

# Can Australia's Biotechnology Industry Survive?

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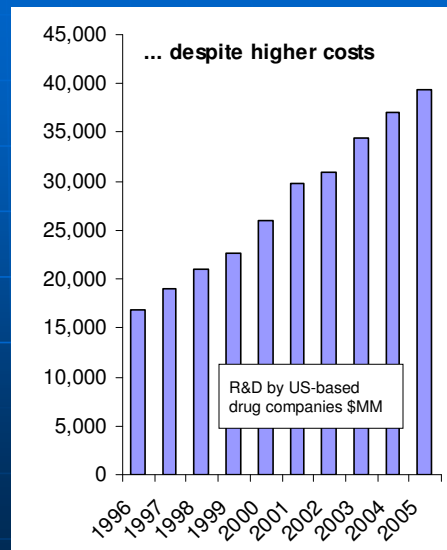
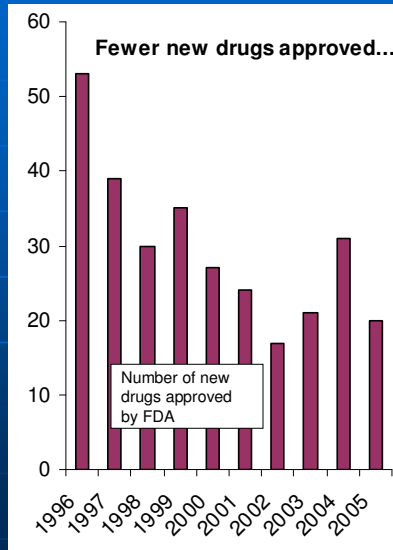
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## Outline

- Industry in transition
  - R&D productivity crisis
  - Vertical restructuring
  - Biogenerics
- Opportunities and challenges
  - For biotech
    - For Australian companies
- Policy and strategy
  - Tough choices ahead

