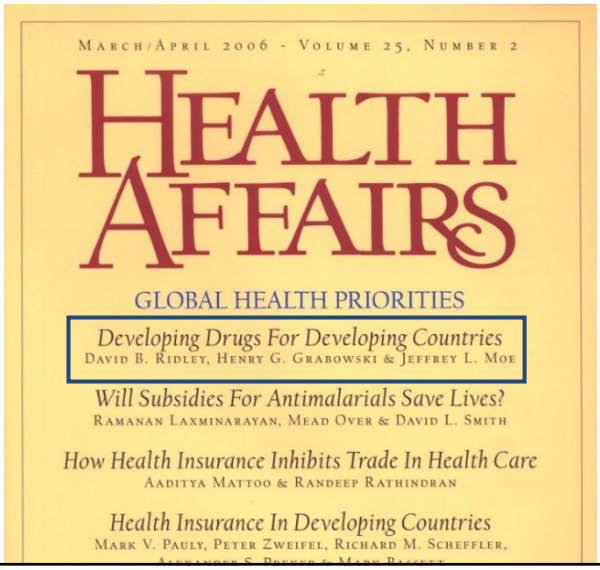
Patents, Exclusivity, Sales, Advance Market Commitment, Priority Review Voucher, Wild Card Extension, Patent Court

Orphan Drug Act



- Jack Klugman's brother wrote an episode of "Quincy" about the orphan drug problem, and a later episode about how a Senator blocked a bill
- Klugman also testified before Congress

Priority Review Voucher



- "After reading their proposal in Health Affairs, I met with Ridley and colleagues to discuss the idea further, and I subsequently drafted an amendment … Indeed, their idea is the heart of my Elimination of Neglected Diseases (END) amendment."
  – Senator Brownback
- Became law in 2007

REPURPOSING DRUGS

Creating Non-Patent Economic Incentives

Bruce E. Bloom
CEO
Cures Within Reach

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JURISDICTIONAL ARBITRAGE

- Can create exclusivity for repurposed indications for drugs from other jurisdictions
- Method of Use Patent and jurisdictional approval would create market exclusivity
- Example:
  - A drug that has never been approved for human use the US, but is generic or proprietary in Japan, is repurposed for a new indication
  - When the drug FDA approved in the US, the company that has the marketing approval (and MOU patent?) is the only one that can market and make a claim about it, and there is no other available drug in the US to use off-label.

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DIFFERENTIAL PRICING OPTIONS

- Pharmacy benefit managers and others with access to e-prescribing and e-health records could use prior authorization systems discriminate between indications, so different prices for the same generic drug could be different for different indications
- Governments could mandate this system as part of e-health/prescribing improvements
- System could limit the cost of the repurposed drug at inception for the new use and reduce it to the generic price for the old indications once a certain profit has been made
- Would create strong incentive for pharma to repurpose
- Many thanks to Ben Roin for his proposal of this system in his article, "Solving the Problem of New Uses"

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TREATMENT FACILITIES THAT REPURPOSE GENERIC DRUG REGIMENS

- Care Oncology Clinics in the UK and US (and others) provide cocktails of repurposed cancer and non-cancer drugs that complement and enhance standard of care oncology
- The medications are well understood, with low side effects, offering a chance for improved outcomes or the same end result with an improved quality of life, and profit for the clinic
- Always sufficient pre-clinical and clinical evidence for these uses
- They capture the outcomes to create more data-feedback loop
- Will be more useful as precision medicine becomes standard of care

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Licks ATTORNEYS

Alternative incentives to patents in Brazil
February 9, 2017

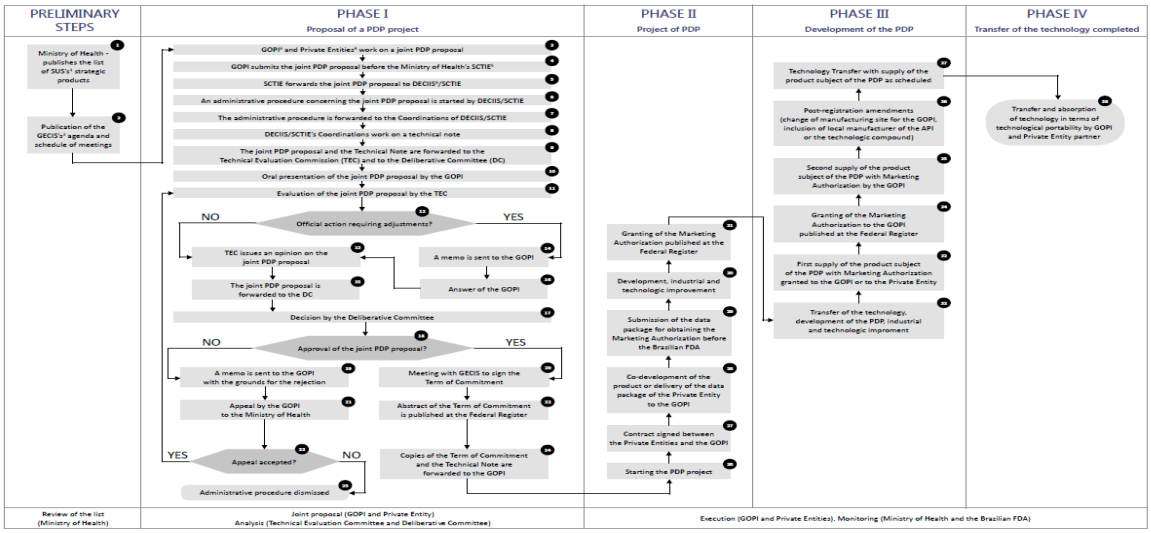
Non-patent incentives

Tech-transfer with the Brazilian government

Partnerships for Productive Development are **long-term government contracts** (5 to 10 years) signed between a **government-owned pharmaceutical industry** (public institutions) and private companies, alone or in consortium (private entity), with the **MoH's approval**, involving the (i) **transfer of the manufacturing technology**; (ii) the **supply of a product** considered strategic for SUS, usually with exclusivity; and (iii) the **nationalization of the API** by one of the private companies

But it is not that simple

Step-by-step in a PDP: from approval to completion



Non-patent incentives

Examples of successful PDPs

Product	Tech-transfer	Total spent as of 2017
Influenza Vaccine	**Sanofi** - Butantan	USD 455 million
Recombinant factor VIII	**Baxter** - Hemobras	USD 430 million
HPV vaccine	**MSD** - Butantan	USD 390 million
Quadrivalent vaccine	**GSK** - Fiocruz	USD 340 million
Infliximab	**Janssen-Cilag** - Fiocruz	USD 250 million