

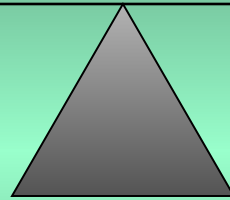
ENFORCING PATENTS ON PHARMACEUTICALS

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Hatch-Waxman Act

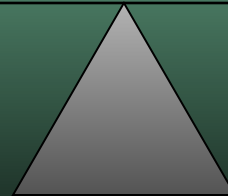
Patent term
extension
due to testing

Exemption from
infringement
due to testing

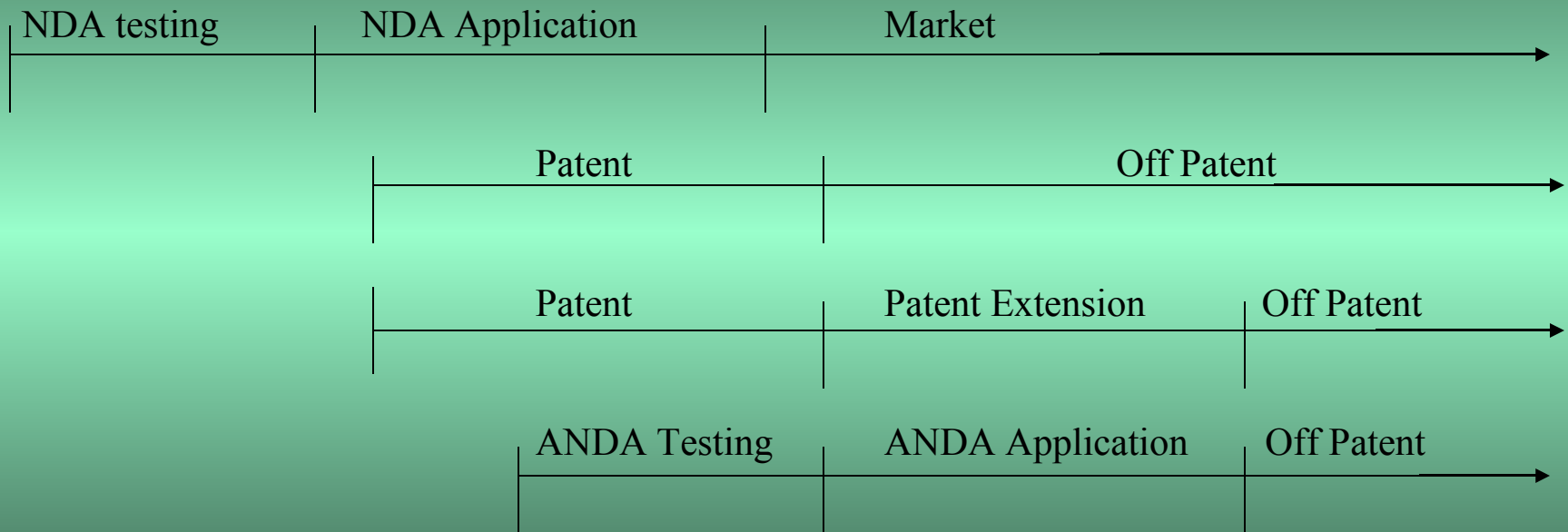


Patent term
extension due
to FDA
application
process

Early determination
of infringement
based on FDA
application



Relative Timelines



Patent Statute

35 U.S.C. § 271(e)

35 U.S.C. § 271(e) defines both infringement and non-infringement in the context of pharmaceutical products

- Non-infringement (§ 271(e)(1)):
“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”
- Infringing (§ 271(e)(2)):
“an application under Section 505(j) of the Federal Food, Drug and Cosmetic Act”

Section 505(j) of the Federal
Food, Drug and Cosmetic Act

21 U.S.C. § 355(j)

The ANDA Application

- A statement that the use of the drug in the application has been approved already. 21 U.S.C. § 355(j)(2)(A)(i)
- A statement that the active ingredient(s) is(are) the same as what has been approved. 21 U.S.C. § 355(j)(2)(A)(ii)(I)-(III)
- A statement showing that the route of administration, the dosage form, and the strength of the drug are the same as the approved drug. 21 U.S.C. § 355(j)(2)(A)(iii)
- A statement of bioequivalence. 21 U.S.C. § 355(j)(2)(A)(iv)
- Proposed labeling. 21 U.S.C. § 355(j)(2)(A)(v)
- Items from 21 U.S.C. § 355(b)(1)(B)-(F)
 - List of ingredients
 - Statement of the composition of the drug
 - Manufacturing specifications
 - Product samples
 - Label samples

