FDA Data Exclusivity Guidance: Emerging Patent Challenges and Opportunities

Navigating Complexities of Exclusivity, New Developments, and the Implications for ANDAs and Hatch-Waxman Litigation

THURSDAY, APRIL 10, 2014

1pm Eastern | 12pm Central | 11am Mountain | 10am Pacific

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FDA Data Exclusivity Guidance: Emerging Patent Challenges and Opportunities
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I. FDA data exclusivity and how it relates to Hatch-Waxman

II. Past guidelines
   A. Five-year data exclusivity
      1. Qualifying subject matter
      2. Limitations on ANDA filing and relation to Hatch-Waxman
   B. Three-year data exclusivity
      1. Qualifying subject matter
      2. Limitations on ANDA filing and relation to Hatch-Waxman

III. FDA’s new draft guidelines and denial of citizen petitions: prospective five-year data exclusivity for some combo drug products
   A. Qualifying subject matter
   B. Limitations on ANDA filing and relation to Hatch-Waxman
   C. Applicability to prospective NDAs

IV. Patent and business strategies to maximize data exclusivity in light of both the new and old landscape
Exclusivity: Basics

Lauren L. Stevens, Ph.D.
The Hatch-Waxman Act


- A compromise with two goals
  - Make available more low cost generic drugs
    - 180 day exclusivity for first filer
    - “Safe harbor”
  - Create incentives for new R&D
    - Public notice of patents and challenges
    - Resolution of patent disputes prior to generic entry
    - Automatic injunction
    - Patent term extension
Summary of Exclusivities

- **NCE**
  - No ANDA/505(b)(2) NDA submission until 5 years after NCE (4 years if Para. IV Cert.); can be extended to 7.5 years by Para. IV Cert.

- **Data**
  - ANDA/505(b)(2) NDA approval prevented until 3-year exclusivity expires

- **Pediatric**
  - Final ANDA/505(b)(2) approval delayed for 6 months

- **Orphan**
  - Final ANDA/505(b)(2) approval delayed for 7 years
The Why and What of FDA Exclusivities

Why are exclusivities awarded?
- New molecular entity approval
- New data leading to new product or use
- Pediatric testing of existing product
- Orphan drug (to treat a rare disease)

What types of exclusivities are awarded?
- Filing exclusivity
  - Blocks FDA from accepting ANDA application.
- Approval exclusivity
  - Blocks FDA from approving ANDA.
What is an NCE?

- New chemical entity (NCE) is a drug that contains no “active” moiety that has been approved in another NDA.

- An “active moiety” is defined in FDA’s regulations at 21 C.F.R. § 314.108(a) to mean “the molecule or ion, excluding those appended portions of the molecule that cause the drug to be an ester, salt (including a salt with hydrogen or coordination bonds), or other noncovalent derivative (such as a complex, chelate, or clathrate) of the molecule, responsible for the physiological or pharmacological action of the drug substance.”
  - Structure-centric → small changes can result in NCE.
5-Year NCE Exclusivity

- The first pharmaceutical company to receive NDA approval for a drug product containing a new chemical entity (NCE) is entitled to a 5-year period of FDA filing exclusivity.

- During this 5-year period, no other company can submit an ANDA to FDA seeking regulatory approval of a drug product containing the same active ingredient.

- Does not prevent new NDA from being filed.

- Runs concurrently with the term of any patent claiming the drug.
NCE Exclusivity with No Patents

- ANDA or 505(b)2 is filed after year 5 of the NDA holder’s NCE exclusivity period.

- Some claim that it takes about 30-months on average to get ANDA approval so effective exclusivity of 7.5 years after NDA approval.
NCE Exclusivity with Patents

- An ANDA filed with a Para. IV certification can be filed at the end of year 4 following approval of the drug.

- BUT:
  - If Para. IV certification leads to Hatch Waxman litigation, then 30-month stay automatically extended to ensure 7.5 years of NCE exclusivity.
  - Only way to shorten this period is for ANDA-filer to prevail quickly in ANDA litigation.
Enantiomers?

