

Patent and Exclusivity Update

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Agenda

- Patent and Exclusivity Team(PET) Introduction:
 - Who we are and what we do
- Relevant Regulations
- Observations
- Exclusivity Issues
 - Pre-MMA products and 180-day exclusivity
 - Pediatric exclusivity: impact on your ANDA
 - Forfeiture of 180-day exclusivity
- Contact Information
- Questions?

MMA Rule and Implementation

The new MMA rule that goes into effect on December 5, 2016 will NOT be a topic of discussion today. All material covered today reflects the regulations currently in effect.

Everyone is strongly encouraged to read the MMA final rule.

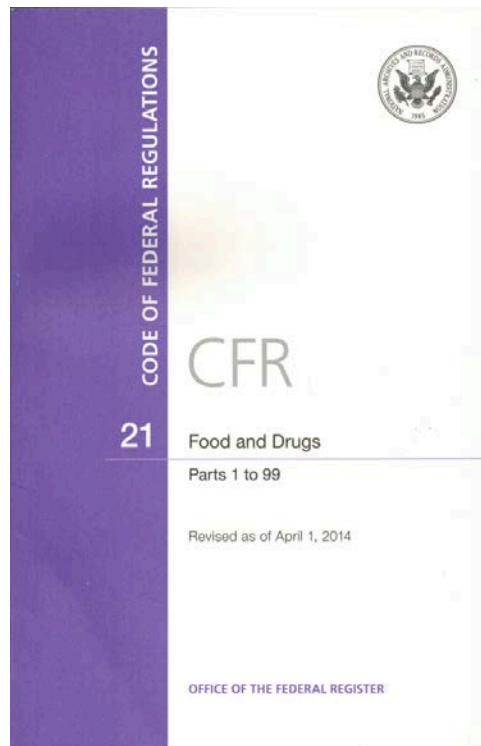
Who We Are

- Iain Margand
- Rinku Patel
- Martin Shimer
- Heather Strandberg
- Ashley Jones/Pat Downs: Project Management support

What We Do

- Complete analyses of legal documents
- Research related to patents/exclusivities
 - Late Listing per 21 CFR 314.94(a)(12)(vi)
 - Patent submission dates
- Determine eligibility for 180-day exclusivity
- Forecast dates
 - Eligibility for Full Approval: “earliest lawful ANDA approval date”
 - Forfeiture dates
- Forfeiture Tracking
- Recertification/Renotification
- Prioritization under MaPP 5240.3
 - Granting Prioritization of First Generic Applications
 - Assisting with other prioritization determinations

Relevant Regulations



Patent Certifications

314.94(a)(12)(i) through (viii): Patent certification

- Types of certifications
- Late submission of patent information
- Disputed patent information
- Amended certifications
 - Infringement
 - Other amendments

Notice of Certification

314.95(a)-(f)

- a. Notice of certification
- b. Sending the Notice
- c. Content of Notice
- d. Amendment to ANDA
- e. Documentation of Receipt of Notice
- f. Approval

Effective Date of Approval

314.107(a)-(f)

- Disposition of Patent Litigation: stays of approval
- Subsequent abbreviated new drug application submission: 180-day exclusivity
- Notification of court actions
- Computation of 45-day time clock

Brief Discussion on Other Topics/Regulations

- Late listed patents: 314.94(a)(viii)(C)(2)
 - Application-specific
 - Changes to NDA are a factor
- Correction of Patent Information: 314.53(f)
- Split Certifications

Aldara Cream NDA 20723

Split Certifications

U-1047: Treatment of biopsy confirmed, primary superficial basal cell carcinoma

U-1048: Works through the induction of interferon and other cytokines

Product 001
 IMIQUIMOD (ALDARA) CREAM 5%

Patent Data

Product No	Patent No	Patent Expiration	Drug Substance Claim	Drug Product Claim	Patent Use Code	Delist Requested
001	7696159	Apr 1, 2024	DS		U-1047 U-1048	
001	7696159*PED	Oct 1, 2024				

