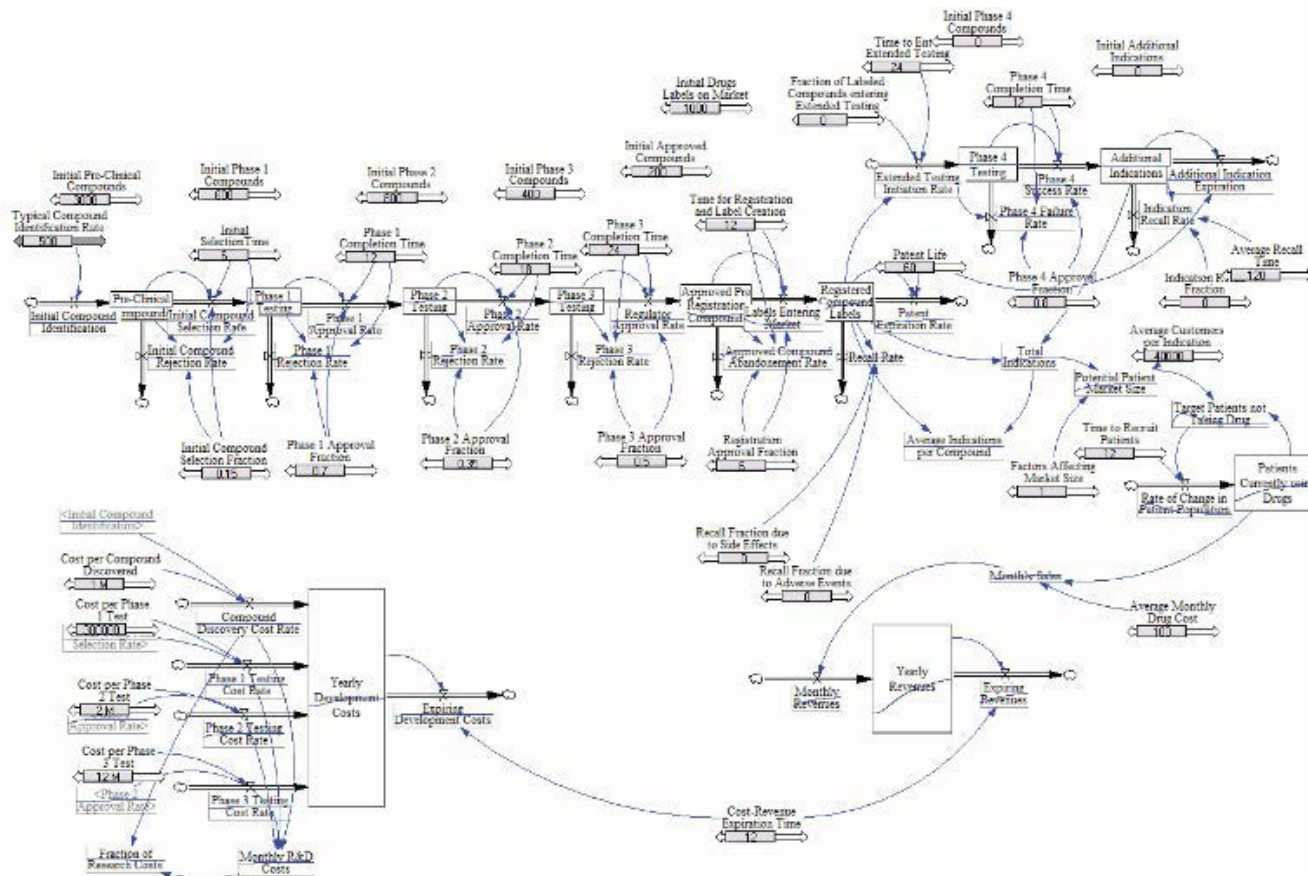


The Evolving Economics of Pharmaceuticals

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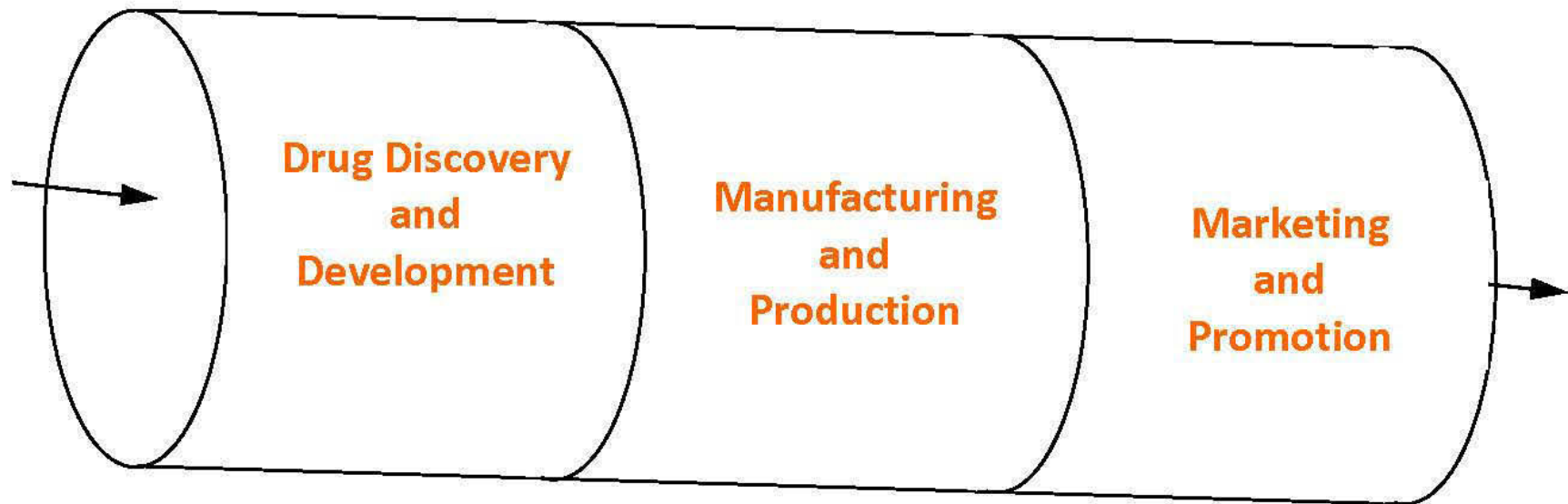
September 12, 2013

Drug Development is a Complex System



Courtesy of Professor Nancy Leveson. Used with permission.

Drug Development is a Complex System



- Not actually a linear process
- Essentially all aspects of the process can now be outsourced

Of Particular Interest . . .

- ❑ Largest firm has market share of less than 10.0% (but major firms have more market power than this suggests).
- ❑ Biotech industry total sales comparable to one or two of the large pharma firms.
- ❑ Drugs account for about 12% of annual \$2+ trillion health care costs in U.S., and growing.
- ❑ Drug prices are higher in the U.S. than just about anywhere else in the world.

Key Themes

- ❑ U.S. Government and pharmaceutical industry are closely intertwined (by the way of the FDA).
- ❑ Changes in prescription drug policy has largely been driven by disasters.
- ❑ Each major policy change was, at first, anticipated to adversely affect the industry, but wound up increasing its market power.

Disasters and Policy Changes

- ❑ In 1937, S. E. Massengill, a U.S. pharma firm introduced a liquid form of the antibiotic, sulfanilamide by dissolving it in ethylene glycol (anti-freeze).
- ❑ More than 100 people died of poisoning.
- ❑ In 1938, congress gave the FDA authority to act in these kinds of events, creating “by prescription only” category.
- ❑ Pharma firms were to separately identify drugs for self-medication (now called, “over the counter”) vs. “by prescription only”.

Disasters and Policy Changes *(continued)*

- “By prescription only” drugs became those that, “He who orders does not buy, and he who buys does not order” (Sen. Estes Kefauver, 1960’ s).
- Result was demand for drugs was insensitive to price.
- 1960’ s: Senate hearing on bill to reduce drug firms’ market power.
- Thalidomide disaster—new anti-nausea drug for pregnant women, never licensed in the U.S., but led to phocomelia syndrome (children born without hands or feet) in European countries.