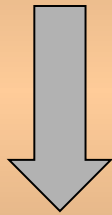
The ANDA Application continued

- Certification as to each patent “which claims the listed drug referred to in the application.” 21 U.S.C. § 355(j)(2)(A)(vii)
 - No patent information has been filed. 21 U.S.C. § 355(j)(2)(A)(vii)(I)
 - The patent has expired. 21 U.S.C. § 355(j)(2)(A)(vii)(II)
 - The date on which the patent will expire. 21 U.S.C. § 355(j)(2)(A)(vii)(III) (known as a Paragraph III certification)
 - The patent is invalid or will not be infringed. 21 U.S.C. § 355(j)(A)(vii) (known as a Paragraph IV certification)
- Statement. 21 U.S.C. § 355(j)(2)(A)(viii)
 - If the patent is a method of use patent, a statement that the patent does not claim the use in the application

The ANDA Application Process

The ANDA
Application

21 U.S.C. § 355(j)(2)(A)



Notice to patent holder when a
Paragraph IV Certification is made

21 U.S.C. § 355(j)(2)(B)

Contents of the Notice to Patent Holder

Statute 21 U.S.C. § 355(j)(2)(B)

Regulation 21 C.F.R. § 314.95

FDA Action After an ANDA Filing

Approval or disapproval within 180 days. 21 U.S.C. § 355(j)(5)(A)

- Paragraph I or II certification, approval is immediate.
21 U.S.C. § 355(j)(5)(B)(I)
- Paragraph III certification, approval is effective when the patent expires.
21 U.S.C. § 355(j)(5)(ii)
- Paragraph IV certification, approval is immediate unless an infringement suit on the certified patent is brought before 45 days from the notice to the patent holder. 21 U.S.C. § 355(j)(5)(B)(iii)
 - If suit is brought, approval is delayed 30 months
 - If the suit decides the patent is invalid or not infringed, approval is effective on the date of the decision. 21 U.S.C. § 355(j)(5)(B)(iii)(I)
 - If the suit decides the patent is infringed, approval is effective not earlier than the expiration of the patent. 21 U.S.C. § 355(j)(5)(B)(iii)(II) and 35 U.S.C. § 271(e)(A)

The First Filed ANDA Application

If you are a second or subsequent ANDA application, approval cannot be made until 180 days after either the date of the first commercialization of the first ANDA filer's drug or the date of a court decision rendering the patent invalid or not infringed.

21 U.S.C. § 355(j)(5)(b)(iv)

Patent Term Restoration and Periods of Exclusivity

- Term Restoration. 35 U.S.C. § 156
- Periods of exclusivity.
 - New indications – 3 years. 21 U.S.C. § 355(c)(3)(D)(iii)
 - New chemical entities – 5 years. 21 U.S.C. § 355(c)(3)(D)(ii)
 - Pediatric use – 6 months. 21 U.S.C. § 355a(a) (not to be confused with § 355(a)!)
 - Rare disease – 7 years. 21 U.S.C. § 360cc(a)

Bayer AG v. Elan Pharm. Research Corp.,

54 U.S.P.Q. 2d 1710 (Fed Cir. 2000)

- Bayer owned a patent on a form of the vasodilator, nifedipine.
- The patent claimed a specific surface area of the crystals to enhance absorption into the blood.
- The asserted claim:
 - A solid pharmaceutical composition comprising as an active ingredient an effective amount of nifedipine crystals with a specific surface area of 1.0 to 4 m²/g, in admixture with a solid diluent, to result in a sustained release of nifedipine.
- Elan's ANDA biopatch used a raw material crystal size of 6.15 m²/g but the ANDA did not have a specification for the crystal size. Elan's dosage strength was 30 mg.
- Elan amended its ANDA to limit the raw material crystal size to greater than 5 m²/g. It also set up internal testing procedures for crystal size.
- Bayer filed suit under 35 U.S.C. § 271(e)(2). Elan moved for summary judgment and the district court granted the motion.

