Litigation Webinar Series

Hatch-Waxman 101

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FISH & RICHARDSON

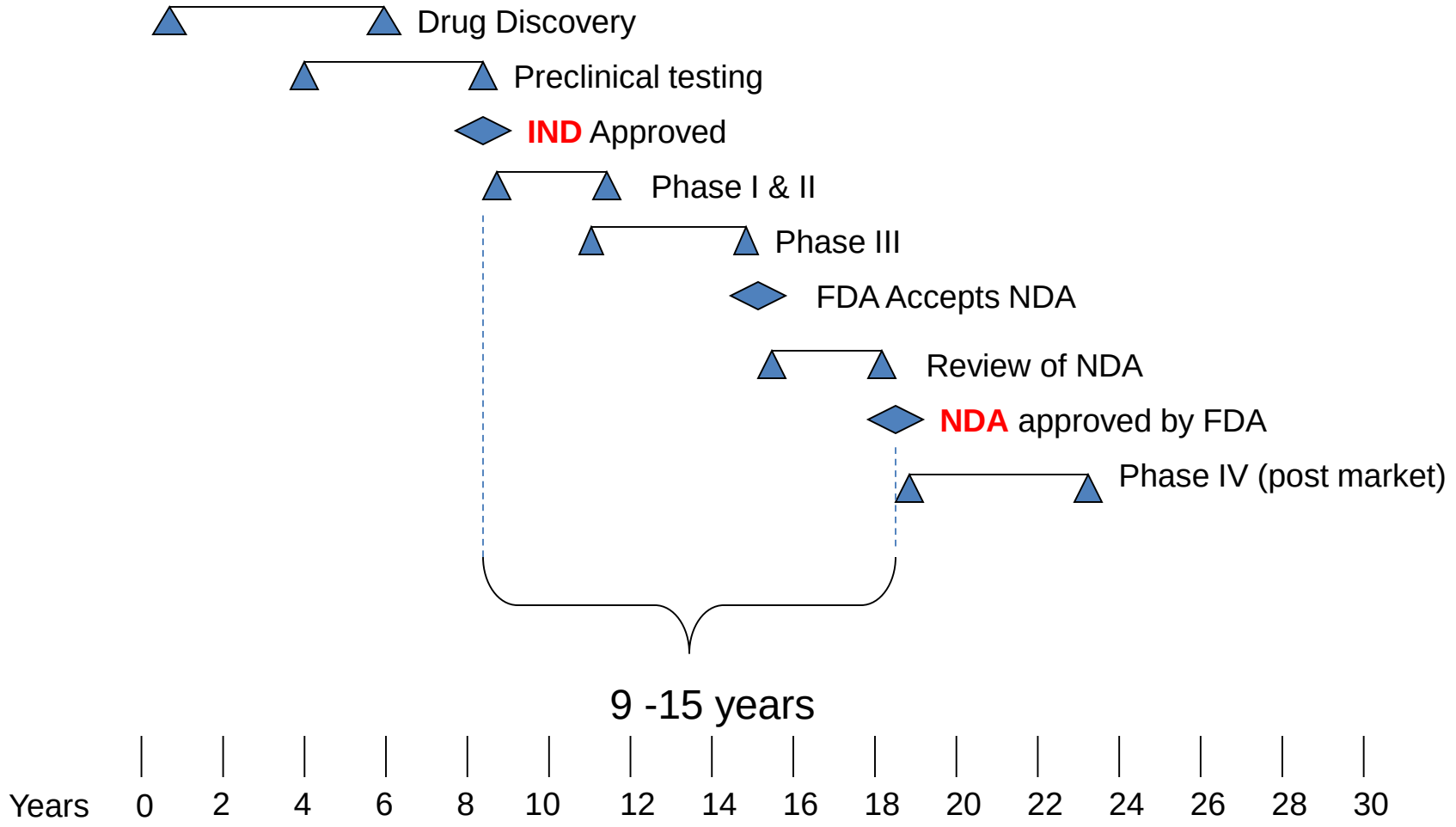
Overview

- Hatch-Waxman Series
- Housekeeping
  - CLE Contact: Jane Lundberg
    - lundberg@fr.com
  - Questions
  - Materials: www.fr.com/webinars
- #fishwebinar

