Linking patents to products

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- In general: no straightforward linkage [exception: de Rassenfosse et al. (2018)]
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- Drug makers are required to report all patent protection to the FDA
- Lists are published annually as the FDA’s Orange Book
  - All patents (& regulatory exclusivities) associated with brand-name, small-molecule drugs
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**This paper:** a user’s guide to the challenges and opportunities of this unique resource
This paper

We introduce a newly digitized, open-access dataset of Orange Book records [1985-2016]

- Annual editions provide snapshots at specific points in time
- New dataset provides a comprehensive portrait of legal protections over drug lifecycles
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• New dataset provides a comprehensive portrait of legal protections over drug lifecycles

Focus on two challenges:

1. Orange Book records are self-reported by firms and not audited by the FDA
   ⟷ Validation exercises against external benchmarks
2. The appropriate use of the Orange Book may differ across researchers and questions
   ⟷ Detailed use case: calculating market exclusivity
Outline

The Orange Book

The NBER Orange Book Dataset

How complete and accurate are records?

Use case: market exclusivity

Takeaways
Background

Patents and regulatory exclusivities added under Hatch-Waxman Act (1984)
(Drug Price Competition and Patent Term Restoration Act)

- Modern regime for competition for brand-name and generic drugs
- Includes a variety of features intended to accelerate entry of generic drugs
Patents

**Eligible:** Patents with > 1 claim covering drug substances, products, and methods of use

- Must list any patents that “could reasonably be asserted” [21 U.S.C. § 355(b)(1)(A)(viii)]
- Patents issued after drug approval must be listed within 30 days of issuance
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Ineligible: Patents on manufacturing processes, packaging, metabolites, intermediates
Firms face strong incentives to list all eligible patents

- Potential generic entrants are required to *challenge* every Orange Book patent
  - Legal certification that patent is either invalid or not infringed
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Key feature: Infringement suits filed in response to Paragraph IV challenges

⇒ Generic approval blocked for 30 months while suit is pending
Regulatory exclusivities

**Exclusivities:** Delays and prohibitions on approval of competitor drugs, awarded by FDA

1. New chemical entity (NCE) exclusivity: 5 years
2. Orphan drug exclusivity (ODE): 7 years
3. Pediatric (PED) exclusivity: 6 months
4. Generating Antibiotic Incentives Now (GAIN) exclusivity: 5 years
5. 180-day exclusivity (Generic Drug Exclusivity): 180 days
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Generic-blocking exclusivities

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Orange Book patent and exclusivity data - 1985-2016

These data files provide digital versions of the US Food and Drug Administration (FDA)'s Orange Book patent and exclusivity tables for years 1985-2016 (no Orange Book was published in 1986). PDF versions of the Orange Books were obtained via a Freedom of Information Act (FOIA) request, and data from these PDF files was either hand-entered or parsed in order to create the digital files.
Data Resources

Four data files:

1. **FDA Drug Patents**: Full listing of patent records
   [edition, FDA application no., generic name, trade name, patent no., patent expiration]

2. **FDA Patent Use Codes**: Details on approved indications/uses [1998-present]

3. **FDA Drug Exclusivity**: Full listings of all exclusivities

4. **FDA Drug Exclusivity Codes**: Details on exclusivity types
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Dataset does not include all information in FDA Orange Book

- *e.g.*, the Products file, which identifies therapeutically equivalent alternatives for drugs
- Paper provides directions to expand coverage to more recent years
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Of the 2,458 new (small molecule) drugs approved between 1985 and 2015:

- $\sim 80\%$ of drugs have at least one form of legal protection
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Of the 2,458 new (small molecule) drugs approved between 1985 and 2015:
  • ∼80% of drugs have at least one form of legal protection

Of the 796 new molecular entities approved between 1985 and 2015:
  • ∼96% of innovative drugs have at least one form of legal protection

* Note: does not include patent listings for biologics (some are listed in FDA's Purple Book)
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Of the 2,458 new (small molecule) drugs approved between 1985 and 2015:

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Of the 796 new molecular entities approved between 1985 and 2015:

- \( \sim 96\% \) of *innovative* drugs have at least one form of legal protection

\[ \Rightarrow \] Consistent with documented importance of IP in pharmaceutical markets

[Cohen, Nelson, Walsh 2000; Levin et al. 1987]
Drug coverage

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Exclusivity coverage

Exclusivity is granted by the FDA and recorded directly by the agency

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Two simple validation exercises:

1. Confirm that Orange Book records of ODE match an FDA list of orphan designations
2. Confirm that Orange Book records of PED match an FDA list of pediatric studies
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⇒ Exclusivity records are **complete** and **accurate**
Patent coverage reflects a mix of legal requirements and firm strategy

- Expect coverage to vary across drugs and firms
- May also vary over time: documented increase in listing of “secondary patents”

[Kapczynski, Park, and Sampat 2012; Hemphill and Sampat 2011]
Patent coverage

Three validation exercises:

1. Comparison to IQVIA/Ark [Kyle, Sampat, Shadlen 2020]
   - Many drug patents (on the order of 60%) are not listed in the Orange Book
   - But the vast majority that are “likely to constrain generic entry” are listed
Patent coverage

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⇒ Records of all “important” drug patents are complete
Patent expiration

Patents may not always expire 20 years after filing...

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Patent expiration

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We investigate whether OB records reflect four changes to expiration dates:

1. Agreement on Trade-Related Aspects of IP Rights (TRIPS)
2. Patent Term Extension (PTE)
3. Patent Term Adjustment (PTA)
4. Maintenance Fee Non-Payment

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⇒ High-level: all changes are accurate except maintenance fees

- Substantial problem: \(\sim45\) percent of OB patents expire before full-term
- Accurate measures of patent term require additional USPTO records
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Calculating exclusivity: combining records

The “right” calculation of market exclusivity is a function of the research question

- **Nominal**: How much market exclusivity do various legal protections confer?
- **Expected**: How long can a firm expect to be shielded from competition?
- **Realized**: How much time actually elapsed before generic entry?
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Exercise: compare measures of exclusivity to observed generic entry

- **Sample**: 1,673 new drugs approved between 1985 and 2014
- **Median drug**: 13 years of market exclusivity
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Paper provides detailed advice for calculation of “legal protection periods”
Measure #1: NCE

**Test:** NCE is granted & enforced by FDA $\implies$ expect to bind

Use case: market exclusivity
Measure #1: NCE

Test: NCE is granted & enforced by FDA ⇒ expect to bind

Use case: market exclusivity
Measure #2: Earliest patent

**Test:** Early expiring patents likely stronger than later expiring $\implies$ expect minimal generic entry

[Hemphill and Sampat, 2011; Branstetter, Chatterjee, and Higgins, 2016; Gupta, 2021]
**Measure #2: Earliest patent**

**Test:** Early expiring patents likely stronger than later expiring $\implies$ expect minimal generic entry

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**Use case: market exclusivity**
Measure #3: Latest patent

**Test:** Latest expiring patents are often invalidated/unenforced $\implies$ expect more generic entry

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**Measure #3: Latest patent**

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Using the Orange Book for research

Key advantages:

- Unique opportunity to study linkages between patents and products
  - Rich resource for understanding pharmaceutical markets
- Variables facilitate a wide variety of linkages to other datasets
  - Drug name, sponsor, patent number, FDA application number
- **Good news:** Records are generally complete and accurate
  - Exception: maintenance fee non-payment
Using the Orange Book for research

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“Calculating exclusivity” $\implies$ Appropriate use of data is based on questions of interest