## The research productivity crisis

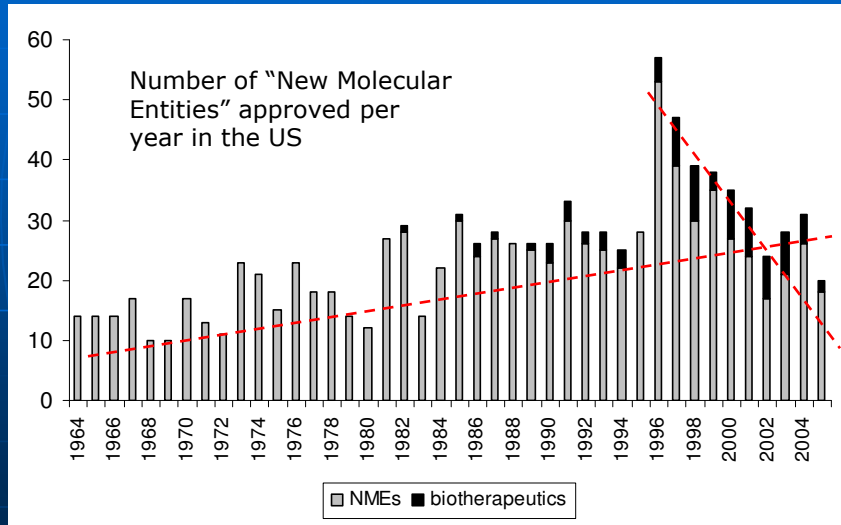


Source: New York Times, FDA, PhRMA

## “The business model is broken”

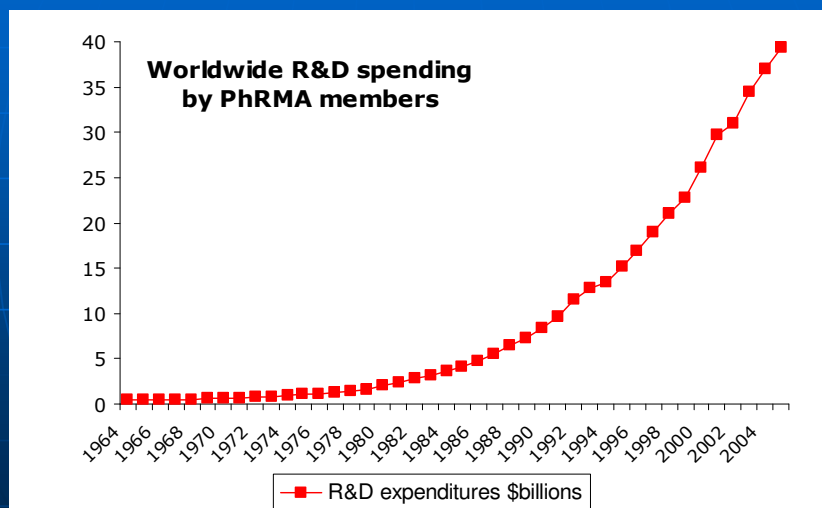
- Global biomedical R&D budget ~ \$100bn
  - substantial contributions from taxpayers
- Fertile science base, 4000 molecules in the pipeline, yet only about 20 NMEs + 5 new biologics per year
- Limited progress against major disease burdens (most cancers, Alzheimer's, schizophrenia, autoimmune diseases etc.)
- **Soaring health care costs & limits to willingness to pay**

## Measuring output: counting new drugs



Source: FDA, Tufts CSDD

## Inputs to drug development



Source: PhRMA, NIH Biomedical R&D Price Deflator

## R&D cost per successful new drug

Millions of 2000  
constant US dollars

Includes failed projects  
and cost of capital



Source: Tufts CSDD

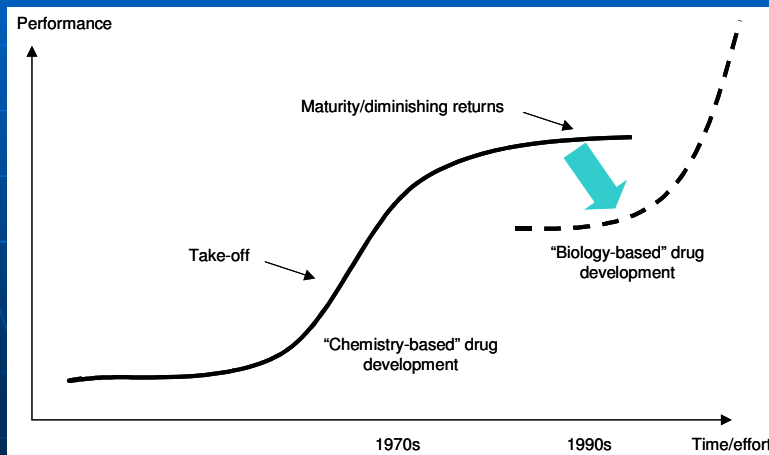
## Why is R&D spending rising?

- "Mining out"
- Input price inflation
- Failure rates in the development process
- Increased opportunities
- Re-tooling
- Re-structuring of the industry

## Structural change in the global biopharmaceutical industry

### Industry transformation

- Biopharmaceuticals is going through a familiar process of disruptive (i.e. costly) technological change from "chemistry" to "biology"