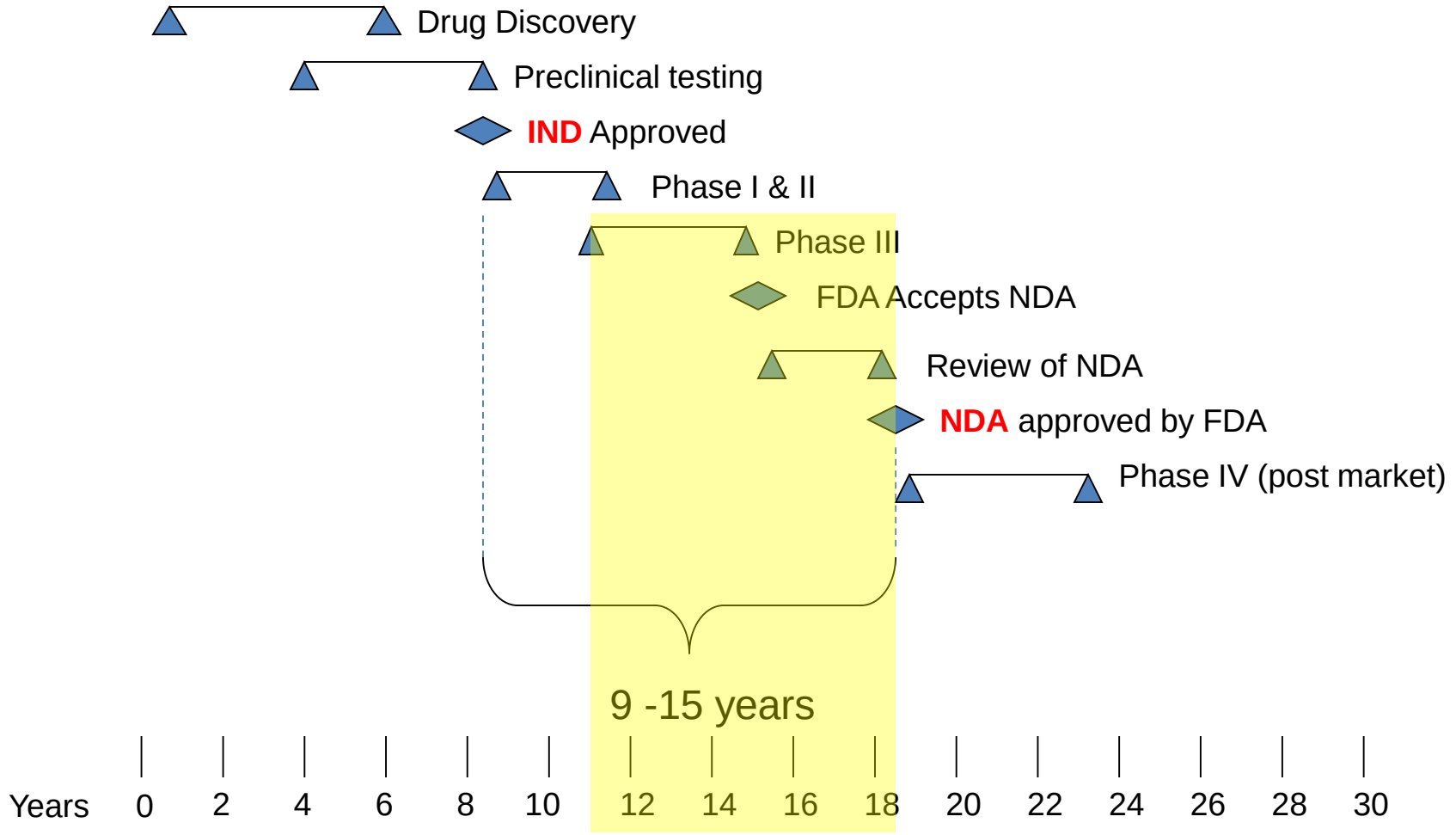
Upcoming Webinar

Hatch-Waxman 102
January 25, 2018
1:00 – 2:00 pm ET

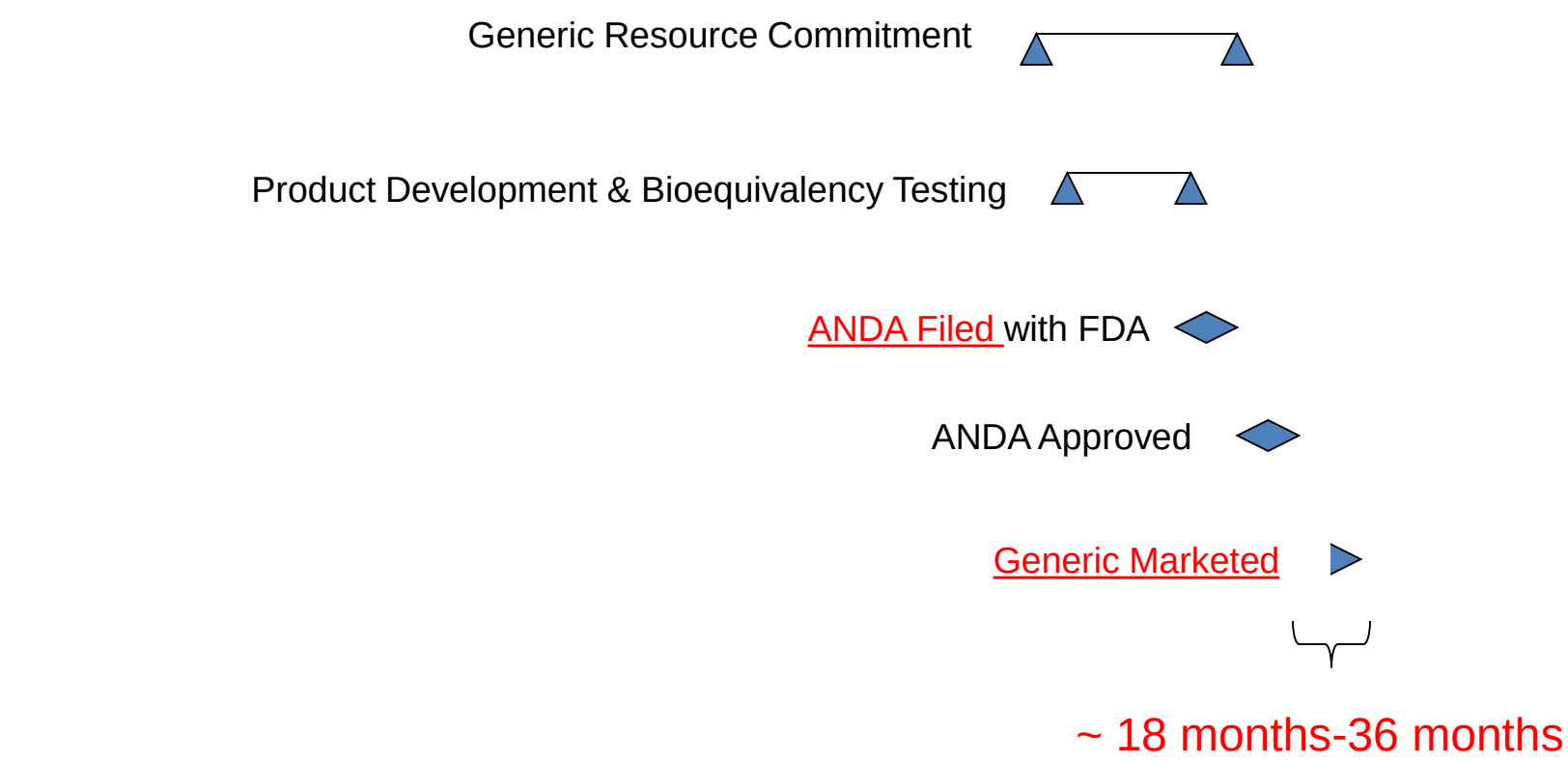
Drug Discovery & Development



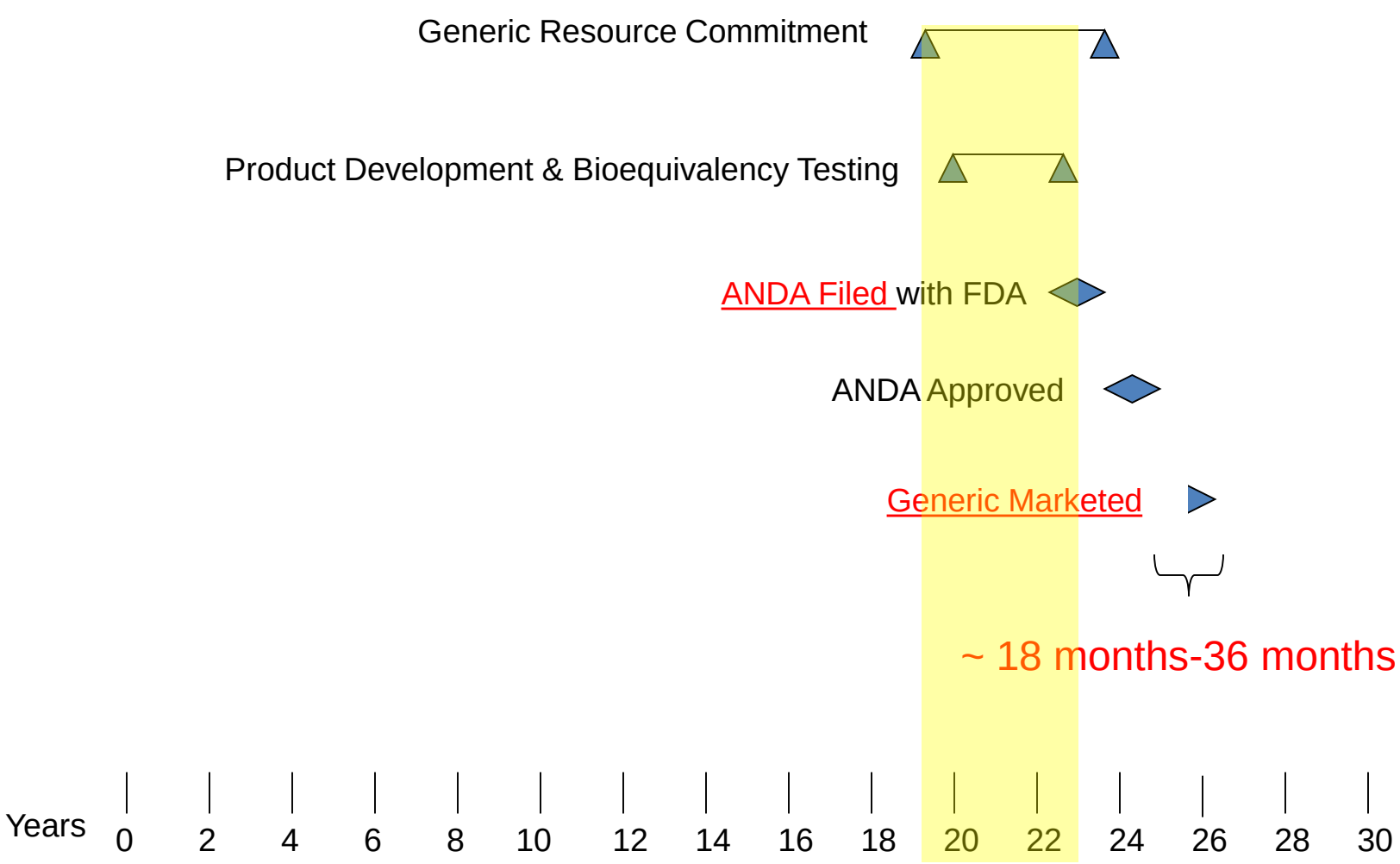
Drug Discovery & Development



Generic Timeline



Generic Timeline



The Great Compromise

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Hatch-Waxman Act Is a Compromise

