

Understanding the 180-Day Exclusivity Forfeiture Provisions of the MMA

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Pre-MMA

- **180-day exclusivity triggered by the earlier of:**
 - (1) court decision (appellate); or**
 - (2) commercial marketing.**

- **Problem: Exclusivity Parking**
 - Use it or lose it
 - If others are ready, let them go ahead



MMA 180-Day Exclusivity Period

- **“Subject to subparagraph (D), if the application contains a [P.IV] certification and is for a drug for which a first applicant has submitted an application containing such a certification, the application shall be made effective on the date that is 180 days after the date of the first commercial marketing of the drug . . . by any first applicant.”**

21 USC 355(j)(5)(B)(iv)(I)

- **Application: first ANDA with a P.IV certification was filed on or after Dec. 8, 2003**



“First Applicant”

- “...‘first applicant’ means an applicant that, on the first day on which a substantially complete application containing a [P.IV] certification is submitted for approval of a drug, submits a substantially complete application that contains and lawfully maintains a [P.IV] certification....”

21 USC 355(j)(5)(B)(iv)(II)(bb)

- “substantially complete” = “sufficiently complete to permit a substantive review”

21 USC 355(j)(5)(B)(iv)(II)(cc)



Forfeiture Events

- (I) Failure to Market**
- (II) Withdrawal of Application**
- (III) Amendment of Certification**
- (IV) Failure to Obtain Tentative Approval Within 30 Mos.**
- (V) Agreement With Another Applicant, the Listed Drug Application Holder, or a Patent Owner**
- (VI) Expiration of All Patents**

21 USC 355(j)(5)(D)(I)-(VI)



FDA Practice

- **“It is FDA’s practice to make decisions on eligibility for 180-day exclusivity only in the context of specific ANDAs that are otherwise eligible for approval.”**
- **When FDA must make an approval decision for an ANDA, it will inform the applicant that it is**
 - (1) a first applicant and entitled to exclusivity
 - (2) a first applicant that has forfeited its exclusivity
 - (3) eligible only for TA due to another’s exclusivity
 - (4) eligible for FA because another forfeited exclusivity
- **FDA will consider whether there has been a forfeiture when approval of a subsequent ANDA may be blocked by a first applicant’s exclusivity.**



(I) Failure to Market

The first applicant fails to market the drug by later of

(aa) the earlier of

(AA) 75 days after final approval; or

(BB) 30 months after ANDA submission;

Or

(bb) The date that is 75 days after the date as of which, as to each of the patents that qualified the FA for exclusivity, at least one of the following has occurred:

(AA) Final decision of invalidity or noninfringement.

(BB) Settlement order entering final judgment.

(CC) NDA holder delists patent from Orange Book.



Granisetron Decision

Docket No. 2007N-0389 (Jan. 17, 2008)

- **Teva's ANDA "submitted" 6/1/04**
 - "submission" date = date accepted for review
- **p.III to '808; sect. viii to '340; and p.IV to '548**
 - '808 exp. 12/29/07 (42+ mos. after ANDA filing)
- **HLR did not sue Teva on '548 patent**
- **ANDA approval on 12/31/07**
- **(aa) date = 12/1/06**
 - 30 mos. after filing < 75 days after approval (3/15/08)
- **But no (bb) date:**
 - No suit vs. Teva; no DJ action; no delisting request
- **Take home:**
 - no (bb) date → no forfeiture (plain language reading)



Granisetron Decision

Docket No. 2007N-0389 (Jan. 17, 2008)

- **Problem noted in footnote 6:**
 - Inherent in the “failure to market” provisions is the possibility that a first applicant could enter into a settlement agreement with the NDA holder or patent owner in which a court does not enter a final judgment of invalidity or non-infringement, and that subsequent applicants would be unable to initiate a forfeiture with a declaratory judgment action
 - “This potential scenario is not one for which the statute currently provides a remedy”
- **Solution: expanded DJ jurisdiction (*Caraco v. Forest*)**



Acarbose Decision

Docket No. 2007N-0445 (May 7, 2008)