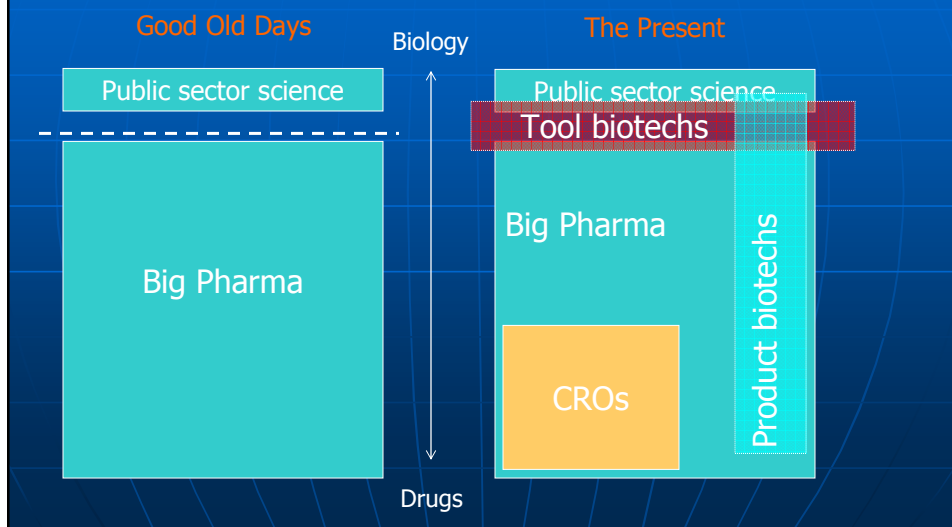


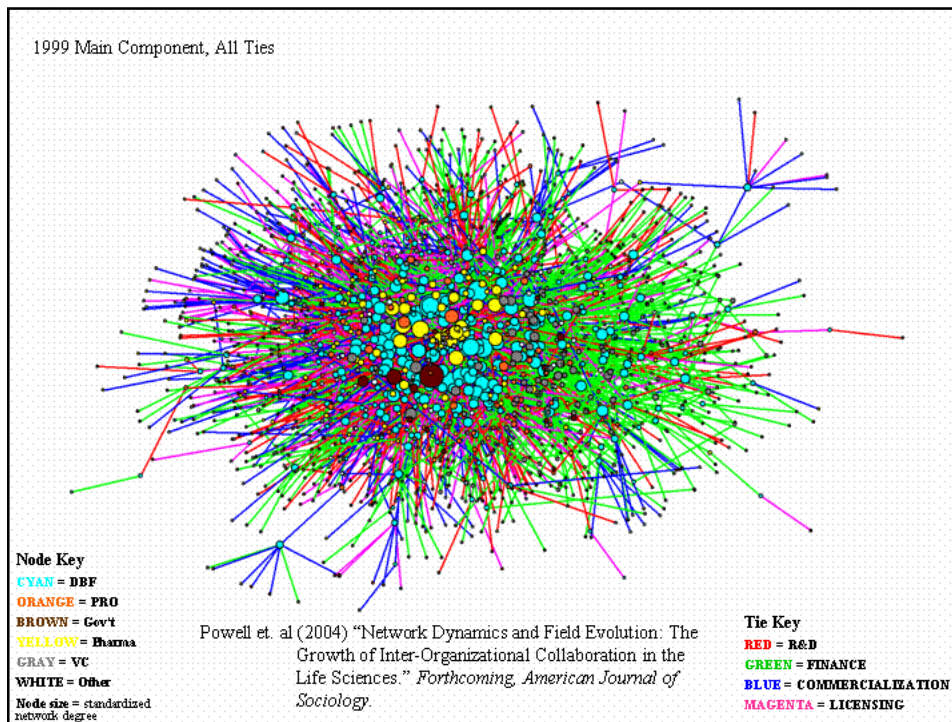
## Transition and vertical dis-integration

- Driven by new science and new actors
  - Also
    - Bayh-Dole Act - university tech transfer
    - availability of venture capital
    - changing IP rules - *Diamond v. Chakrabarty*
- Associated costs? Borne by whom?
- Efficiency compared to old vertically integrated structure?

See Cockburn, I. "The Changing Structure of the Pharmaceutical Industry." *Health Affairs*, 2004, 23(1):10-22.

## Historical evolution of industry structure





## Implications for productivity/value creation

- Vertically dis-integrated industry has important advantages
  - Entrepreneurial energy, speed, flexibility
  - Explicit pricing of risk (in licensing contracts)
  - Efficient specialization and division of labor

**= \$\$\$ on the table**
  
- Also disadvantages compared to integrated firms
  - Fewer transactions in tacit knowledge
  - Governance problems
  - Poor resource allocation if "wrong" prices

**= \$\$\$ down the drain**

## Impact of vertical dis-integration

- Market for knowledge in basic science
  - Previously “free” spillovers from upstream basic research now explicitly priced and paid for by downstream firms
    - = **potential value capture for biotechs**
- Struggle between universities, biotechs, and Big Pharma
  - Defensive investments to improve bargaining
  - Mergers beyond optimal scale/scope
  - Strong IP over upstream research prompts dissipative racing behavior
  - Patent thickets and other transactions costs
    - = **value destruction**

## “The Big Squeeze”

- Big Pharma
  - “Strategy of the Commons” – SNPs Consortium
  - Obtaining their own upstream IP
  - Consolidation
  - Buyers market for technology
- Open Science fights back
  - Public domain data, tools
  - GPL, copyleft concepts
- Biogenerics, manufacturing costs, margins

**Solution: more IP?**

## IP is a double-edged sword

Are more patents preferred to less?