The Act was legislatively negotiated to strike:

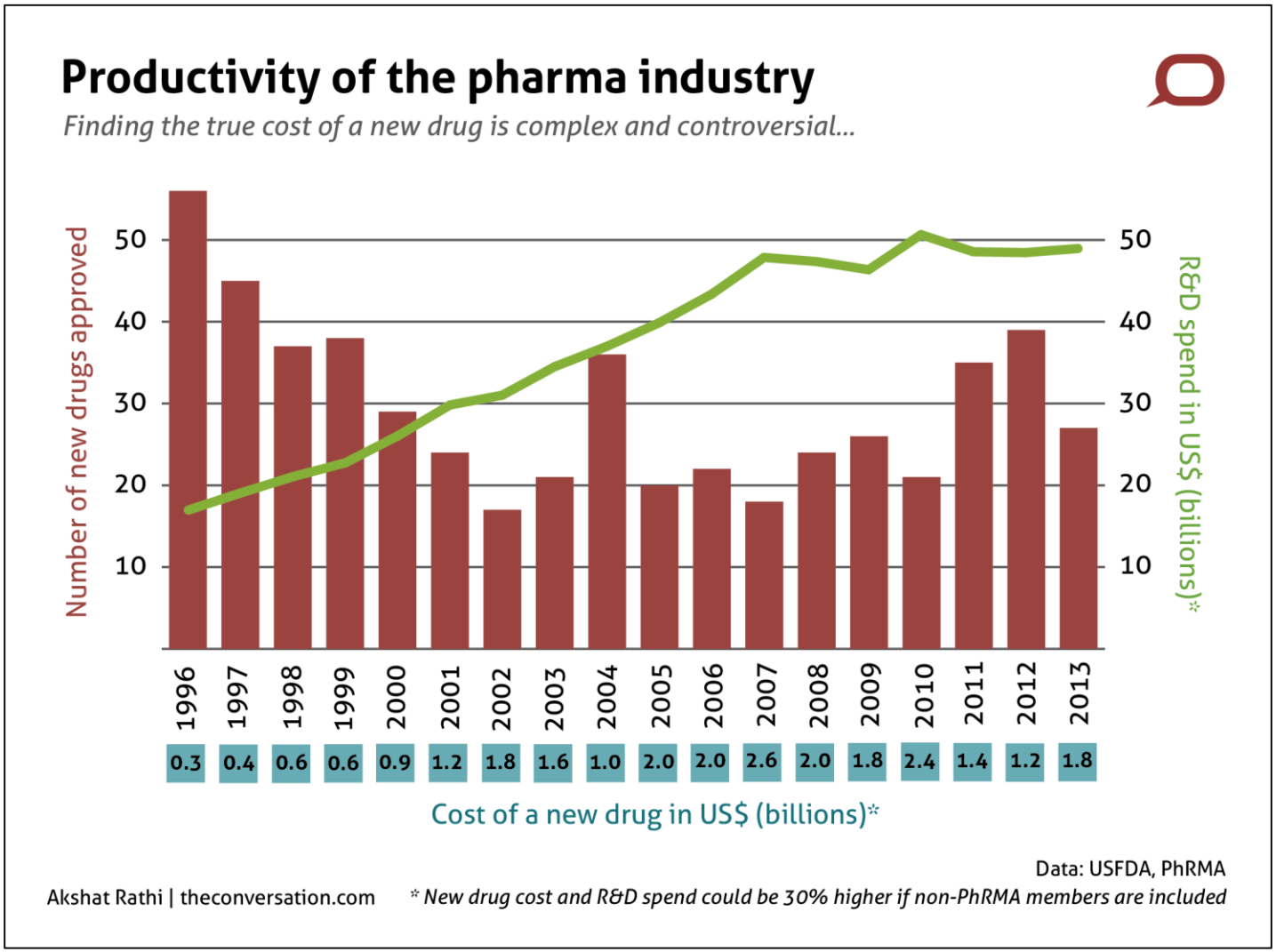
> "a balance between two potentially competing policy interests—inducing pioneering development of pharmaceutical formulations and methods and facilitating efficient transition to a market with low-cost, generic copies of those pioneering inventions at the close of a patent term."