- **Cobalt's ANDA "submitted" 3/22/05**
- **p.IV to '769 patent**
 - '769 exp. 12/29/07 (42+ mos. after ANDA filing)
- **Bayer did not sue; Cobalt filed DJ, but then dismissed**
- **Bayer requested delisting of '769 on 4/16/07**
- **ANDA approval on 5/7/08**
- **(aa) date = 9/22/07**
 - 30 mos. after filing < 75 days after approval (7/21/08)
- **(bb) date = 6/30/07 (75 days after delisting)**
- **Result: Cobalt forfeited on 9/22/07**



Acarbose Decision

Docket No. 2007N-0445 (May 7, 2008)

- **Distinguished *Ranbaxy v. Leavitt* (D.C. Cir. 2006)**
 - Rule: FDA may not delist a patent if p.IV ANDA has been filed, thereby depriving applicant of 180-day exclusivity
 - Pre-MMA case, therefore the court did not purport to render a decision on patent delisting under MMA
- **Rejected argument that forfeiture under (bb) (CC) should apply only if the withdrawal of patent information is pursuant to 21 USC 355(j)(5)(C)(ii) (counterclaim to infringement action, alleging a patent is improperly listed, seeking withdrawal)**
 - Scope of provision is broad; plain language controls
- **Cobalt sued FDA 5/8; voluntarily dismissed 5/16**



(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).”**
- **Administrative withdrawal due to poor quality ANDA?**



(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.”**
- **21 CFR 314.94(a)(12)(viii)(A) requires amendment of a p.IV to a p.III after a final judgment of infringement**



(IV) Failure to Obtain Tent. 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.”**
- **FDAAA – 21 USC 355(q)(1)(G) (2007)**
 - If approval was delayed due to a citizen petition, 30-month period extended by amt. of time to resolve pet.
- **Metoprolol; Famotidine: no decision b/c no subseq.**
- **Irinotecan: Watson forfeits b/c > 30 mos. to TA**



(IV) Failure to Obtain Tent. Approval

- **Acarbose**

- “filed” = “submission” = accepted for review = 3/22/05
- no tentative approval before 9/22/05
- However, “Cobalt’s failure to obtain a tentative approval within 30 months was caused – in part – by the agency’s change in or review of BE requirements.”
- FDA identified the 100 mg strength tablet as the product to be used in Cobalt’s in vivo BE study
- On Aug. 8, 2006, FDA: “Cobalt 100 mg not acc.”
- Cobalt then used a different strength
- “Because FDA changed the requirements for the BE study, Cobalt did not forfeit its exclusivity.”



(V) Anticompetitive Agreement

- **The first applicant enters into an agreement with another ANDA applicant, the NDA holder, or the patent owner, and there is a final decision of the Federal Trade Commission or an appeals court “that the agreement has violated the antitrust laws.”**
- **The only forfeiture provision that applies retroactively to all ANDAs, regardless of whether the first P.IV certification was made before Dec. 8, 2003**



(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.”**
- **Puts to rest Mylan’s argument in amlodipine case**



P.III/P.IV Hypo

- **Cmpd. Pat. expires 2015; Form. Pat. expires 2018**
- **Generico plans ANDA for noninfringing formulation, therefore p.III Cmpd. Pat., p.IV Form. Pat.**
- **When should Generico file its ANDA?**
- **Problem: if file now, might get court decision more than 75 days before Cmpd. Pat. expires → forfeiture**
- **Possible Solutions:**
 - Wait until 30 mos. before Cmpd. Pat. expiration to file
 - File now, delay court decision (or final judgment as result of settlement) until <75 days before Cmpd. Pat. expiration
 - Avoid lawsuit on p.IV (Granisetron)



Lessons

- **Failure to Market**

- may need to delay p.III/p.IV filings, if want excl.
- Fn. 7 in Granisetron decision: “the race to earn 180-day exclusivity by submitting the first ANDA to challenge a patent may result in the submission of ANDAs that may also contain one or more p.III certifications to patents that do not expire until well into the future.” “We have received ANDAs for which...the sponsor has no intention to obtain approval and market the generic drug for 12 years or more.”

- **Failure to Obtain Tentative Approval**

- Must file quality ANDA, to ensure TA w/in 30 mos.



Questions?

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