- Permissible when a single patent has both drug substance and/or drug product claims as well as use claims.
- Permissible when a single patent has multiple approved uses within a single use code.
- Permissible when a single patent has multiple approved use codes
- Also must consider any exclusivities that may or may not overlap with use codes defined for use patents

Observations

What Industry is Doing Well

- Certifying to all listed patents
- Providing timely notice.....generally
- Submitting documentation of notice for original PIV certifications
- Requesting prior authorization before sending notice of PIV certification
- Notifying FDA of filing of first civil action complaint

Areas for Improvement

- Timely submission of notice for amendments
- Documentation of timely notice for amendment
- **Notifying FDA of the entry of all final court orders or judgments within 10 days: 314.107(e)**
- Providing notice of commercial launch:
314.107(c)(1)(i)
 - Notice needed for launch of First Generic with 180-day
 - Notice needed on exclusivity punts: sponsor may still be eligible for 180-day exclusivity
 - Notice needed when launching an Authorized Generic
- Some challenges with maintaining congruent certifications

Areas for Improvement continued

- Amending to PIII or notifying FDA of appeal
- Providing **complete** copy of complaint
- Clearly stating intent with respect to unexpired exclusivity
 - Carving-out
 - Awaiting expiration

Congruent Certifications

- Method that ANDA sponsor chooses (PIV or section viii statement) to address a specific use code
- Must be consistent across all patents that are associated with that use code or similarly worded use codes

FDA requests for copy of Settlement Agreement

- Sponsor's are not normally required to submit copy of settlement agreement to their ANDA
- However, when a judgment references 271(e)(4)(A) and indicates that the date of approval shall be a date not earlier than the expiration of the patent(s)-in-suit, except as permitted by settlement and license agreement, FDA will refrain from approving without additional supporting documentation related to the settlement and license agreement



Exclusivity Issues



Pre-MMA 180-day Exclusivity

Pre-MMA

Patent-by-Patent

Separate exclusivity periods awarded for each patent. These can be held by different applicants and may run at different times. This creates confusion and diminishes value of some applicants exclusivity periods

Post-MMA

Product-by-Product

A single period of 180-day exclusivity, though this exclusivity can still be shared by multiple applicants

Why are we still discussing pre-MMA exclusivity in 2016?

- Pre-MMA exclusivity lives on!
- Generally results in second round of exclusivity but can be a third.....
- Can happen many years after initial ANDA approval(s) and first round of exclusivity has run
- Not obvious to most of industry-may even surprise party being granted exclusivity
- Determination of Topiramate Sprinkle Capsules Exclusivity:

<http://www.fda.gov/downloads/AboutFDA/CentersOffices/CenterforDrugEvaluationandResearch/UCM135323.pdf>

Pediatric Exclusivity

- Six month period that “attaches” to existing patents or exclusivities for an active moiety
- This exclusivity period can NOT be carved out of labeling
- Exclusivity period itself also can NOT be challenged
- Exclusivity period is NOT an extension of the patent



Pediatric Exclusivity Example:

Epzicom NDA 21652

Product 001
ABACAVIR SULFATE; LAMIVUDINE (EPZICOM) TABLET EQ 600MG BASE;300MG

Patent Data

Product No	Patent No	Patent Expiration	Drug Substance Claim	Drug Product Claim	Patent Use Code	Delist Requested
001	5905082	May 18, 2016	DS	DP		
001	5905082*PED	Nov 18, 2016				
001	6294540	May 14, 2018	DS	DP	<u>U-257</u>	
001	6294540*PED	Nov 14, 2018				
001	6417191	Mar 28, 2016		DP	<u>U-257</u>	
001	6417191*PED	Sep 28, 2016				