Novo Nordisk A/S, et al. v. Caraco Pharmaceutical Laboratories, Ltd., et al., No. 2010- 1001 (Fed. Cir., April 14, 2010), at 2.

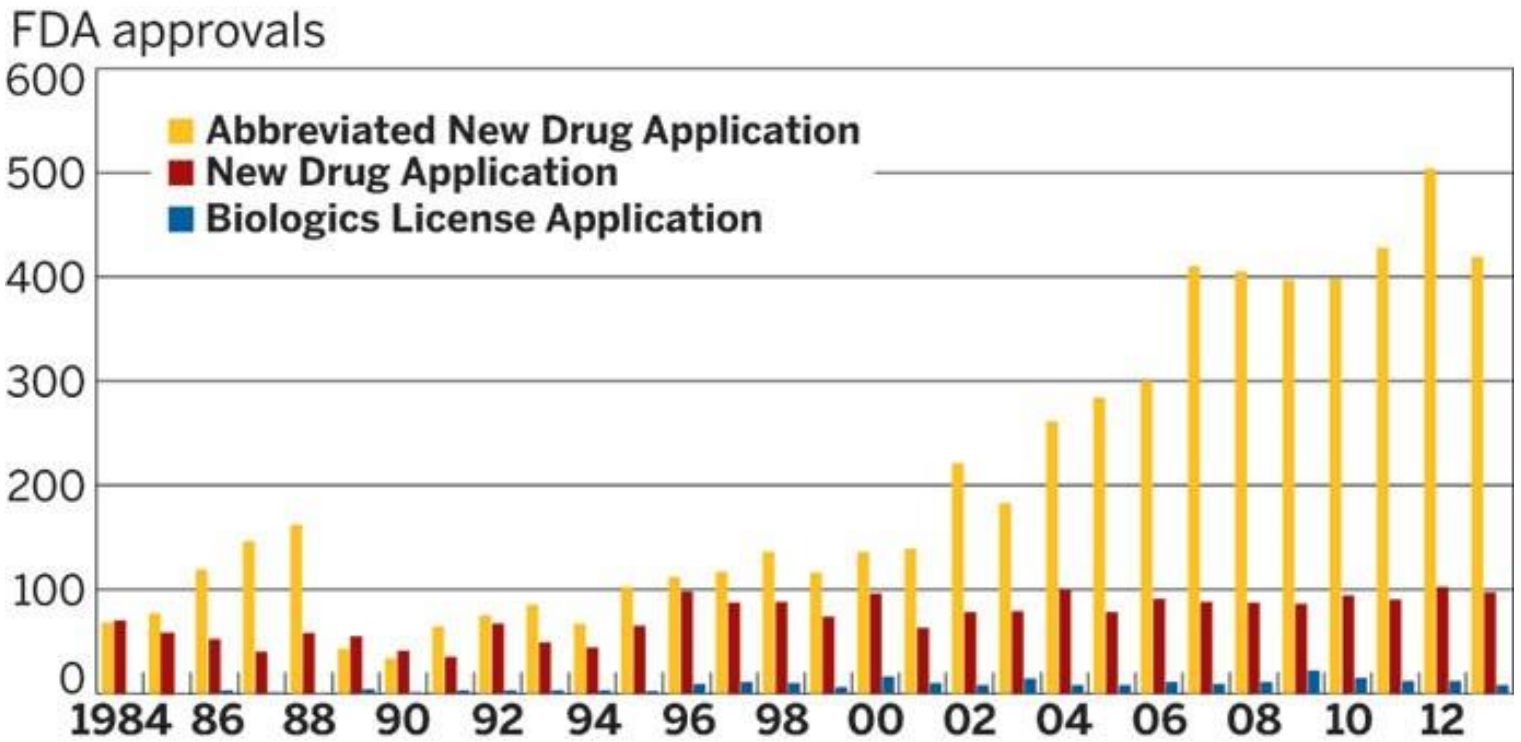
The Compromise

- Brand Industry (§ 505(j)(5)(F):
  - 5 year “filing” exclusivity (“data exclusivity”) for new chemical entities (NCE)
  - 3 year “marketing” exclusivity based on new clinical trials
  - Patent Term Extension for time patented product is under review by FDA
- Generic Industry:
  - Use of Abbreviated New Drug Applications (ANDAs)
  - 180-Day Generic Drug Exclusivity for first Paragraph IV filer(s)
  - Ability to develop product free of worry of infringement suit (Safe Harbor)
- Both
  - Opportunity for Court to decide patent issues pre-launch

It's Working


Productivity of the pharma industry
Finding the true cost of a new drug is complex and controversial...
Number of new drugs approved
R&D spend in US$ (billions)*
50
40
30
20
10
1996 1997 1998 1999 2000 2001 2002 2003 2004 2005 2006 2007 2008 2009 2010 2011 2012 2013
0.3 0.4 0.6 0.6 0.9 1.2 1.8 1.6 1.0 2.0 2.0 2.6 2.0 1.8 2.4 1.4 1.2 1.8
Cost of a new drug in US$ (billions)*
Data: USFDA, PhRMA
Akshat Rathi | theconversation.com
* New drug cost and R&D spend could be 30% higher if non-PhRMA members are included

It's Working


FDA approvals
600
500
400
300
200
100
0
Abbreviated New Drug Application
New Drug Application
Biologics License Application
1984
86
88
90
92
94
96
98
00
02
04
06
08
10
12

How Does it Work . . .

