Overview of the U.S. Patent Term Extension Process

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Presentation Topics

- General Requirements for, and Contents of, Patent Term Extension (PTE) Application
- The PTE Application Process – Collaboration between U.S. PTO and Regulatory Agency
- Availability of Interim Extensions
- Scope of Protection During Extension Period & Issued Raised During Enforcement

Application for Patent Term Extension

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Application for PTE– General Requirements

PTE only available for a patent that has been issued during clinical development and/or regulatory review period for the first approved commercial use of a drug, biologic or medical device product. 35 U.S.C. § 156

- Patent claims product, method of using a product, or method of manufacturing a product
- Term of patent not expired before PTE application submitted
- Term of patent not previously extended
- First permitted commercial marketing or use of product under which regulatory review period occurred
- Must submit application within 60 days of regulatory agency approval

Application for PTE– General Requirements

- **60 Day rule**
  - Approval date = day 1; 60 calendar days, not business days
  - Exception now applies to approval notice sent after 4:30 pm (eastern time zone), in which case day 1 is the next business day
    - Rule change avoids problem created by "after hours" approval notice from FDA that was an issue in *Medicines Company v. Kappos* (E.D. Va. 2010)
- **Post-Covid PTE applications are filed electronically**
- **Pre-Covid PTE applications delivered in paper form**

Application for PTE– General Requirements

- **First Approved Use of "Drug Product"**
  - "Drug Product" is defined as "active ingredient of a new drug … including any salt or ester of the active ingredient, as a single entity or in combination with another active ingredient." *See* 35 U.S.C. § 156(f)(2).
  - USPTO equates active ingredient and its salt or its ester to be the same
    - PTE Application for approval of Prilosec OTC (omeprazole magnesium) denied, because the first approval was for Prilosec (omeprazole base). *Petition to Director In re: PTE Application for U.S. Patent No. 5,817,338.*
  - Court decisions confirm that PTE is ***not*** precluded for all salts/esters
    - *Glaxo Operations UK Ltd. V. Quigg*, "active ingredient" refers to the molecule in the drug product *to be administered* (cerufoxime axetil); newly approved drug was a separately patentable ester even though salts had been approved earlier

Application for PTE– General Requirements

- **First Approved Use of "Drug Product" cont.**
  - Court decisions confirm that PTE is not precluded for all salts/esters
    - *Photocure ASA v. Dudas* (Fed. Cir. 2010), court overturned PTO decision denying PTE application for drug product containing the active ingredient methyl aminolevulinate HCl ("MAL HCl") based on the earlier approval of aminolevulinic acid HCl ("ALA HCl")
    - Court relied heavily on the following facts:

      (i) MAL HCl was a "new drug" that required full FDA approval

      (ii) MAL HCl was separately patentable over prior art ALA HCl

      (iii) the pharmacological properties of MAL HCl differ from those of ALA HCl
    - PTO has made clear that it does not construe *Photocure* decision as requiring consideration of those criteria

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Application for PTE– General Requirements

- **First Approved Use of "Drug Product" cont.**
  - Combination product where both/all components were previously approved is ***not*** eligible
    - *Arnold P'ship v. Dudas* (Fed. Cir. 2004), court ruled that term of patent directed to combination of hydrocodone and ibuprofen could not be extended, because both components have been available as separate drugs
  - Combination product where at least one component was not previously approved is eligible (but only for patent directed to the combination or the previously unapproved component, its method of use or manufacture)
    - GARDASIL® 9 HPV vaccine, PTE Application for US7476389 approved, where pentavalent vaccine formulation had prior marketing approval but four of the new subcomponents were not covered by that prior approval
    - See also KAZANO® and OSENI® example (*infra page 11)*

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Application for PTE– General Requirements

- **First Approved Use of "Drug Product" cont.**
  - New formulation of previously approved drug product is ***not*** eligible
    - *Fisons PLC v. Quigg,* (Fed. Cir. 1989), where the court upheld PTO denial of extension of Fisons patents directed to "innovative use or dosage forms of cromolyn sodium". Fisons had developed stable liquid dosage forms, but first approved use of cromolyn sodium (for an inhalation capsule form) contained the same active ingredient.

