NJIPLA's 25th Annual Pharmaceutical / Chemical Patent Practice Update

First Applicant Generic Exclusivity and Forfeiture Thereof

December 7, 2011

Andrew S. Wasson
Frommer Lawrence & Haug LLP

Editor, FDALawyersBlog
http://www.fdalawyersblog.com

FROMMER LAWRENCE & HAUG LLP

Hatch-Waxman Amendments

- Goal
  - Increase access to lower-cost generic alternatives while at the same time maintaining incentives for innovators
- History
  - 1984 Drug Price Competition and Patent Term Restoration Act
  - 2003 Medicare Prescription Drug Improvement and Modernization Act (MMA)
- Balance
  - Innovative Products
    - Patent listings
    - 30-month stays
    - Patent term extension
    - Exclusivities (NCE, Orphan, Pediatric)
  - Generics
    - ANDA and 505(b)(2) NDA approval mechanism
    - 180-day exclusivity for first PIV ANDA

2003 Medicare Prescription Drug Improvement and Modernization Act (MMA)

- 180-day exclusivity:
  - Act authorizes FDA to approve an ANDA with a PIV certification upon the date that is 180 days after the date of the first commercial marketing of the drug (including the commercial marketing of the listed drug) by any first applicant
- First Applicant:
  - "[A]n applicant that, on the first day on which a substantially complete application containing a certification described in paragraph (2)(A)(vii)(VI) is submitted for approval of a drug, submits a substantially complete application that contains and lawfully maintains a certification described in paragraph (2)(A)(vii)(IV) for the drug." 21 U.S.C. § 355(j)(5)(B)(iv)(II)(bb)
- Under MMA, first applicant can forfeit first applicant exclusivity
  - Added to reduce possibility of "parking" first applicant exclusivity
  - Prior to MMA, a first applicant could block subsequent filers by not marketing and entering into an agreement with brand

Six Forfeiture Events

I. Failure to Market
II. Withdrawal of Application
III. Amendment of Certification
IV. Failure to Obtain Tentative Approval
V. Agreement with another applicant, the listed drug application holder, or a patent owner
VI. Expiration of All Patents

Failure to Market – 21 U.S.C. § 355(j)(5)(D)(i)(I)

(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) of this section is withdrawn by the holder of the application approved under subsection (b) of this section.

Failure to Market – 21 U.S.C. § 355(j)(5)(D)(i)(I)

(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) of this section is withdrawn by the holder of the application approved under subsection (b) of this section.

Failure to Market – 21 U.S.C. § 355(j)(5)(D)(i)(I)

(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) of this section is withdrawn by the holder of the application approved under subsection (b) of this section.

Failure to Market – 21 U.S.C. § 355(j)(5)(D)(i)(I)

(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) of this section is withdrawn by the holder of the application approved under subsection (b) of this section.

Failure to Market – 21 U.S.C. § 355(j)(5)(D)(i)(I)

(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) of this section is withdrawn by the holder of the application approved under subsection (b) of this section.

Granisetron

- Drug Product: Kytril (graniestron hydrochloride) injection
- ANDA filer: Teva
- ANDA filing date: 6/1/2004
- ANDA approval date: 12/31/2007
- Three patents listed on the Orange Book
  - Teva ANDA contained a PIV, a PIII, and a Section viii statement
- No action brought against Teva on the PIV patent

Granisetron Injection

Relevant Provision	Analysis
Later of	
(aa) the earlier of	
(AA) 75 days after ANDA approval	12/31/07 + 75 days = 3/15/2008
(BB) 30 months after filing	6/1/2004 + 30 months = 12/1/2006
(bb) 75 days after at least one of	
(AA) final decision patent is valid or infringed	
(BB) settlement/consent decree patent is valid or infringed	
(CC) patent delisted	

Granisetron Injection

Relevant Provision	Analysis
Later of	
(aa) the earlier of	12/1/2006
(AA) 75 days after ANDA approval	12/31/07 + 75 days = 3/15/2008
(BB) 30 months after filing	6/1/2004 + 30 months = 12/1/2006
(bb) 75 days after at least one of	
(AA) final decision patent is valid or infringed	
(BB) settlement/consent decree patent is valid or infringed	
(CC) patent delisted	

