



Regulatory Education for Industry (REdI): **GENERIC DRUGS FORUM**

Sheraton | Silver Spring, MD | April 22-23, 2015

Hatch-Waxman 101

Maryll Toufanian, J.D.
Capt. Martin Shimer, R.Ph.



Hatch-Waxman Agreement

Grand bargain for Brand and Generic Industries

- **Brand Industry Gains (section 505(j)(5)(F)):**
 - **5-year New Chemical Entity (NCE) Exclusivity**
 - **3-year New Clinical Studies Exclusivity**
 - **Patent Term Extension to account for time patented product is under review by FDA**
- **Generic Industry Gains:**
 - **Ability to obtain approval through ANDAs**
 - **Ability to challenge brand drug patents prior to marketing in court**
 - **180-day Generic Drug Exclusivity**



Key HW Concepts in FD&C Act

- ***Listing of patents***
- ***Certifying to Patents***
- ***Notification of Patent Challenge***
- ***30-month Stay of Approval***
- ***180-Day Exclusivity***



What brand must do: “list” patents

- **NDA sponsor must identify in NDA those patents reasonably related to drug product, drug substance, or method of using drug for which approval is sought.**
- **FDA “lists” patents identified by NDA sponsors in “Orange Book” (OB).**
- **Sections 505(b)(1)(G); (c)(2); 21 CFR 314.53**



What generics must do: “certify”

- **Certify*** with respect to each patent listed for that RLD in the OB (Section 505(j)(2)(A)(vii); 21 CFR 314.95) :
 - patent information has not been filed (“paragraph I certification”) = FDA can approve ANDA when ready
 - the patent has expired (“paragraph II certification”) = FDA can approve ANDA when ready
 - the date the patent will expire (“paragraph III certification”) = FDA can approve ANDA when patent expires and ANDA is ready
 - the patent is invalid or not infringed by the drug product proposed in the ANDA (“paragraph IV certification” or “PIV”) = complex approval landscape



What brand must do: “list” patents

- **NDA sponsor must submit patents for listing within 30 days of approval of NDA or supplement, and patent issuance by PTO**
- **If submitted after 30-day period – pending ANDAs do not have to certify to patent; patent will not block ANDA approval = “late listed” patent**
- **Result: patents will block approval only of PIV ANDAs submitted after late-listed patent**

What follows from PIV certification: Section 505(j)(2)(B)

After FDA notifies applicant that ANDA is sufficiently complete to review, applicant must notify NDA/patent holder of Paragraph IV certification.



Notice Requirements

Section 505(j)(2)(B)(iv)/21 CFR 314.95: Content

- **Statement that an application that contains data from bioavailability or bioequivalence studies has been submitted under this subsection for the drug with respect to which the certification is made to obtain approval to engage in the commercial manufacture, use, or sale of the drug before the expiration of the patent referred to in the certification; and**
- **Statement of the factual and legal basis of the opinion of the applicant that the patent is invalid or will not be infringed.**



What Follows from Notice

- **NDA sponsor can sue when it receives notice.**
- **Infringement lawsuit can start prior to ANDA approval and marketing = big gain for generics.**
- **If NDA sponsor sues within 45 days of notice, ANDA approval is stayed for 30 months.**
- **No lawsuit within 45 days = FDA can approve ANDA when ready**



Notice (cont.)

- **Timing of Notice: within 20 days from ANDA “receipt” acknowledgement letter**
 - **unless in an amendment post-receipt: then must notify immediately**
- **Sufficiency of notice: not policed by FDA**
- **Issues:**
 - **premature notice**
 - **failure to provide documentation of notice to ANDA**



What follows from PIV certification

ANDA approval depends on patent litigation:

Section 505(j)(5)(B)

Litigation Status	Regulatory Action
Lawsuit pending before 30-month stay expires	We can only tentatively approve ANDA
Lawsuit still pending at 30 months	We can approve ANDA
Generic wins	We can approve ANDA
Dismissal/Settlement	We can usually approve ANDA on agreed date
Brand wins	We can only tentatively approve ANDA until patent expires



I. How Hatch-Waxman Works

- **Tentative Approval**
 - **ANDA ready for approval but blocked by patent, exclusivity, or stay = only eligible for tentative approval (TA)**
 - **Full approval not automatic after TA – must show ANDA still meets requirements for approval at time of full approval, e.g., cGMPs still good**
 - **TA'd ANDAs must request full approval**



180-day Exclusivity

Section 505(j)(5)(B)(vi):

- **Reward for ANDA applicants that challenge patents, potentially hastening generic market entry**
- **180-day exclusivity is only available to “First to File” (FTF) ANDAs containing PIV certification**
- **Practical Effect: FTFs eligible for 180 days of marketing before FDA can approve non-FTF PIV ANDAs**
- **Commonly there are multiple FTFs = shared exclusivity for FTF cohort, e.g., NCE-1 ANDAs**