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Hatch-Waxman Act – Key Concepts

- “Easier” routes of approval
- Exclusivities
- List of relevant patents
- Generic certification and notice re: patents
- Patent Challenge/Safe Harbor
- Stay of Approval
- 180-Day Exclusivity

“Easier” Routes to Drug Approval (21 USC § 355)

- 505(b)(1) or New Drug Application (“NDA”)
  - Full clinical trials, patent declaration
- 505(b)(2) or “paper NDA”
  - New drugs – partial clinical trials, reliance on published safety and efficacy data, patent declaration
  - Generic drugs – partial clinical trials, reliance on unpublished safety and efficacy data, patent certification
- 505 (j) or Abbreviated New Drug Application (“ANDA”) – true generic
  - Clinical trials often not required, reliance on data for the approved branded drug, patent certification
  - Can petition FDA to change active ingredient (combination drug), route, dosage or strength
  - Inactive ingredient changes permitted in some cases

Exclusivities

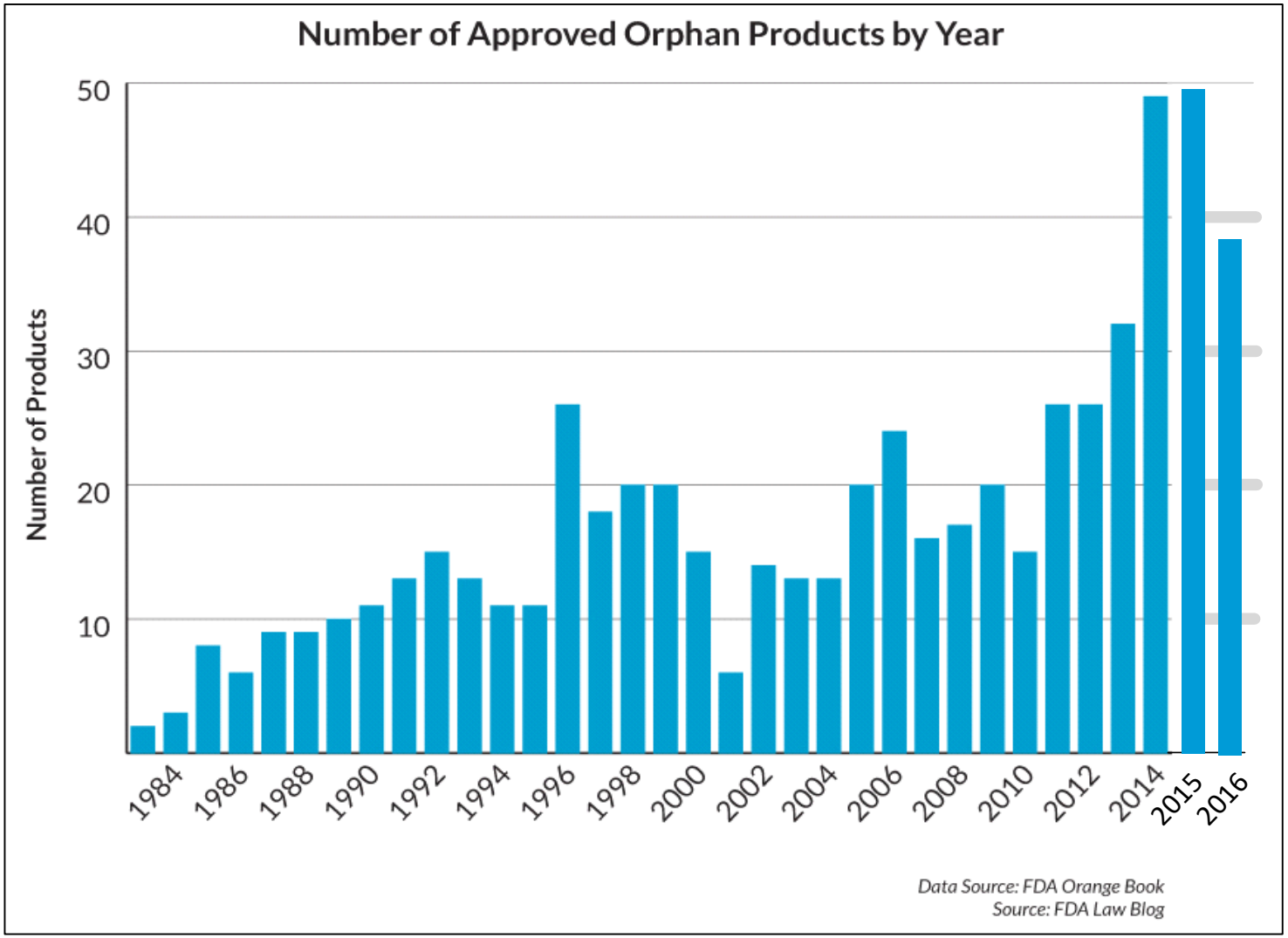
- Scope: drugs, combinations regulated as drugs, new antibiotics (since 1997)
- 5 year “data” exclusivity
  - New active moieties only
  - No generic or 505(b)(2) application can be filed for 5 years
  - 4 year exclusivity if Orange Book listed patent is challenged
- 3 Year “marketing” exclusivity
  - Clinicals required; must be essential to approval; change in dosage, new patient regulation, new indications, Rx to OTC
  - No generic or 505(b)(2) can be approved for 3 years
- Pediatric Exclusivity
- Orphan Drug Exclusivity