- Freedom to operate searches are increasingly complicated and costly: large patent estates raise everyone's costs
- Threats from external IP
  - Small companies often have limited resources to endure IP battles, can't afford time to negotiate licenses
  - Single product companies very vulnerable
  - Tough to fight competitors with deep pockets and credible threat to countersue (Big Pharma), or apparent immunity from IP suits (universities)
- Investors shy away from IP problems

## “Propertization” of science

- Profit motive and property rights may weaken key institutions of Open Science  
(Publication, sharing, peer review)
- Anticommons, patent thickets, access to data
- Long term social costs
  - Degradation of “truth-telling” function
  - Conflict within public institutions
  - Market-driven versus curiosity-driven agenda
    - Areas of inquiry
    - Time horizons

## Harvard Grad Student Newsletter (April 1st 2000 edition)

As of June 1, 2000, the Biomedical and Biological Sciences (BBS) Program of the Harvard Division of Medical Sciences will become a publicly owned corporation and have its equities freely traded on the stock market (Nasdaq symbol HBBS). The event is viewed as a landmark paradigm shift in financing graduate programs and basic biomedical research...

### Highlights of the deal:

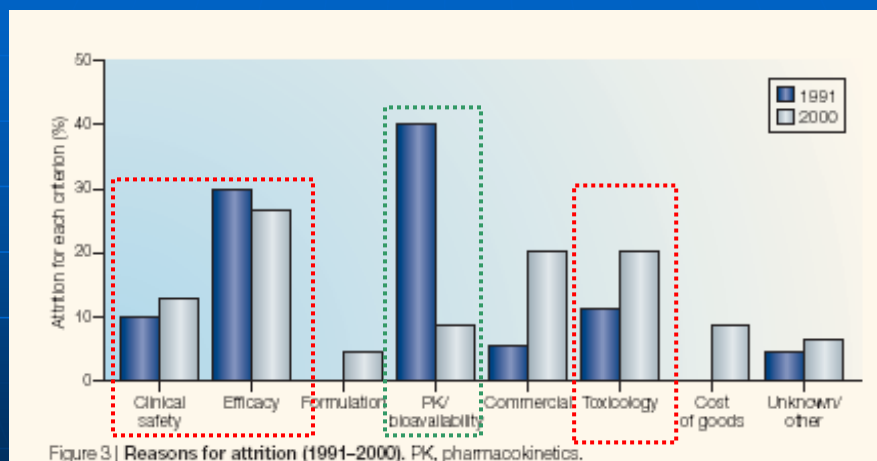
- IPO to finance
  - hostile takeover of MIT Mol. Biol. Dept and Millennium Pharmaceuticals
  - merger with UCSF
- Dean and senior administrators to hold Series A Preferred Stock
- Stock options and performance bonuses for faculty and students
- Right of first refusal on marketable technologies discovered at affiliated labs
- Harvard to hold 51% of equity, major minority investors: NIH, Mass General Hospital, Stanford endowment, Hale & Dorr LLP, Pfizer
- Tracking stocks for Cell Biology, Biological Chemistry, Molecular Pharmacology, and Genetics departments

Fixing the drug development process

## Attrition undermines productivity

- Great success in discovery of drug candidates, but
- High failures rates in clinical development
  - 2/3 fail in Phase II
  - Nearly 1/2 of survivors then fail in Phase III
- (Late) failures are very costly!

## Why do (so many) drugs fail? Science



Kola and Landis, NRDD, August 2004

## How could failures be reduced?

- Rethinking regulatory review processes and standards
- Capacity building and workforce development in investigative medicine
- Scientific progress in translational medicine
  - Systems biology, whole-organism disease pathology etc.