Application for PTE– General Requirements

- **Multiple, Distinct "First Approvals" On Same Day**
  - LYRICA® (pregabalin)
    - Two separate NDAs: NDA 21-446 for method of treating neuropathy and NDA 21-723 for method of treating post-herpetic neuralgia
    - PTE awarded for two patents: (i) 300 days for US6197819 (covering compound/salt) and (ii) 533 days for US6001876 (covering treatment of pain, including post-herpetic pain)

Application for PTE– General Requirements

- **Multiple, Distinct "First Approvals" On Same Day**
  - NESINA® (alogliptin benzoate), KAZANO® (alogliptin benzoate and metformin HCl), and OSENI® (alogliptin benzoate and pioglitazone HCl)
    - Three separate NDAs: NDA 22-271 for use of alogliptin benzoate for glycemic control of type 2 diabetes; NDA 22-414 for combination of alogliptin benzoate and metformin HCl for treating type 2 diabetes; and NDA 22-426 for combination of alogliptin benzoate and pioglitazone HCl for treating type 2 diabetes
    - PTE awarded for three patents: (i) 262 days for US8173663 (covering method of treating type 2 diabetes for NESINA®); (ii) 101 days for US8288539 (covering compound for KAZANO®); and (iii) 5 years for US6329404 (covering composition for OSENI®)

Application for PTE– General Requirements

- **At least one claim must read on the approved product**
  - *Angiotech v. Lee* (E.D. Va 2016) concerned Angiotech's PTE Application for US5811447 based on the approval of its drug-eluting stent
    - The PTO denied the PTE Application—and the court agreed—because the claims were directed to a method of stenting a mammalian blood vessel that included a step of administering a drug
    - None of the claims specified that the drug was administered by the stent

Application for PTE– Application Contents

- **Application Contents/Requirements**
  - Applicant must be patent owner or its agent (licensee's agent with power)
  - Complete identification of the approved product
  - Complete identification of statutory basis for regulatory review
  - Date commercial marketing approval was received (i.e., day 1 of 60)
  - Statement that PTE Application filed within 60-day period; identification of last day to file
  - For drug product, identification of each active ingredient and a statement that product has not previously been approved
  - Complete identification of the patent for which extension is sought, and a copy of that patent (or reissue if application)

Application for PTE– Application Contents

- **Application Contents/Requirements cont.**
  - Copies of any Terminal Disclaimers, Certificates of Correction, Reexamination Certificate
  - Statement that the patent claims the product, method of use, or method of manufacturing the product (e.g., use claim chart)
  - Statement of relevant dates for the regulatory review (e.g., present log/table of all activity chronologically)
    - INDs (list all, first exemption of the approved product controls), any clinical holds, filing of NDA, BLA, PMA (class III devices); if submitted as modules, then list all
    - Description of all activities during regulatory review period (all requests from and submissions to reviewing agency)
  - Statement/opinion that patent is eligible for PTE (*see supra* page 4)

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Application for PTE– Application Contents

- **Application Contents/Requirements cont.**
  - Show PTE calculation: RRP – PGRRP – DD – ½(TP-PGTP)

    where RRP = regulatory review period (see above re: multiple INDs)

    PGRRP = pre-grant regulatory review

    DD = time during which applicant did not act with due diligence

    TP = testing phase

    PGTP = pre-grant testing phase
  - PTE capped at 5 years/total extended patent term of 14 years
  - Statement acknowledging duty to disclose any material information relevant to PTE
  - Pay the required fee (currently $1180)