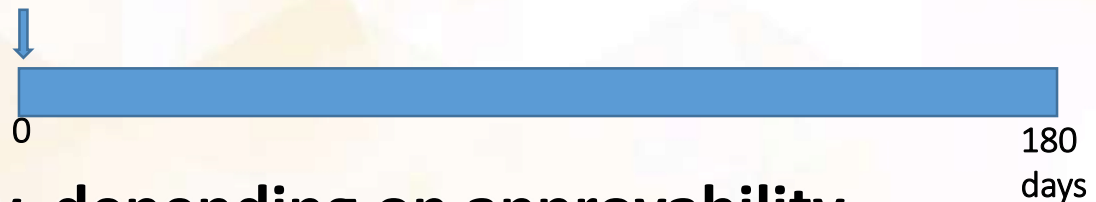


I. How Hatch-Waxman Works

- **Shared 180-day exclusivity**

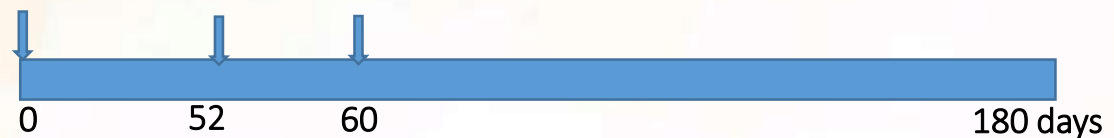
- **FTF ANDAs may enter market at once if approval-ready**

ANDA A, ANDA B, ANDA C



- **or sequentially, depending on approvability**

ANDA A ANDA B ANDA C



- **or sequentially depending on intent to market**

ANDA A ANDA B ANDA C



- **All exclusivity ends at first triggered 180-day mark**



***“Section viii” Carve-Outs**

Section 505(j)(2)(A)(viii): permits “section viii statement” = not seeking approval of the use covered by a use patent or exclusivity

- Permissible so long as generic product safe and effective for remaining conditions of use**
- Effect: ANDA with labeling carved out can be approved absent other PIV – not blocked by FTF ANDAs**
- Legality of approving generic without carved-out label upheld by courts**



New Drug Exclusivities

- **Five-year New Chemical Entity (NCE) Exclusivity**
- **Three-year “Hatch-Waxman” Exclusivity**
- **Pediatric Exclusivity**
- **Orphan Drug Exclusivity**
- **GAIN Exclusivity**

Pediatric Exclusivity



Pediatric (Ped) Exclusivity

- **Is:**

- granted by FDA
- unique as the only exclusivity that also attaches to listed patents
- study resulting in 6 months of ped exclusivity may also result in 3 year Hatch Waxman exclusivity
- results in 6 months if sponsor “fairly responds” to Written Request
- attaches to all drug products that contain the same active moiety provided they are held by the same sponsor

- **Is Not:**

- an extension of a patent
- subject to challenge via PIV certification
- 6 month ped exclusivity can not be “carved-out” of labeling in traditional sense



Pediatric Exclusivity

Appl No	Prod No	Patent No	Patent Expiration	Drug Substance Claim	Drug Product Claim	Patent Use Code	Delist Requested
N021153	001	5690960	Nov 25, 2014		Y	U - 373	
N021153	001	5690960	Nov 25, 2014		Y	U - 729	
N021153	001	5690960	Nov 25, 2014		Y	U - 770	
N021153	001	5690960*PED	May 25, 2015				
N021153	001	5714504	Feb 3, 2015		Y	U - 373	
N021153	001	5714504	Feb 3, 2015		Y	U - 729	
N021153	001	5714504	Feb 3, 2015		Y	U - 770	
N021153	001	5714504*PED	Aug 3, 2015				
N021153	001	5877192*PED	Nov 27, 2014				
N021153	001	5900424	May 4, 2016	Y		U - 373	
N021153	001	5900424	May 4, 2016	Y		U - 729	
N021153	001	5900424	May 4, 2016	Y		U - 770	
N021153	001	5900424*PED	Nov 4, 2016				



Pediatric Exclusivity for Nexium

- **Ped window for '960 currently extends from 11/25/2014 until 5/25/2015**
- **Ped window for '504 extends from 2/3/2015 until 8/3/2015**
- **Ped window for '424 extends from 5/4/2016 until 11/4/2016**



Impact on ANDAs

- **ANDA sponsor may not maintain a PIV cert to expired patent**
 - **ANDA sponsor considered to have PII cert**
- **ANDA sponsor blocked from Full AP during ped window unless:**
 - **They have secured a pediatric waiver from the NDA holder**
 - **They have a holding/ruling from a Court finding the patent in question, invalid, not-infringed or unenforceable.**



Key MMA Changes to Hatch-Waxman

180-Day Exclusivity – Forfeiture

FTF can forfeit 180-day exclusivity: section 505(j)(5)(D)

- Failure to obtain a tentative approval in 30 months
- Failure to market within a specified time after approval
- Expiration of all patents with which exclusivity is associated
- Withdrawal of the ANDA or all paragraph IV certifications
- Entering into an agreement that is in violation of antitrust laws as determined by final decision by FTC or court based on FTC or DOJ complaint



Key MMA Changes to Hatch-Waxman

180-Day Exclusivity - Forfeiture

Pre-MMA:

Patent-by-Patent.

- Separate exclusivity periods would be awarded for each patent.
- Complicated landscape.

Post-MMA:

Product-by-Product.

- This means there should only be one period of generic drug exclusivity (though perhaps shared by more than one applicant).



Key MMA Changes to Hatch-Waxman

180-Day Exclusivity - Trigger

Pre-MMA:

Either of two events could trigger the exclusivity period:

- **A court decision that the patent was invalid or not infringed**
- **First commercial marketing by an applicant eligible for exclusivity**

Post-MMA:

Only first commercial marketing by an applicant eligible for exclusivity triggers exclusivity.

Questions?

Evaluation: surveyMonkey.com/s/GDF-D1S5