Pediatric Exclusivity

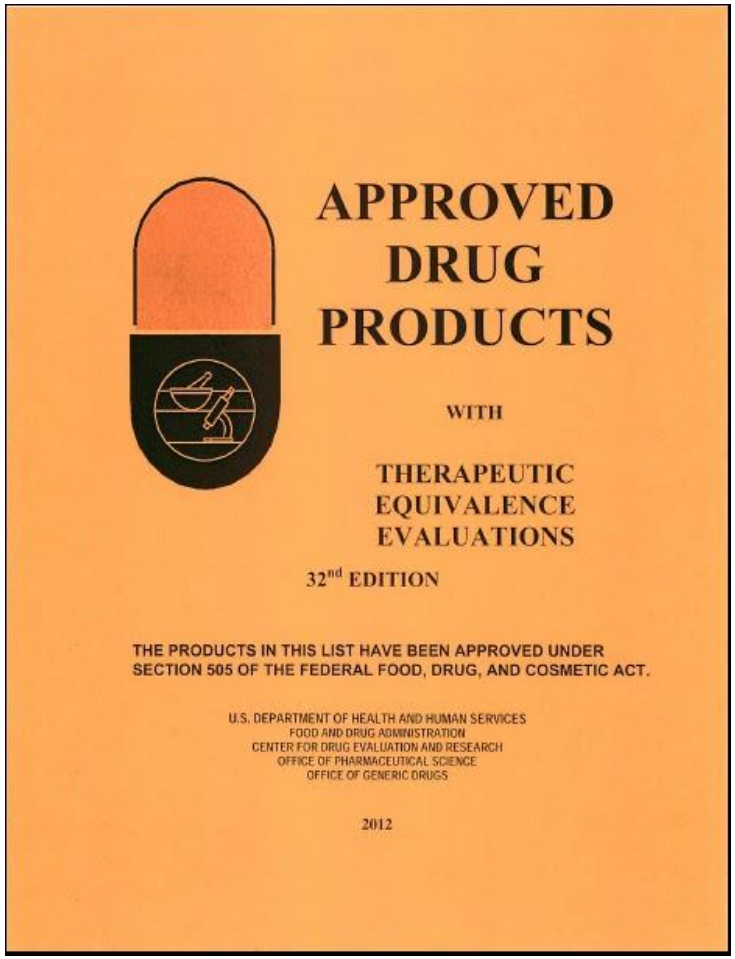
- Scope: clinical studies in pediatric populations
- Drugs and biologics (2009 ACA)
- Protects active moiety; all indications, dosages, strengths
- Adds 6 months protection to all other exclusivities
- Listed patents also get 6 months of protection
- Protects combination drugs containing active moiety

Orphan Drug Exclusivity

- Scope: population <200,000 or no expectation of cost recovery
- Drugs and biologics
- 7 years protection
- No FDA approval for same product for same indication unless clinically superior
  - clinical superiority means drug is not the “same”
- OD designation must be made before NDA/BLA submission
- Tax credits, fee waivers, grants


Number of Approved Orphan Products by Year
Number of Products
50
40
30
20
10
1984
1986
1988
1990
1992
1994
1996
1998
2000
2002
2004
2006
2008
2010
2012
2014
2015
2016
Data Source: FDA Orange Book
Source: FDA Law Blog

Listings of Patents – The Orange Book



Orange Book Listing

Eligibility

- Patent must claim a drug or method of using a drug for which a claim of patent infringement could reasonably be asserted
- 2003 Orange Book Reforms – no packaging patents, metabolites or intermediates

FDA Form 3542 – Patent Information

- Use patents must be identified on label
- Patent “use code” provided for each method patent
- Signed under “penalty of perjury”
- New patents (after NDA approved) must be filed within 30 days to perfect issue date in OB

Timing

- NDA Sponsor must submit within 30 days of approval of NDA or supplement and patent issuance
- If submitted after 30 days, pending ANDAs do NOT have to certify

Orange Book Listing - Use Code

- Tool for FDA – identifies language on label protected by method patents
- Drafted by pioneer based on reasonable claim construction
- 240 character max
- *Caraco v. Novo Nordisk* (Supreme Court 2012) – use code cannot prevent generic from marketing a drug for an approved use not claimed by the patent

“Section viii” Carve Out – 505(j)(2)(A)(viii)

- Permits a generic to “carve out” of label approved uses that it is not seeking approval for
  - Generic product must still be safe and effective for remaining approved uses
  - Impact: ANDA with carved out label can be approved absent another PIV (i.e. no First to File blocking approval)

35 USC 271(e)(2) filing of ANDA or 505(b)(2) is an act of infringement “if the purpose is to obtain approval … to engage in the commercial manufacture, use or sale of a drug … before the expiration of such patent.”

Patent Certification

For each patent listed in the Orange Book, Generics must certify one of the following:

- Paragraph I – patent information has not been filed
  - FDA can approve ANDA whenever ready to
- Paragraph II – patent has expired
  - FDA can approve ANDA whenever ready to
- Paragraph III – date patent will expire
  - FDA can approve ANDA when patent expires and ANDA is ready to be approved
- Paragraph IV – such patent is invalid or will not be infringed by the manufacture, use, or sale of the drug for which the application is submitted
  - Much more complicated approval window

Paragraph IV Certification

- Generic applicant must state:
  - That an application that contains data from a bioequivalence or bioavailability study has been submitted;
  - Seeking approval to engage in the commercial manufacture, use, or sale of the listed drug before the expiration of the listed patent(s); and
  - The factual and legal basis that the ANDA applicant believes that the patent is invalid or will not be infringed
- Generic must send notice letter within 20 days from ANDA “receipt” acknowledgement letter from FDA
- *FDA does not police the sufficiency of the notice letter*

Safe Harbor (35 USC § 271(e)(1))

- § 271(e)(1): “It shall not be an act of infringement to make, use, offer to sell within the US or import into the US a patented invention … solely for uses reasonably related to the development and submission of information under a Federal Law which regulates the manufacture, use or sale of drugs or veterinary biological products.”

Safe Harbor (35 USC § 271(e)(1))

- Scope of Safe Harbor: Supreme Court decision in *Merck v. Integra* says Safe Harbor "extends to all uses of patented inventions that are ***reasonably related to the development and submission of any information under the FDCA***. This necessarily includes preclinical studies of patented compounds that are appropriate for submission to the FDA in the regulatory process. There is simply no room in the statute for excluding certain information from the exemption on the basis of the phase of research in which it is developed or the particular submission in which it could be included."