Application for PTE– Application Contents

- **Problems with Application Contents/Requirements**
  - Complete identification of the approved product not a problem for small molecule, antibody, protein, vaccine, etc.
  - YESCARTA® PTE Application initially failed to provide a sufficient description of the CAR-T cell therapy
    - PTO inquired of Applicant as to whether earlier approved antibody directed to the same cancer cell-surface protein was actually the first approval
    - PTO found Applicant's description of the "*non-variable* vector comprising chimeric DNA encoding a *non-variable* chimeric antigen receptor" insufficient to distinguish the CAR T-cells of YESCARTA® from other approved products
    - PTO is supposed to rely ***only*** on what is in the application, but PTO acquired the vector and CD28 sequences from WHO records and asked FDA to confirm those sequences which distinguish YESCARTA® from other approved products

Application for PTE– Application Contents

- **Duty to disclose material information to PTO**
  - In *In re Zetia (Ezetimibe) Antitrust Litigation* (E.D. Va. 2019), the defendant argued that the patent owner in seeking patent term extension for the '721 patent without disclosing that certain claims were invalid for inherent anticipation.
  - If filing multiple PTE Applications for different patents based on the same approval, you ***must*** disclose this
    - With multiple patents possibly covering the approved product, you may still be assessing which is the best patent to extend
    - PTO will identify the PTE Application as approved subject to the Applicant picking with patent to extend
  - Multiple first approval examples; those were also disclosed to the PTO
  - For combinations, disclose prior approvals for “shared” active ingredients

PTE Application Process

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Application for PTE– Application Process

- **Initial Review by PTO (3-4 months)**
  - PTO will review Application for required components
  - PTO will review its records (assignment, maintenance fees)
  - PTO review the claims to assess whether the claims cover the product, method of use, or method of manufacturing the product
- **PTO First Request of Regulatory Agency (3-4 months)**
  - Whether product that is subject to PTE Application was subject to regulatory review and approval
  - Whether the regulatory review in question was the first approval for product
  - Whether PTE Application was timely filed

Application for PTE– Application Process cont.

- **Further Review by PTO (~1 month)**
  - If reviewing agency identifies an earlier approval, then the PTO may deny the PTE Application
  - If reviewing agency confirms that product approval was the first, then PTO will request agency to assess regulatory review periods and diligence
- **Second Request of Regulatory Agency (~9-10 months)**
  - Will assess testing/review periods, whether applicant acted with diligence
  - Due diligence standard: "…whether the applicant exhibited that degree of attention, continuous directed effort, and timeliness as may reasonably be expected from, and are ordinarily exercised by, a person during a regulatory review period."

Application for PTE– Application Process cont.

- **Second Request of Regulatory Agency cont.**
  - All relevant factors considered, which may include:
    - Time between approval of investigational exemption and start of trial
    - Length of time for clinical trials
    - Length of review periods for comparable products
    - Applicant compliance/failure to comply with agency requirements
    - Delay solely attributable to agency
    - Interruption of testing or submission of data caused by government action
    - Unavailability of key persons
    - Physical destruction of essential testing facilities or essential data
    - Whether ordinary and necessary measures to minimize delay were implemented
    - Delay caused by financial considerations

Application for PTE– Application Process cont.

- **Second Request of Regulatory Agency cont.**
  - Decision is published, opening 180 day period for third parties to challenge diligence
    - Four due diligence petitions over the last ~40 years
    - two were withdrawn
    - one was taken into consideration in reducing the regulatory review period (i.e., FDA revised its calculation of regulatory delay)
    - one was denied because the issue raised (lack of agency between PTE applicant and party receiving marketing approval) was within the PTO's purview
  - Upon conclusion of the challenge window, agency will send letter confirming that the review period is closed

Application for PTE– Application Process cont.