- Federal Drug Administration Amendments Act, 2007 (“FDAAA”)

- An enantiomer can qualify as an NCE/NME only if:
  - Applicant elects to have enantiomer not be considered the same active ingredient as racemate;
  - The single enantiomer has not been previously approved except in the approved racemic drug;
  - The NDA includes full new clinical investigations;
  - The clinical studies were not used for the racemate.
Enantiomers (cont’d)

- Sponsor agrees **not** to seek, for 10 years, approval of the enantiomer for a use in a “therapeutic category” for which the racemate is approved, or for a use for which any other enantiomer of the racemate is approved.
- The labeling of the enantiomer drug for which “new active ingredient” status is elected **must** “include a statement that the non-racemic drug is **not** approved, and has **not** been shown to be safe and effective, for any condition of use of the racemic drug.”
- Five-year exclusivity for enantiomer.
- Enantiomer cannot be approved for racemate’s use(s) until 10 years after approval of enantiomer NDA.
FETZIMA (levomilnacipran)

- Extended-release Capsules, 20 mg, 40 mg, 80 mg and 120 mg, approved on July 25, 2013 for Major Depressive Disorder
- Levomilnacipran is an enantiomer of the previously approved racemate, milnacipran HCl (SAVELLA), which was approved for fibromyalgia.

-----------------------------------------INDICATIONS AND USAGE-----------------------------------------
FETZIMA is a serotonin and norepinephrine reuptake inhibitor (SNRI) indicated for the treatment of Major Depressive Disorder (MDD) (1).

Limitation of Use: FETZIMA is not approved for the management of fibromyalgia. The efficacy and safety of FETZIMA for the management of fibromyalgia have not been established (1).
Salts?

- Generally, a salt of an approved drug is not considered a new active moiety and so is not eligible for NCE/NME exclusivity.
Esters?

- NCE exclusivity will not be awarded to a new ester of a previously approved active ingredient.
- FDA had also recognized that in exceptional cases, it could award NCE exclusivity to a “stable ester”
  - “[a]n ester that is stable, both in vitro and in vivo, is considered to be the active moiety, because the de-esterified molecule is devoid of activity . . .”
  - FDA granted NCE exclusivity to ISMO (isosorbide mononitrate) in 1991, on the basis that the esterified molecule itself was a new active moiety, even though the underlying molecule (isosorbide) had previously been approved.
Yes? Maybe? No!

- TORISEL (temsirirolimus) - an ester form of the previously approved drug RAPAMUNE (sirolimus)
  - 2007 – 5-year NCE exclusivity awarded.
  - On May 29, 2012, FDA reversed its award of NCE exclusivity.

- VERAMYST (fluticasone furoate) – a different ester form of fluticasone propionate
  - 2007 – No determination of exclusivity.
Bright-Line Rule

The TORISEL and VERAMYST letter decisions confirm that FDA will apply a “chemical-structure-based” rule, rather than an “activity-based” approach, in determining the active moiety of a new product for purposes of NCE exclusivity.

- FDA will look only to the chemical bond between the base molecule and its appendages, and will not consider whether the underlying molecule is therapeutically active, or how the appended portions are cleaved off *in vivo* or otherwise behave in the body.
Amides?

- VYVANSE (Lisdexamfetamine) – an amide of dextroamphetamine and lysine.
- Awarded 5-year NCE exclusivity.
  - Consistent with regulations which define non-ester covalently bonded appendages to be part of the active moiety.
  - Did not take into account the pharmacological activity of lisdexamfetamine.
- Upheld by the DC Circuit in *Actavis Elizabeth LLC v. FDA*, 625 F.3d 760, 765 (D.C. Cir. 2010).
- FDA relied heavily on that exclusivity determination in its letter decisions re: esters.
Prodrugs?