- Bottom line – actions related to seeking FDA approval are not infringement

Patent Challenge

- Filing of ANDA is an “artificial act” of infringement
- NDA sponsor can sue when it receives notice
- Infringement suit can begin ***before*** ANDA approval
- If suit brought within 45 days of notice, ANDA approval is stayed for 30 months
  - *Computation of 45-day time clock.* (1) The 45-day clock described in paragraph (b)(3) of this section begins on the day after the date of receipt of the applicant's notice of certification by the patent owner or its representative, and by the approved application holder. When the 45th day falls on Saturday, Sunday, or a Federal holiday, the 45th day will be the next day that is not a Saturday, Sunday, or a Federal holiday. https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=314.107
- If no suit within 45 days, FDA can approve ANDA at its discretion

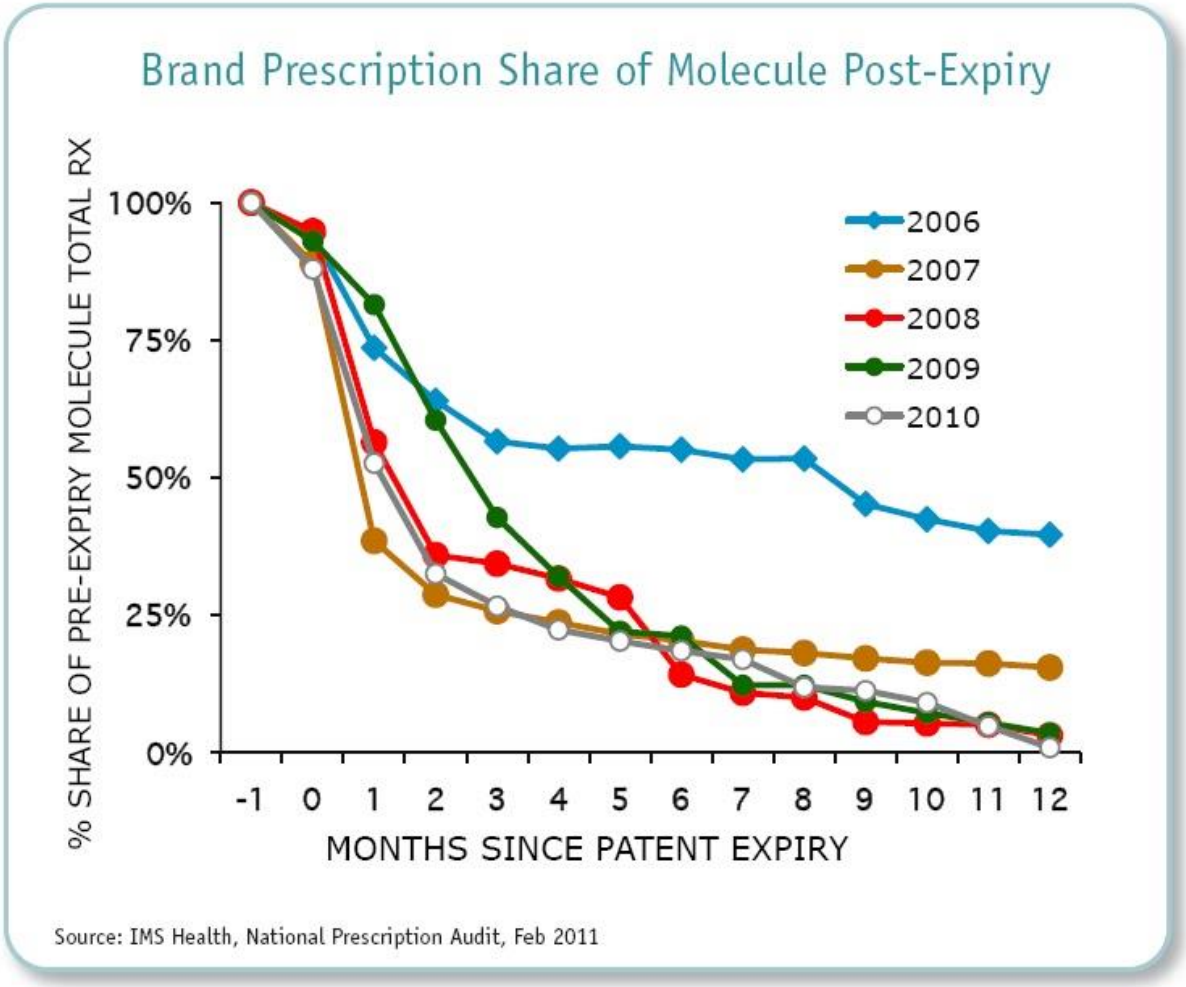
Stay of Approval

- Approval stayed pending outcome of suit (up to 30 months)
  - Can be shortened or extended by Court
  - Only get one 30-month stay
    - Later listed patents require certification but do not impact first to file status or 30-month stay
- Tentative Approval
  - ANDA ready for approval but blocked by patent, exclusivity or stay
  - Only eligible for “tentative” approval
- Full approval not automatic
  - Must be requested
  - Will not be given until “block” is cleared
    - Expiration of 30-month stay
    - Generic wins
    - Settlement of case