- **PTO Completes Evaluation (~2-3 months)**
  - Independently calculates to PTE available and assesses whether 5 year maximum extension or 14 extended term maximum would be exceeded
  - Sends notice letter to PTE Applicant confirming total available extension
  - PTO will issue a Certificate of Correction listing PTE (unless Applicant challenges)
- **Applicant can challenge by requesting reconsideration (within 1 month) and, if still not satisfied, then Applicant can bring in action in federal court (E.D. Va)**
- **PTO maintains list of patents with granted PTE**
  - https://www.uspto.gov/patents/laws/patent-term-extension/patent-terms-extended-under-35-usc-156

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Availability of Interim Extensions

Interim Extensions

- **Patent Owner Has Filed NDA/BLA/PMA**
  - During period of regulatory review but ***prior*** to regulatory approval, the patent to be extended will expire
  - Applicant can file request for interim extension
    - Include all information required for PTE Application (for product under review); no statement for date of approval and statement regarding 60 day window
    - First request must be filed within window of 6 months to 15 days prior to expiration of patent; subsequent requests must be filed within window of 60 to 30 days before expiration of the prior extension
    - Request must include statement that regulatory review period has begun, but has not concluded, for product that is the subject of the patent
  - Extensions for one year periods; must re-apply; 5 year maximum

Interim Extensions

- **Interim Extension denied**
  - *Genetics IVF v. Kappos* (E.D. Va 2011), Patent Owner filed a first interim extension request during the regulatory review period but failed to timely file the second interim extension request within the 60 to 30 day window
  - Error was discovered during the final 30 days and a second interim request was filed roughly a week before close of the first extension
  - PTO denied the second interim request as untimely, and the court agreed that PTO lack any authority to excuse the tardiness of the request

Interim Extensions

- **Patent Owner Has Filed PTE Application**
  - Where PTE Application is filed but PTO/regulatory agency review is not complete, Applicant can file request for interim extension
  - Director ***shall*** extend the term of the patent for periods up to one year, if:
    - The patent would expire before a certificate for extension can be issued or denied
    - It is determined that the patent is eligible for extension (consistent with PTO initial review)
  - Multiple extensions (up to1 year) are possible; PTO authorized to extend ***until*** a decision regarding approval/denial of the certificate of extension is entered

Interim Extensions

- **Interim Extension denied**
  - *Somerset Pharm. Inc. v. Dudas* (Fed. Cir. 2007), Patent Owner filed a PTE Application for EMSAM® (selegiline formulated in a transdermal patch) and then filed request for interim extension
  - Patent Owner filed a civil complaint to compel the PTO to act on the interim extension request, which was denied by the lower court and then Somerset appealed on an expedited basis
  - The same day that the appellate court granted the motion to expedite the appeal, the PTO denied the PTE Application on its merits (not based on first approved use) as well as the request for interim extension
  - Because PTO denied the PTE Application, the court had no authority to compel the PTO to grant the interim request because that is only available before grant or denial of the PTE Application

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Scope of Protection During Extension Period & Issues Raised During Enforcement

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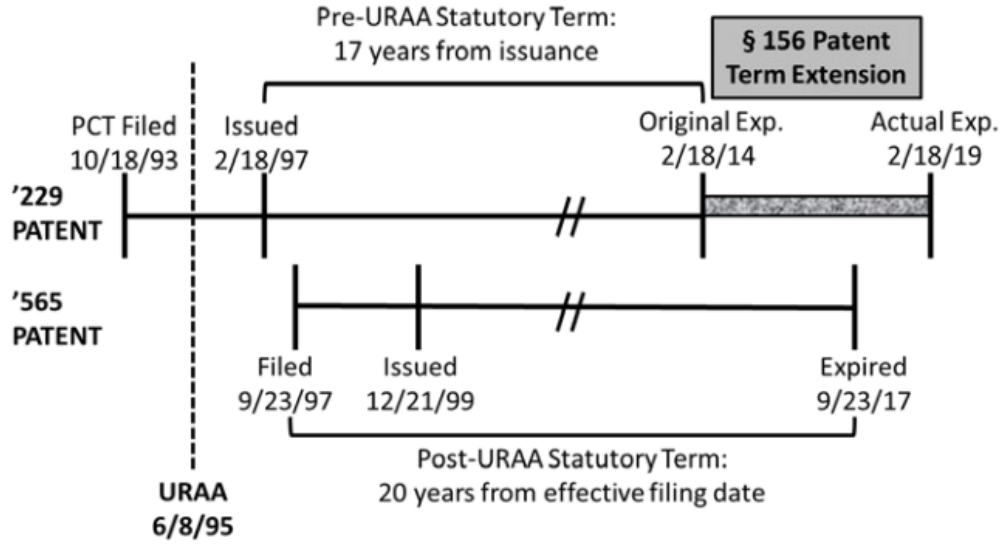
Issues Raised During Enforcement