- **EMEND** (fosaprepitant dimeglumine) - a phosphamide derivative (a type of covalent derivative) and a pro-drug of the previously-approved active ingredient in EMEND (aprepitant).
- Not an ester, salt (including a salt with hydrogen or coordination bonds), nor other noncovalent derivative (such as a complex, chelate, or clathrate) of the molecule aprepitant.
- As a non-ester covalent derivative of aprepitant, under 21 CFR § 314.108, fosaprepitant dimeglumine is a new chemical entity entitled to 5 years of exclusivity.
3-Year Data Exclusivity

“[I]f a supplement to an application approved under subsection (b) . . . contains reports of new clinical investigations (other than bioavailability studies) essential to the approval of the supplement and conducted or sponsored by the person submitting the supplement, the Secretary may not make the approval of an application submitted under this subsection for a change approved in the supplement effective before the expiration of three years from the date of the approval of the supplement under subsection (b)”

• Section 505(j)(5)(F)(iv) of the FD&C Act
3-Year Exclusivity with Patents

Generic needs to certify against the patent.
30-Month stay!
3-Year Exclusivity with No Patents

ANDA Filed

Approval

Patent Issued and Listed

End of 3-yr Exclusivity

Generic needs to certify against the patent
No 30-month stay!
ANDA can be approved at the end of 3-yr exclusivity
3-Year Data Exclusivity

- New clinical indications for approved products
- Formulations
- Dosing regimens
- Patient populations
- OTC Switch
- Other aspects of labeling? (to be discussed later)
3-Year (Data) Exclusivity

- NDA must contain new reports of one or more new clinical investigations essential to FDA’s approval of the new drug.

- 3-year exclusivity period runs irrespective of, but concurrent with, any applicable patent term

- **Caveats:**
  - During the 3-year exclusivity period other companies may submit ANDAs to FDA but no approval until 3 year period expires.
  - Data exclusivity for new indication: generic carve-out (i.e., “skinny-label”).
“New Clinical Investigations”

- Investigations conducted on humans “the results of which have not been relied on by FDA to demonstrate substantial evidence of effectiveness of a previously approved drug product for any indication or of safety for a new patient population and do not duplicate the results of another investigation that was relied on by the agency to demonstrate the effectiveness or safety in a new patient population of a previously approved drug product”

- “Essential to approval” – with regard to an investigation, there are no other data available that could support approval of the application.
  - The change could not be approved without the investigation.
“New Clinical Investigations”

- SEROQUEL (quetiapine fumarate) Tablets
- Investigations:
  - Metabolic data submitted in response to FDA request
    - Data came from 15 clinical trials, each conducted for reasons other than generating this particular data and none conducted on pediatric patients
    - FDA asked for a table summarizing the data, which was included in the label
  - Also two sNDAs related to pediatric uses.
  - FDA approved the pediatric sNDAs as well as the proposed labeling changes, including the data table.
  - AZ requested exclusivity based on the data table.
“New Clinical Investigations”

- FDA argued that AstraZeneca reads the statute to provide for exclusivity for any labeling change
  - even if the change was initially submitted through general correspondence (and not a supplement), and
  - it was unrelated to the purpose for which the supplement was submitted, and
  - the change occurred only coincidentally and contemporaneously with the changes relating to the new clinical investigations that were the subject of the supplements.
SEROQUEL (cont’d)

- FDA argued table was not entitled to a period of exclusivity
  - “[C]hanges in labeling that involve the addition of warnings or other similar risk information are generally not entitled to 3-year exclusivity”
  - Table contains only “generally applicable safety information”
  - Table does not include data from any indications for which Seroquel still had exclusivity, including pediatric indications
  - Table was not “a change approved” in any supplement, and only changes approved in a supplement are entitled to a statutory period of exclusivity

- DC Dt. Ct. agreed.

- Ct. Appeals for Dt. Ct. agreed.
  - Labeling changes in table were neither “a change approved” in the pediatric supplements nor submitted as a separate supplement.
“Old” Antibiotics?