Bayer AG v. Elan Pharm. Research Corp. continued

- The district court held there was no direct infringement based on the ANDA specification.
- The district court held there was no infringement under the doctrine of equivalents because Bayer narrowed the claim from 1 to 6 m²/g to 1 to 4 m²/g based on an obviousness rejection.
- The Federal Circuit affirmed:

“The focus, under Section 271(e)(2)(A), is on what the ANDA applicant will likely market if its application is approved, an act that has not yet occurred. ‘ . . .[t]his hypothetical inquiry is properly grounded in the ANDA application and the extensive materials typically submitted in its support.’”
- Because there are civil and criminal penalties that attach to selling and distributing a drug outside of the approved specification, the only drug that Elan could sell is one that does not literally infringe the patent.

Bayer AG v. Biovail Corp, No. 01-1329 (Fed. Cir. Feb. 7, 2002)

- Bayer sued Elan on its 60 mg nifedipine ANDA and on its commercial 30 mg tablet.
- The district court dismissed both cases based on collateral estoppel.
- The Federal Circuit held that the 30 mg case was different than the previous ANDA case because “infringement under § 271(e)(2)(A) by submission of an ANDA is not synonymous with infringement under § 271(a) by a commercial product. Evidence of actual infringement (contrasted with evidence of a ‘hypothetical’ infringement) may differ in substance and may become available only after manufacture of the composition. Therefore, at a minimum, Bayer did not have a full and fair opportunity to litigate the issue of infringement by the commercial tablets because those tablets were not available until after ANDA approval.”

Bayer AG v. Biovail Corp, No. 01-1329 (Fed. Cir. Feb. 7, 2002)

continued

- The Federal Circuit held that the 60 mg ANDA case might be different than the 30 mg ANDA case because evidence from the 30 mg commercial tablet suggested that the crystals condensed over time to reduce the surface area to within the claimed range and that this evidence had not been available in the 30 mg ANDA case and that the claim interpretation in that case did not explicitly cover whether the condensed crystals would fall within the claims.
- The Federal Circuit remanded.

Mylan Pharmaceuticals Inc. v. Thompson,
60 U.S.P.Q. 2d 1576 (Fed. Cir. 2001)

- Bristol-Meyers owned a patent on a method of administering Bupirone hydrochloride.
- Mylan filed an ANDA with a paragraph III certification. Mylan was set to ship product at midnight on November 22, 2000, the exact moment Bristol-Meyers' patent expired.
- 11 hours before the patent was to expire, Bristol-Meyers delivered a copy of a new patent to the FDA to be listed in the Orange Book.
- After a cursory investigation as to whether the patent covered the listed product, the FDA agreed to list the new patent.
- The new patent covered the administration of the metabolite of Bupirone.

Mylan Pharmaceuticals Inc. v. Thompson,
60 USPQ 2d 1576 (Fed. Cir. 2001) continued

- Mylan sued the FDA seeking to delist the new patent.
- The district court entered a preliminary injunction ordering the FDA to delist the patent and to approve Mylan's product.
- The Federal Circuit reversed. Mylan's action was based on declaratory judgment jurisdiction. In determining whether there is a case or controversy, a court should examine the forward-facing lawsuit. In this case the forward-facing lawsuit would be an action under § 271(e)(2) based on a paragraph IV certification.
- The patent statutes provide no recognizable defense to patent infringement that the patent in the Orange Book is improperly listed.
- Because Mylan's defense is not recognizable, there is no jurisdiction to maintain the suit.

**In re Buspirone Patent Litigation, MDL No. 1410
(S.D.N.Y. Feb 14, 2002)**

- Bristol-Meyers sued Mylan and others for patent infringement under § 271(e)(2).
- The district court held that the patent claim did not cover the administration of Buspirone which subsequently was metabolized in vitro to the claimed metabolite.
 - First, the claim calls for the “administration” of the metabolite. The specification only talked about the oral administration of the metabolite.
 - Second, the prosecution history showed that the patent was not allowed until Bristol-Meyers eliminated references to “Buspirone” and “pro drug”.
 - Third, the patent would be anticipated if interpreted to cover the administration of Buspirone which had been done publicly since 1986.

In re Buspirone Patent Litigation MDL No. 1410
(S.D.N.Y. Feb 14, 2002) continued

- The district court refused to dismiss antitrust counts against Bristol-Meyers. The Noerr-Pennington doctrine does not apply because the communications with the U.S. Government, the FDA, were with an agency that exercised no independent review of the statements being made to it. The result was that Bristol-Meyers was able to obtain automatic injunctions against the generic manufacturers by making false statements to the FDA about what the metabolite patent covered.
- The district court also broke new ground and found that Bristol-Meyers' conduct asserting the metabolite patent could support patent misuse and Walker-Process claims.