- **Obviousness-type double patenting considerations**
  - Terminal Disclaimer links together the terms of two or more patents such that those patents will expire on the same day
  - *Merck v. Hi-Tech Pharmacal* (Fed. Cir. 2007), ANDA challenger argued that the grant of the PTE is incompatible with the existence of the Terminal Disclaimer, but court held that it is not, noting:
    - The expiration date of the patent set by the Terminal Disclaimer remains in place
    - The computation of the PTE is from the expiration date resulting from the Terminal Disclaimer; the purpose of the Terminal Disclaimer remains fulfilled
    - At the same time, the purpose of the PTE is also fulfilled

Issues Raised During Enforcement cont.

- **Obviousness-type double patenting considerations cont.**



  - *Novartis v. Ezra* (Fed. Cir. 2018), ANDA challenger argued that obviousness-type double patenting should limit the term of a PTE extended, 17 year term (pre-GATT) patent, but the court held that it cannot invalidate because (i) the patent, under its pre-PTE expiration date remained valid and (ii) the PTE was validly obtained

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Issues Raised During Enforcement

- **Improper Calculation of PTE**
  - Pregrant portions of testing or regulatory delay are excluded
  - *In re Sugammadex* (D. New Jersey 2023), Merck sued various ANDA challengers for infringement of its reissue patent covering BRIDION® (sugammadex sodium), which had received 5 years of PTE
  - ANDA defendants argued that the period of pre-grant delay should count not from the issue date of the original patent but instead from the date that Merck's reissue patent was granted, which would have eliminated over 3 years of the PTE. The court disagreed, holding that the grant date of the original patent is the critical date for calculating PTE

Issues Raised During Enforcement

- **Scope of Protection Afforded by PTE**
  - *Pfizer v. Dr. Reddy's Labs* (Fed. Cir. 2004) addressed the provision of 35 U.S.C. § 156(b)(2), which limits the "rights derived" from PTE to "any use approved for the product"
  - Pfizer obtained PTE for its approved product, Norvasc® (amlopidine besylate), and Dr. Reddy's filed a "paper NDA" for amlopidine maleate (relying on Pfizer's data for both salts) during the extended term
  - Dr. Reddy's acknowledged that amlodipine maleate was covered by the patent claims, but argued that the term extension applies only to the besylate salt because that is the registered product
  - The court looked to the language of 35 U.S.C. § 156(f)(2), which specifies that salts/esters of the active ingredient are the same product, concluding that "the active ingredient is amlodipine, and that it is the same whether administered as the besylate salt or the maleate salt"

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Issues Raised During Enforcement

- **Scope of Protection Afforded by PTE cont.**
  - *Biogen Internat'l v. Banner Life Sciences* (Fed. Cir. 2004) has a similar fact pattern
  - Biogen obtained PTE for its approved product, FECFIDERA® (dimethyl fumarate) for treating multiple sclerosis, and Banner filed a "paper NDA" for monomethylfumarate (relying on Biogen's data) during the extended term. DMF is converted to MMF in the body.
  - Claims covered administering DMF, MMF, or a combination for treating multiple sclerosis
  - The court distinguished *Pfizer* on the basis that the active ingredient in *Pfizer* was the same for both salts, but in *Biogen*, because DMF was the ester of MMF, and not vice versa, MMF was not the same active ingredient or salt/ester thereof and did not fall within the scope of Biogen's patent term extension

Thank You

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