- VANCOCIN (vancomycin hydrochloride (HCl)) capsules first approved in 1986 for the treatment of antibiotic-associated pseudomembranous colitis caused by *C. difficile* and for the treatment of enterocolitis caused by *Staphylococcus aureus* (including methicillin-resistant strains).

- On December 14, 2011, FDA approved sNDA for VANCOCIN.
  - Updates to the prescribing information supported by two Phase 3 clinical safety and efficacy studies to evaluate the safety and efficacy for the treatment of *C. difficile*-associated diarrhea.
“Old” Antibiotics?

- Those antibiotic drugs for which the first application was received before the enactment of FDAMA on November 21, 1997 are not eligible for the three-year exclusivity period for “any condition of use” for which the Old Antibiotic was approved before October 8, 2008.

- “Condition of use” - a significant new use for an Old Antibiotic, such as a new indication, not merely minor differences in labeling related to previously approved uses for Old Antibiotics.
VANCOCIN Prescribing Information

INDICATIONS & USAGE

VANCOCIN HCL capsules are indicated for the treatment of enterocolitis caused by Staphylococcus aureus (including methicillin-resistant strains) and antibiotic-associated pseudomembranous colitis caused by C. difficile-associated diarrhea.

VANCOCIN CAPSULES are also used for the treatment of enterocolitis caused by Staphylococcus aureus (including methicillin-resistant strains).

DOSAGE & ADMINISTRATION

Adults
Oral Vancocin HCL VANCOCIN CAPSULES is used in treating antibiotic-associated pseudomembranous colitis caused by C. difficile-associated diarrhea and staphylococcal enterocolitis. The usual adult total daily dosage is 500 mg to 2 g administered orally in 3 or 4 divided doses for 7 to 10 days.

- **C. difficile-associated diarrhea**: The recommended dose is 125 mg administered orally 4 times daily for 10 days.

- **Staphylococcal enterocolitis**: Total daily dosage is 500 mg to 2 g administered orally in 3 or 4 divided doses for 7 to 10 days.

Pediatric Patients
The usual daily dosage is 40 mg/kg in 3 or 4 divided doses for 7 to 10 days. The total daily dosage should not exceed 2 g.
No Exclusivity

- Does not constitute approval for a new condition of use within the meaning of 505(v).
  - Antibiotic-associated pseudomembranous colitis caused by *C. difficile* and *C. difficile*-associated diarrhea are not mutually exclusive indications.
    - The labeling changes only clarified the previously approved indication.
  - “New” dosing regimen (125 mg orally 4 times a day for 10 days) encompassed within the prior regimen of 500 mg to 2 g administered orally in 3 or 4 divided doses for 7-10 days.
  - Labeling changes related to clinical study data for CDAD, nephrotoxicity and geriatric use merely relate to and provide additional details regarding the previously approved indication for treatment of CDAD in already identified patient populations.
FDA’s New Draft Guidelines
New Draft Guidelines

- FDA issued Feb. 21, 2014
- Prospective application only
  - “If the new interpretation is adopted, FDA intends to apply the new interpretation prospectively. Therefore, this guidance does not apply to fixed-combination drug products that were approved prior to adopting the new interpretation.”
- Grant five years of NCE data exclusivity to combination drug products with at least one new active moiety.
- Paradoxically, at the same time, the FDA denied the petitions that led to the new draft guidelines.
For any combo drug product in which at least one active moiety is new, the NDA filer can get five-year data exclusivity, even if the drug product also contains an active moiety previously approved. If the combo drug product contains no new active moiety, but only at least one moiety that has previously been approved, the NDA filer gets three years' data exclusivity.

Data exclusivity periods of 5- and 3-years run irrespective of, but concurrent with, any applicable patent term, and stops approval of any ANDAs before certain time periods.
- Five-year data exclusivity sets a time bar on the filing of any ANDA after approval;
- Three-year data exclusivity sets only a time bar on ANDA approval, no time bar on the filing of an ANDA.
Commentary to Draft Guidelines

- Comments due April 21, 2014.
- “in recent years, FDA has adopted policies aimed at encouraging the development of fixed-combinations because, among other things, such combinations have been shown to improve treatment response, lower the risk of developing resistance, and lower the rates of adverse events.”