## Freeing up pre-clinical data

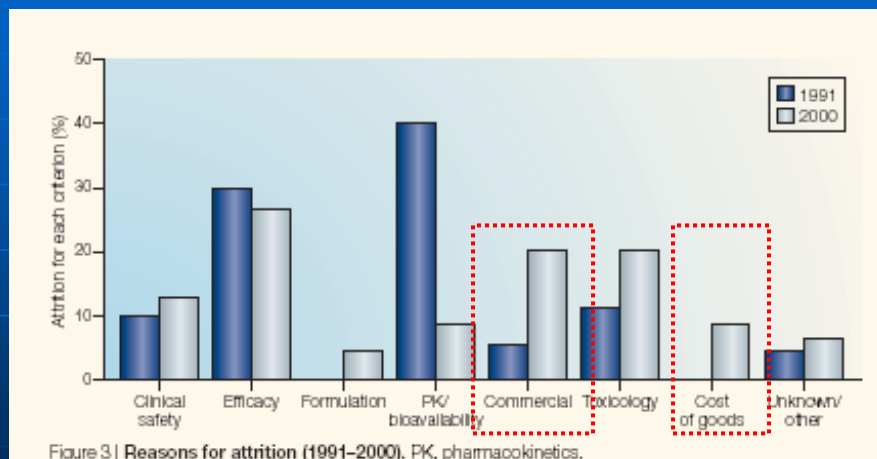
- Wider access to “pre-competitive” data
  - Intermediaries
  - Consortia
  - Public-private partnerships
  - Public provision of data: NIH Molecular Libraries Initiative

= Good news or bad news for biotech?

## Large scale biology

- Systems biology and 'omics are massive projects in every sense: problems likely infeasible for single institutions
  - Solutions will emerge from **linkages** among many sources of data (biophysical, sequences, population variation, disease epidemiology...)
  - Requires free access, sharing, cooperation
  - Incompatible with IP-driven/exclusion based commercialization strategies?

## Why do (so many) drugs fail? Economics



Kola and Landis, NRDD, August 2004

## Blockbuster-nomics

- One-size-fits-all products for large markets look economically irresistible
- But these markets are increasingly crowded and competitive, requiring larger and more expensive trials



higher economic hurdles

→ increased failure rates

→ higher ex post costs

## Kicking the blockbuster habit

- New business models focused on “targeted therapeutics”
- Regulatory acceptance of subpopulation studies (BiDil®)
- Policies to make smaller markets more attractive (Orphan Drug Act)

= Good news or bad news for biotech?

## Biogenerics

### Generics are coming

- First “biosimilars” now being approved (EPO)
- The small molecule patent expiration “cliff” probably doesn’t apply:
  - Manufacturing costs and gross margin
  - Bioequivalence challenges
  - Likely to get brand-based rather than price-based competition (e.g. HGH, insulin, oral contraceptives)
- But business models built on \$10<sup>4</sup>/patient/year unlikely to be sustainable...

See Grabowski, Cockburn, Long “The Market for Follow-on Biologics: How Will It Evolve?” *Health Affairs*, 2006, 25(5):1291-1301.

## Policy and Strategy

### Ways out of this mess

1. New institutions to exploit the exponentially growing, ever more complex science base
  - More shared research resources, particularly in pre-clinical research
    - Incentives to contribute?
    - Limits on use?
  - Hack down the patent thicket
  - Think hard about terms of access to university research

## Ways out of this mess

### 2. Build and sustain critical capacity in investigational and translational medicine

- Funding models for academic medical centers
  - without the clinical trials franchise
- Resources for training
- Incentives to attract scarce talent

## Ways out of this mess

### 3. Enhance efficiency of the market for knowledge

- More explicit price competition
  - Auctions?
- Reduce bargaining costs
  - Standardized contracts
  - Patent pools

## Ways out of this mess

### 4. Rethink business strategy

- New business models
  - Collaboration vs. competition
  - Open Source biology
- More attractive markets
  - Ag-bio
  - Bioremediation
  - Energy, industrial processes

Whither biotech?

## Classic models for biotech

- License out/get acquired
  - At what price?
- Grow into a FIPCO
  - Time/talent/treasure?

Still viable?

## Meanwhile, Down Under...

- Economics of clusters don't look good
  - Distance
  - Sub-optimal scale
  - Quality/quantity of local academic science base?
  - No "anchor tenant" WHY?
  - Location choice: costs of the PBS?
- Catch-up & competition
  - IP: too little, too late?
  - Low cost countries
  - Beggar-thy-neighbour subsidy games

## Tough choices

- “Double down”
  - More subsidies, more infrastructure, more IP, more long term funding, more human capital imports...
- Refocus
  - Ag-bio, bioremediation, bioenergy...
  - Translational/clinical medicine
- Radical re-think
  - Research services model
  - IP-free zone for basic research

Questions/comments?

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