Granisetron Injection

Relevant Provision	Analysis
Later of	
(aa) the earlier of	12/1/2006
(AA) 75 days after ANDA approval	12/31/07 + 75 days = 3/15/2008
(BB) 30 months after filing	6/1/2004 + 30 months = 12/1/2006
(bb) 75 days after at least one of	
(AA) final decision patent is valid or infringed	No
(BB) settlement/consent decree patent is valid or infringed	No
(CC) patent delisted	No

No forfeiture if (aa) has occurred but (bb) has not occurred

Dorzolamide/Timolol

- Drug Product: Cosopt Ophthalmic Solution (dorzolamide hydrochloride and timolol maleate)
- ANDA filer: Hi-Tech
- ANDA filing date: 10/11/2005
- ANDA approval date: 10/28/2008
- Three patents listed on the Orange Book
  - Hi-Tech ANDA contained a PIV certification
- Merck successfully sued Hi-Tech on one patent and no action taken on other two

Dorzolamide/Timolol

Relevant Provision	Analysis
Later of	
(aa) the earlier of	
(AA) 75 days after ANDA approval	10/28/2008 + 75 days = 1/11/2009
(BB) 30 months after filing	10/11/2005 + 30 months = 4/11/2008
(bb) 75 days after at least one of	
(AA) final decision patent is valid or infringed	
(BB) settlement/consent decree patent is valid or infringed	
(CC) patent delisted	

Dorzolamide/Timolol

Relevant Provision	Analysis
Later of	
(aa) the earlier of	4/11/2008
(AA) 75 days after ANDA approval	10/28/2008 + 75 days = 1/11/2009
(BB) 30 months after filing	10/11/2005 + 30 months = 4/11/2008
(bb) 75 days after at least one of	
(AA) final decision patent is valid or infringed	
(BB) settlement/consent decree patent is valid or infringed	
(CC) patent delisted	

Dorzolamide/Timolol

Relevant Provision	Analysis
Later of	4/11/2008
(aa) the earlier of	4/11/2008
(AA) 75 days after ANDA approval	10/28/2008 + 75 days = 1/11/2009
(BB) 30 months after filing	10/11/2005 + 30 months = 4/11/2008
(bb) 75 days after at least one of	
(AA) final decision patent is valid or infringed	NO
(BB) settlement/consent decree patent is valid or infringed	NO
(CC) patent delisted	Yes, 4/26/2006 + 75 days = 7/10/2006

Forfeiture because (aa) occurred and (bb) occurred and no marketing before 4/11/2008
FDA rejected argument that forfeiture was improper because of the existence of another patent that blocked final approval = “no fault forfeiture”

Losartan

- Drug Product: Cozaar (losartan potassium)
- ANDA filer: Teva
- ANDA filing date: 12/18/2003
- ANDA approval date: 4/26/2010
- Four patents listed on the Orange Book
  - Teva ANDA contained a PIV certification for one (’075 patent)
- No action brought against Teva on the PIV patent
- Merck asked FDA to delist ’075 patent: 3/18/2005
  - FDA makes public: 4/18/2008

Losartan (Cozaar)

Relevant Provision	Analysis
Later of	
(aa) the earlier of	
(AA) 75 days after ANDA approval	4/06/2010 + 75 days = 6/20/10
(BB) 30 months after filing	12/18/2003 + 30 months = 6/18/2006
(bb) 75 days after at least one of	
(AA) final decision patent is valid or infringed	
(BB) settlement/consent decree patent is valid or infringed	
(CC) patent delisted	

Losartan (Cozaar)

Relevant Provision	Analysis
Later of	
(aa) the earlier of	6/18/2006
(AA) 75 days after ANDA approval	4/06/2010 + 75 days = 6/20/10
(BB) 30 months after filing	12/18/2003 + 30 months = 6/18/2006
(bb) 75 days after at least one of	
(AA) final decision patent is valid or infringed	
(BB) settlement/consent decree patent is valid or infringed	
(CC) patent delisted	