- In 2013, the Agency was petitioned to revise its current interpretation of the 5-year NCE exclusivity provisions with respect to certain fixed-combinations.
  - “FDA’s existing interpretation might encourage an applicant to submit an NDA for a single-entity product before it submits an NDA for a fixed-combination to secure 5-year NCE exclusivity for the single entity and protect the later-approved fixed-combination with that exclusivity under the umbrella policy.”

- “the new interpretation urged by the petitioners would be beneficial to the public health.”
- “Under the revised interpretation, the term drug in the eligibility clause of the statutory provisions, and in the regulatory definition of new chemical entity, refers to drug substance, not drug product.”
Citizen Petitions Denied

- Hogan Lovells, on behalf of Gilead Sciences, Inc., submitted a citizen petition dated January 8, 2013, requesting 5-year NCE exclusivity for cobicistat and elvitegravir, the new active moieties in the fixed-combination Stribild (cobicistat; elvitegravir; emtricitabine; tenofovir disoproxil fumarate) (NDA 203100) (FDA-2013-P-0058).

- Buchanan Ingersoll & Rooney PC, on behalf of Ferring Pharmaceuticals, Inc., submitted a citizen petition dated January 29, 2013, requesting 5-year NCE exclusivity for picosulfate, the new active moiety in the fixed-combination Prepopik (citric acid; magnesium oxide; sodium picosulfate) (NDA 202535) (FDA-2013-P-0119).

- Ropes & Gray LLP, on behalf of Bayer HealthCare Pharmaceuticals Inc., submitted a citizen petition dated April 19, 2013, requesting 5-year NCE exclusivity for dienogest, the new active moiety in the fixed-combination Natazia (estradiol valerate; dienogest) (NDA 022252) (FDA-2013-P-0471).
Strategies
“Skinny Labeling”: Scenario

• NME approved for hypertension

• After further studies also approved for
  • Left ventricular dysfunction (LVD) due to heart attack
  • Diabetic neuropathy (DN) in diabetic patients

• NME exclusivity expires

• Patent protection on NME and use in hypertension expires;

• Does 3 year data exclusivity on use in hypertension prohibit FDA from approving ANDA with labeling for use of the NME to treat hypertension but no labeling for LVD or DN?
“Skinny Labeling” Scenario (con’t)

- If approved, generic product label will only describe use in hypertension.

- Doctors and pharmacists aware that the active ingredient also approved for left ventricular dysfunction and diabetic neuropathy.

- Brand company worried that doctors and pharmacists will substitute generic for brand product for those other indications, notwithstanding the different labels.
“Skinny Labeling” is Allowed

- 21 C.F.R. § 314.94(a)(8)(iv) states:
  - “differences between the applicant’s proposed labeling and labeling approved for the [Reference Listed Drug “RLD”] may include... omission of an indication or other aspect of labeling protected by patent or accorded exclusivity under [FDC Act § 505(j)(5)(D)].”

- Skinny labeling allowed in face of 3-year data exclusivity for carved out indications, see Bristol-Myers Squibb Co. v. Shalala, 91 F.3d 1493 (D.C. Cir. 1996), and orphan drug exclusivity. See Sigma Tau Pharma. Inc. v. Schwetz, 288 F.3d 141 (4th Cir. 2002)

- Skinny labeling detracts from value of 3-year data exclusivity and method of use patents for later developed indications.
Skinny Labeling in Practice

- Brand companies have filed citizen petitions with FDA, arguing that carve-outs should not be allowed for various reasons, such as patient safety.