Disasters and Policy Changes *(continued)*

- ❑ 1962 Drug amendments gave FDA authority to pre-approve drugs entry to market based on drug firm generated data on safety and efficacy (from clinical trials).
- ❑ High cost of clinical trials created large barriers to enter the industry; only large firms could afford.
- ❑ Result was greater market power for the firms in the industry—price inelasticity, high drug prices, large profits until patents ran out (and generic competition could enter).
- ❑ Drove “blockbuster” mentality.

The “Integrated” Pharmaceutical Firm

- ❑ 1944: Some 19 U.S. companies produced penicillin; the largest 5 accounted for 90% of the total sales.
- ❑ Only 1 of these 5 was integrated: combining manufacturing, packaging and sales.
- ❑ Professor Selman Waxman of Rutgers University discovered streptomycin—a new antibiotic that would revolutionize the market for antibiotics.
- ❑ Even more important—Waxman pioneered screening soil samples for the presents of agents (that kept soil relatively harmless) that had human therapeutic value.
- ❑ Waxman’s discovery allowed existing drug firms and new entrants to integrate “backward” into research and development.

Prices, Profitability and Market Power

- ❑ Developing a new drug costs in excess of \$1 billion (according to Tufts Center for the Study of Drug Development).
- ❑ This includes cost of failures and the “opportunity cost” of capital.
- ❑ Only about one-third of eventually marketed drugs make more than enough to cover their development costs.
- ❑ Monopolies on new drugs are protected by patents and the companies earn substantial profits on them.

Prices, Profitability and Market Power *(continued)*

- ❑ Until the patents expire, generic competition emerges and market prices quickly drop.
- ❑ Drug prices highest in the U.S. (where prices are largely free from controls) and much lower in most European countries and Japan (where government has implemented price controls).
- ❑ Profits on sales in U.S. market fuel worldwide R&D.
- ❑ U.S. headquartered firms historically lead the way in producing innovative molecules that become drugs.