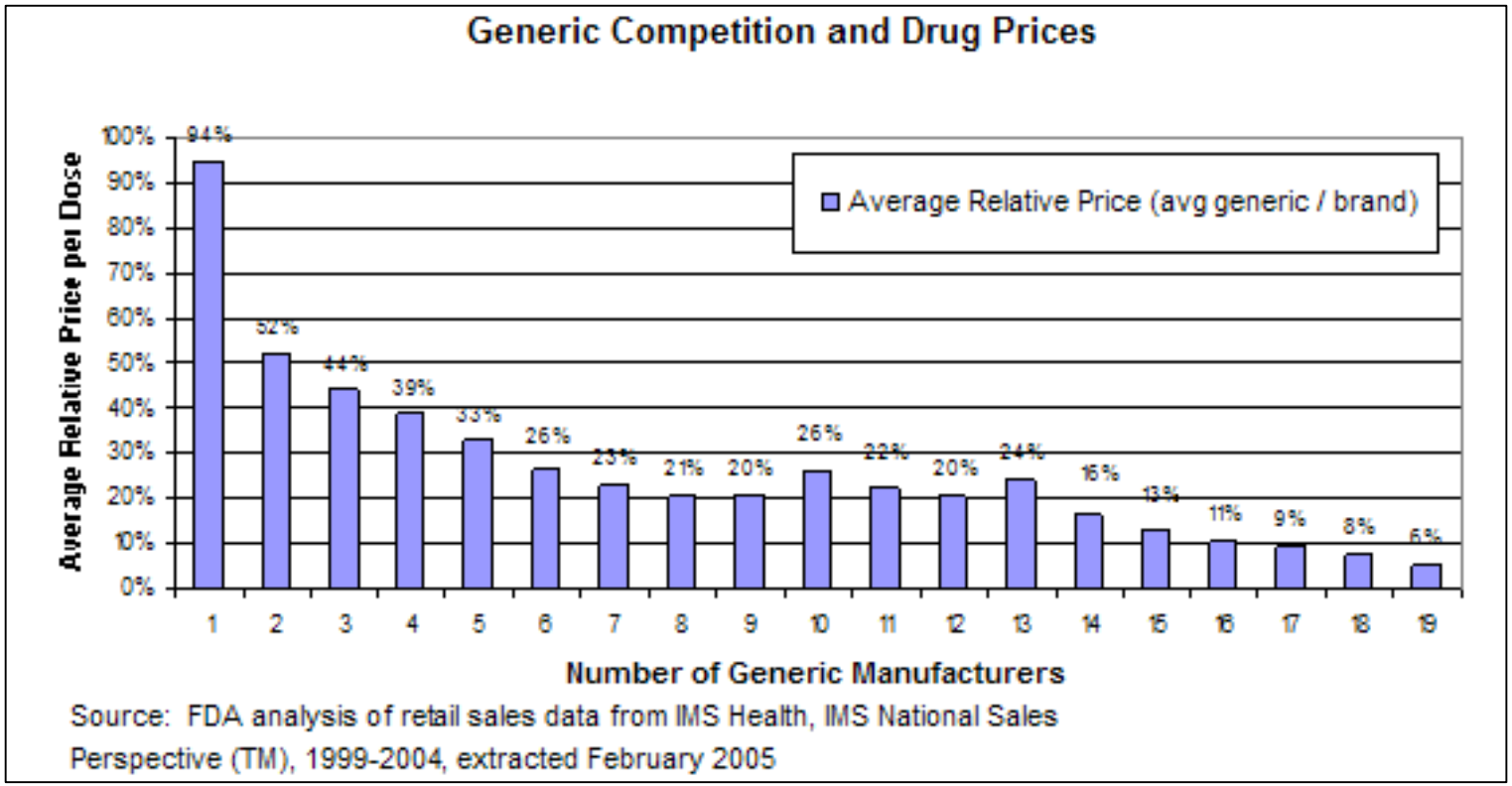
180-Day Exclusivity

- Protects first generic to challenge listed patent
  - No other application can be approved until the expiration of 180-days of marketing by the first to file applicant
- Can be shared (same day first to file)
- Immensely valuable to generic because of states' mandatory substitution laws

What Happens after Generic Entry



Drug Prices Based on Number of Generics in Market



Source: FDA analysis of retail sales data from IMS Health, IMS National Sales Perspective (TM), 1999-2004, extracted February 2005

Shared 180-Day Exclusivity

First-to-file ANDAs may enter market at once if approved

Or sequentially depending on approval

Or sequentially depending on their intent to market

ALL EXCLUSIVITY ENDS AFTER FIRST TRIGGERED 180-DAY MARK

21 USC § 355(j)(5)(D)

(D) **Forfeiture of 180-day exclusivity period**.— (i)Definition of forfeiture event.—In this subparagraph, the term “forfeiture event”, with respect to an application under this subsection, means the occurrence of any of the following:

(I) **Failure to market**.—The first applicant fails to market the drug by the later of—

(aa) the earlier of the date that is—

(AA) 75 days after the date on which the approval of the application of the first applicant is made effective under subparagraph (B)(iii); or

(BB) 30 months after the date of submission of the application of the first applicant; or

(bb) with respect to the first applicant or any other applicant (which other applicant has received tentative approval), the date that is 75 days after the date as of which, as to each of the patents with respect to which the first applicant submitted and lawfully maintained a certification qualifying the first applicant for the 180-day exclusivity period under subparagraph (B)(iv), at least 1 of the following has occurred:

(AA) In an infringement action brought against that applicant with respect to the patent or in a declaratory judgment action brought by that applicant with respect to the patent, a court enters a final decision from which no appeal (other than a petition to the Supreme Court for a writ of certiorari) has been or can be taken that the patent is invalid or not infringed.

(BB) In an infringement action or a declaratory judgment action described in subitem (AA), a court signs a settlement order or consent decree that enters a final judgment that includes a finding that the patent is invalid or not infringed.

(CC) The patent information submitted under subsection (b) or (c) is withdrawn by the holder of the application approved under subsection (b).

(II) **Withdrawal of application**.— The first applicant withdraws the application or the Secretary considers the application to have been withdrawn as a result of a determination by the Secretary that the application does not meet the requirements for approval under paragraph (4).

(III) **Amendment of certification**.— The first applicant amends or withdraws the certification for all of the patents with respect to which that applicant submitted a certification qualifying the applicant for the 180-day exclusivity period.

(IV) **Failure to obtain tentative approval**.— The first applicant fails to obtain tentative approval of the application within 30 months after the date on which the application is filed, unless the failure is caused by a change in or a review of the requirements for approval of the application imposed after the date on which the application is filed.

(V) **Agreement with another applicant, the listed drug application holder, or a patent owner**.— The first applicant enters into an agreement with another applicant under this subsection for the drug, the holder of the application for the listed drug, or an owner of the patent that is the subject of the certification under paragraph (2)(A)(vii)(IV), the Federal Trade Commission or the Attorney General files a complaint, and there is a final decision of the Federal Trade Commission or the court with regard to the complaint from which no appeal (other than a petition to the Supreme Court for a writ of certiorari) has been or can be taken that the agreement has violated the antitrust laws (as defined in section 12 of title 15, except that the term includes section 45 of title 15 to the extent that that section applies to unfair methods of competition).

(VI) **Expiration of all patents**.— All of the patents as to which the applicant submitted a certification qualifying it for the 180-day exclusivity period have expired.

180-Day Forfeiture Events - §505(j)(5)(D)

Generic can forfeit its 180-day exclusivity by:

1. Failing to obtain tentative approval in 30 months
2. Failing to market within specified time after approval
3. Expiration of all patents with which exclusivity is associated
4. Withdrawal of the ANDA or all of the Para. IV certifications
5. Enters into an agreement that is a violation of the antitrust laws

Questions?

Thank you!

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Principal, San Diego

Please send your NY CLE forms or questions about the webinar to marketing at lundberg@fr.com.

A replay of the webinar will be available for viewing at fr.com

#1 Patent Litigation Firm *(Corporate Counsel, 2004–2016)*