- The scorecard (as of September 2008)*
  - 8 Decisions allowing carve out
  - 1 Decision disallowing carve out
    - Wyeth’s Rapamune® (sirolimus)
    - Basis was safety

Source: http://www.fdalawblog.net/fda_law_blog_hyman_phelps/2008/09/the-skinny-on-s.html
Citizen Petition Regulatory Exclusivity

• Whether or not there are OB-listed patents, a Citizen Petition (CP) can possibly add years of regulatory exclusivity.

• Example Lovenox® drug (sodium enoxaparin: a highly complex mixture derived from pig mucosa).

• CP exclusivity was some 8 years, extending even after OB listed patent was held unenforceable and five year data exclusivity expired.
Getting Hatch-Waxman Exclusivity: Listing U.S. Patents in the Orange Book

- NDA sponsor lists in the Orange Book (OB) patents that cover the drug or approved methods of use.

- NDA-holder lists in the OB patents on the “drug [NCE, novel product-by-process, solid state form of NCE, and formulation] or method of using the drug[approved indication(s)]” for which “infringement [use absent a license] could reasonably be asserted”
  - Submit signed patent declaration to achieve listing
  - 21 U.S.C. § 355(b)(1)
  - 21 C.F.R. § 314.53(b)(1)
Getting Hatch-Waxman Exclusivity: Listing U.S. Patents in the Orange Book

- Generally: “Process patents, patents claiming packaging, patents claiming metabolites, and patents claiming intermediates are not covered by this section, and information on these patents must not be submitted to FDA.” But, packaging reciting approved NCE or formulation and solid state “intermediates” converting to approved NCE?

- Listing enables patent holder to file suit under § 271(e)(2) after receiving generic ¶ IV notice to bar immediate FDA approval of the generic ANDA and achieve 30-month stay.

- To avoid late listing, new patent listings for approved drugs must be filed within 30 days of patent issuance or within 30 days of approval if patents issue prior to FDA approval.
Implications for NDA Holders

- No 30-month stay for patents listed after the ANDA is filed.

  - Applies to patents submitted for OB listing on or after August 18, 2003.

  - Generally, have at least one OB listed patent when generics can first file their ANDA.

- What about obtaining OB listed patent shortly before 5 year exclusivity expires?
Listability and Exclusivity

- Desirability of having your OB-listable patent issued and listed before 5-year exclusivity expires.
  - Requires ¶ IV certification and can bring HW suit and get 30 month stay

- Consider listing on the day the patent issues if 3-year exclusivity FDA approval already granted or on the day of 3-year exclusivity FDA approval if you already have the Orange Book-listable patent(s).
  - You do not have to observe 30-day listing deadline.
  - Advance preparation and strategizing.

- Desirability of having your OB-listable patent, preferably not easy to design around, issued and listed BEFORE FDA approval of non-NME, such as a drug combination of two old drugs, or any other drug, for which only 3 year exclusivity will be obtained.
Listable Patents

- FDA rules define the type of patents that shall be listed if they are reasonably assertable (21 CFR § 314.53)
  - Drug substance (active ingredient)
    - Polymorphs under certain conditions
  - Drug product (formulation and composition)
  - Product by process (novel products)
  - Method of use that is the subject of a pending or approved application

See also 68 Fed. Reg. 36676, 36677-83 (June 18, 2003).
Patents that Cannot be Listed

- Process (or manufacturing)
- Metabolites
  - But methods of administering metabolites can be listed.
- Intermediates?
- Packaging?
- Product by process, where product not novel

See also 68 Fed. Reg. 36676, 36677-83 (June 18, 2003)

- An applicant . . . shall submit the required information on the declaration form set forth in paragraph (c) of this section for each patent that claims the drug or a method of using the drug that is the subject of the new drug application or amendment or supplement to it and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use, or sale of the drug product.