Prices, Profitability and Market Power *(continued)*

- NIH—historically a pivotal force in facilitating scientific advances to new drugs.
- Trend toward large firms concentrating and directing their worldwide R&D from U.S. sites.
- We get prestige and jobs but also have high drug prices.

Current State of the Industry

- The global pharmaceutical industry has been extremely successful:
 - Developing products that have contributed to health and well-being
 - In terms of profitability and financial performance
- Many observers see troubling economic fundamentals on the horizon
- Examine:
 - The concerns
 - Paths being taken by firms to improve the situation

Total Unaudited and Audited Global Pharmaceutical Market by Region

Image removed due to copyright restrictions. Table of Global Pharmaceutical Markets by Region, IMS Health Market Prognosis, June 2013.

See: http://www.imshealth.com/deployedfiles/imshealth/Global/Content/Corporate/Press%20Room/Total_World_Pharma_Market_Toplevel_metrics_2012-17_regions.pdf.



Of Concern... "Innovation Gap"

Image removed due to copyright restrictions. Graph of New Molecular Entities Approvals from 1995-2012. Data from PhRMA and GAO Report.
See: <http://www.phrma.org/> and <http://gao.gov/>.

Years



Sources: PhRMA and GAO Report



Of Concern...FDA NME Approvals

Image removed due to copyright restrictions. Graph of New Molecular Entities Approvals by the U.S. Food and Drug Administration from 1940-2011. Data from U. S. F. D. A.
See: <http://www.fda.gov/> .

Of concern... "Patent Cliff"

Global Sales Value of Patent Losses

VALUE SALES LOSSES (\$USD Billion)

Image removed due to copyright restrictions. Graph of Global Sales Value of Patent Losses from 2010-2016. Data from IMS, and Sergio Simoes.
See: <http://www.imshealth.com/portal/site/imshealth>.

Of concern...

Increasing Demands of Regulatory Agencies

Image removed due to copyright restrictions. Graph of averages for clinical trials and patient trials for new drug applications from 1977-2001. Data from SkyePharma, Parexel 2003/4, Sergio Simoes. See: <http://www.skyepharma.com/> and <http://www.parexel.com/>.

Of Concern...Cost containment efforts in established and emerging markets

Image removed due to copyright restrictions. Table of cost containment efforts in established and emerging markets. IMAP: Pharma & Biotech Industry Global Report, 2011, page 7.
See:http://www.kurmannpartners.com/fileadmin/user_upload/Industry_Reports/IMAP_Global_Pharma_and_Biotech_Report_2011.pdf

Promising Paths?

Mergers and Acquisitions

- ❑ Have not solved the problems
- ❑ “R&D Paralysis” described in merged, large firms
- ❑ Article published in 2011 in nature drug discovery (LA Mattina, the impact of mergers on pharmaceutical R&D” reports new drug approvals over past 60 years correlates strongly with number of firms active in R&D

Promising Paths?

Shift Strategy Away from Developing Small Molecule Blockbusters

- ❑ “Old” Strategy—Develop small molecule drug for large chronic disease market—patients take drug every day for the rest of their lives
- ❑ “New” Strategy—Develop Biologics and targeted therapies for orphan diseases and other small markets and charge prices of \$10,000+ per course of treatment or per year
- ❑ Develop Biosimilars
- ❑ “Small market blockbusters among top 15 drugs (Global Sales):
 - ❑ 2009: 6
 - ❑ 2016 (Forecast): 8

Promising Paths?

Shift marketing strategy from established to emerging markets

- ❑ Forecast annual market growth rates in established drug markets (North America, Europe, Japan): 3-6%
- ❑ Forecast Annual Growth Rates in Emerging Markets: 12% (to as much as 20% in China)
- ❑ Emerging markets targets by pharmaceutical companies:

Argentina, Brazil, China, Egypt, India, Indonesia, Mexico, Pakistan, Poland, Romania, Russia, South Africa, Thailand, Turkey, Ukraine, Venezuela, Vietnam

Promising Paths? Bring Manufacturing Costs Down

Text quotes removed due to copyright restrictions. Leila Abboud and Scott Hensley. "New Prescription For Drug Makers: Update the Plants," *Wall Street Journal*, September 3, 2003.
See: <http://online.wsj.com/articles/SB10625358403931000>.

Promising Paths? Reduce R&D Costs Via Adaptive Clinical Trials and Drug Approvals

- ❑ Identify Biomarkers to identify which patients will benefit
- ❑ Design clinical trials in stages, leading to fewer total patients in trials
- ❑ License drugs in stages—iteratively gathering evidence through continued registration trials and post-market surveillance

Promising Paths?

Collaboration and Open Source R&D Strategies

- “Patent Free” approaches to early stage research, led by advocacy groups (autism, schizophrenia societies)—hold off patenting through proof of concept phase
- University-Industry collaboration—Lilly and Pfizer offering scientists opportunity for no-fee testing of promising molecules—intellectual property remains with the scientists

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