Losartan (Cozaar)

Relevant Provision	Analysis
Later of	6/18/2006
(aa) the earlier of	6/18/2006
(AA) 75 days after ANDA approval	4/06/2010 + 75 days = 6/20/10
(BB) 30 months after filing	12/18/2003 + 30 months = 6/18/2006
(bb) 75 days after at least one of	
(AA) final decision patent is valid or infringed	NO
(BB) settlement/consent decree patent is valid or infringed	NO
(CC) patent delisted	YES (according to FDA), 3/18/2005 + 75 days = 6/01/2005

Forfeiture because (aa) occurred and (bb) occurred and no marketing before 6/18/2006
However, Teva sued FDA to determine if Merck's patent delisting satisfied (CC)

Teva Pharmaceuticals v. Sebelius, 595 F.3d 1303 (D.C. Cir. 2010)

- D.C. Cir. Rejected FDA's determination that exclusivity was lost
  - "We see nothing in the 2003 amendments to the [FDCA] that changes the structure of the statute such that brand companies should be newly able to delist challenged patents, thereby triggering a forfeiture event that deprives generic companies of the period of marketing exclusivity they otherwise deserve." 595 F.3d at 1318.
  - "The [FDA], however, offers *not a single cogent reason* why Congress might have permitted brand manufacturers to trigger subsection (CC) by withdrawing a challenged patent, outside the [21 U.S.C. § 355(j)(5)(C)(ii)(I) counterclaim scenario." 595 F.3d at 1317."
- FDA granted Teva's 180 exclusivity on remand
- Rehearing en banc denied
- Apotex cert. petition denied

Failure to Obtain Tentative Approval – 21 U.S.C. § 355(j)(5)(D)(i)(IV)

- 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.

- 2007 FDAAA clarified that if an ANDA approval is delayed because of a Citizen Petition, "the 30-month period . . . is deemed to be extended by [the time needed for final agency action on the petition.]"
  - FDCA § 505(q)(1)(G)

Irinotecan

- Drug Product: Camptosar (irinotecan hydrochloride) Injection
- ANDA filer: Watson
- ANDA filed: 7/23/2004
- Tentative approval: 5/04/2007
  - Requirements for ANDA were not changed or reviewed after the ANDA was filed
  - [FDA says very little in its letter, other than stating that the requirements were not changed or reviewed]
- Exclusivity FORFEITED
  - 7/23/2004 + 30 months = 1/23/2007

Acarbose

- Drug Product: Precose (acarbose) Tablets
- ANDA filer: Cobalt
- ANDA filed: 1/10/2005
- Tentative approval: Not within 30 months
- Exclusivity NOT forfeited under this provision
  - Change in the RLD against which Cobalt was to do its bioequivalence study
  - Initailly, FDA asked Cobalt to use 100 mg strength tablet
  - After Cobalt began in vivo bioequivalence studies, FDA stated 100 mg was not acceptable
  - Cobalt had to do additional in vivo studies with other strength

Imiquimod

- Drug Product: Aldara (imiquimod) Cream
- ANDA filer: Nycomed
- ANDA filed: 10/16/2006
- Tentative approval: Not within 30 months
- Exclusivity NOT forfeited under this provision
  - Failure to obtain tentative approval due to FDA's "ongoing review of the requirements for approval of Imiquimod." nitailly, FDA asked Cobalt to use 100 mg strength tablet

Balto and Carrier Letter

- "[R]everse payments do not block markets, exclusivities do."
  - Problem not with pay-for delay but with ineffective failure-to-market provision
- Market acceleration clauses render "use it or lose it" "toothless"
  - Permit first-filer to enter market prior to agreed upon date if subsequent generic challenger prevails in court
- Declaratory Judgment problem not fixed
  - Stems from MMA's requiring subsequent generic filers to win through appellate court on same patents against which first-filer filed
  - To preserve "parking" of exclusivity, brands either don't sue at all or don't sue on all the patents forcing subsequent filers to seek DJ
- Authors propose helping draft legislation that fixes these problems