Hatch-Waxman Certifications

- ANDA filer must certify one of the following:
  - **Paragraph I**: Drug not patented
  - **Paragraph II**: Patent has already expired
  - **Paragraph III**: Date on which the patent listed in the OB will expire and the generic will not go on market prior to that date
  - **Paragraph IV**: Patent listed in the OB is invalid, not infringed or unenforceable
    - 21 U.S.C. § 355(j)(2)(A)(vii) (that is the one that can lead to 30 month stay if patentee believes it reasonably assertable that at least one listed patent claim can be reasonably asserted to be valid, enforceable, and infringed and brings suit within 45 days).
  - “Skinny viii”: listed method patents do not claim a use for which generic is seeking approval
Paragraph IV Certification

- Paragraph IV certification requires notifying NDA holder and patent owner only if patent listed in the OB.
  - Not later than 20 days after the date of the postmark on the notice with which the Secretary informs the applicant that the application has been filed.

- Paragraphs I-III and “skinny viii” do not require notification and may be secret until approval date.
Hatch-Waxman: 30-Month Stay

- 21 U.S.C. § 355(j)(5)(B)(iii): If patentee files suit within 45 days of receiving notice of a Paragraph IV certification, the FDA may not approve the ANDA until the earliest of:
  - Thirty (30) months after the patentee's receipt of notice;
  - Resolution of the suit; or
  - Expiration of the patent.

  - District Court enters judgment of invalidity, noninfringement, or other substantive determination of no cause of action;
  - Settlement order signed and entered that patent is invalid or not infringed;
  - Federal Circuit reverses District Court judgment of infringement or validity; or
  - Federal Circuit enters consent decree.
30-Month Stay is Predicated on Para. IV Certification

- Implications to Patentees:
  - Patentee often obtains claims broad enough to cover design around efforts of generic competitors
    - NCE (salt, crystalline nce and/or salt)
    - formulation (35 USC § 112, ¶ 6 means for?)
    - multiple indications (strategic considerations)
    - very narrow claims covering approved product and bioequivalents thereof
    - and of course, claims to cover literally approved product.

- Certification against NDA holder’s patent listed for other products: 30-month stay available for those other products.

- For one product, only one 30-month stay against the generic manufacturer who certifies against all OB-listed patents under Para. IV.
30-Month Stay

- No 30-month stay if fail to file suit within 45-day window.
  - If the patent holder does not sue within 45 days of notice, ANDA applicant can file a declaratory action suit (21 U.S.C. § 355(j)(5)(C)(i)) under certain circumstances
  - NDA holder is not entitled to a 30 month stay based on the DJ action.

- Limited multiple 30-month stays
  - Conversion of Para. III to Para. IV for patents submitted to FDA prior to ANDA filing.

- Courts have discretion to extend or shorten the stay if “either party to the action fail[s] to reasonably cooperate in expediting the action.” (Id.)
Hatch-Waxman: Timing

- When can Paragraph IV challenge happen?

  - 5 year NCE Exclusivity Granted to drug products containing a New Chemical Entity
    - New Chemical Entity: “a drug that contains no active moiety that has been approved by FDA in any other application submitted under section 505(b) of the act”

  - ANDA or Paper NDA with Paragraph IV can be filed:
    - after 4 years if there is at least one OB listed patent; one year prior to expiration of NCE exclusivity;
    - after 5 years if no OB listed patent.
30-Month Stay Is Added to NCE Exclusivity

- Implications for NDA Holders With OB-Listed Patents
  - ANDA or Paper NDA is filed after year 4 of the NDA holder’s NME exclusivity period.
  - 30-month stay resulting from HW litigation is extended up to 7.5 years after NDA approval.
NCE Exclusivity with No Patents

- Implications for NDA Holders With No OB-Listed Patents
  - ANDA or Paper NDA is filed after year 5 of the NDA holder’s NME exclusivity period.
  - Some claim that it takes about 30-months on average to get ANDA approval so effective exclusivity of 7.5 years after NDA approval.
What is the Difference for NME NDAs?

- About 7.5 years regulatory exclusivity either way.
- But the OB-listed patent can extend many years beyond 7.5.
- A key for patent exclusivity: valid, infringed, enforceable OB-listed patents extending in term as long as legally possible.
Thank You!

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