Pediatric Exclusivity Example



Patent Data

Product No	Patent No	Patent Expiration
001	5905082	May 18, 2016
001	5905082*PED	Nov 18, 2016
001	6294540	May 14, 2018
001	6294540*PED	Nov 14, 2018
001	6417191	Mar 28, 2016
001	6417191*PED	Sep 28, 2016

Epzicom NDA 21652

- '191 patent expired 3/28/2016 associated pediatric exclusivity expired 9/28/2016
- '082 patent expired 5/14/2016 associated pediatric exclusivity expires 11/14/2016

- Overlap of pediatric exclusivity periods in this case such that exclusivity runs from expiration of '191 patent on 3/28/2016 through expiration of pediatric exclusivity associated with '082 on 11/14/2016.
- ANDA CANNOT be approved during pediatric exclusivity period unless NDA holder provides waiver of pediatric exclusivity period



Impact of Pediatric Exclusivity on timing of ANDA approvals

- ANDA not eligible for Full Approval during pediatric exclusivity “window” unless:
 - Applicant has secured a waiver of pediatric exclusivity from the NDA holder
 - Applicant has obtained a ruling from a court finding the patent subject to pediatric exclusivity invalid, not-infringed or unenforceable
- Dismissal of civil action: Must secure waiver
- Not sued within 45 days: Must secure waiver



Pediatric Exclusivity Additional Information

- ANDA sponsor may not maintain a PIV certification to an expired patent
- ANDA sponsors are considered to have a PII certification upon expiration of the patent
- Docket: FDA 2007-P-0351
- CP 2012-P-0661: Response issued January 26, 2015-footnote #20: ANDA approval permissible day after expiration of pediatric exclusivity pursuant to section 505A(b)(1)(B)(ii) of the FD&C Act

Forfeiture Provisions

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

- Failure to obtain a tentative approval within 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

Forfeitures

- PET forecasts and tracks events related to forfeitures
 - Failure to Market
 - Failure to obtain Tentative Approval
- Subsequent applicants often presume forfeiture when the First Filer did not secure TA within 30 months
- If FDA determines that there was a change in or a review of the requirements for approval there is no forfeiture under this forfeiture provision- 505(j)(5)(D)(i)(IV)
- OGD conducts forfeiture analysis when subsequent applicant(s) is/are eligible for Full Approval except for blocking 180-day exclusivity
- Forfeiture determinations currently NOT published

Forfeitures continued

- Letters to ANDA from sponsor
- FDA's practice is not to confirm forfeiture finding
- Shared exclusivity and forfeiture
 - “Nateglinide precedent”:
<http://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/AbbreviatedNewDrugApplicationANDAGenerics/UCM182134.pdf>

Rosuvastatin Exclusivity

- Cohort of First Filers submitted on the NCE-1 date
- No First Filer secured TA within 30 months of submission date
- Exclusivity was shared and potentially subject to mass forfeiture by all First Filers
- Forfeiture analysis completed showing that there was a change in or review of the requirements for approval of at least one First Filer
- Non forfeiture by one First Filer in the cohort preserves exclusivity per the Agency's Nateglinide precedent
- First application approved on April 29, 2016 due to pediatric waiver during ped window for the RE37314 patent
- First approved application launched on May 4, 2016
- 180-day exclusivity awarded to ANDA 79168 upon approval issued on July 19, 2016
- Exclusivity for 79168 triggered by May 4, 2016 Marketing of ANDA 79167

Exclusivity for ANDA 79168

Exclusivity Code	Exclusivity Expiration
PC	Oct 29, 2016

Exclusivity for ANDA 79167

Exclusivity Code	Exclusivity Expiration
There is no unexpired exclusivity for this product in the Orange Book database.	

Contact Information

- New PET mailbox: CDER-OGDPET@fda.hhs.gov
- Information to be sent to mailbox:
 - Commercial launch notice
 - Court decisions which immediately impact when your ANDA can be approved
 - Exclusivity relinquishments
 - Pediatric waivers
 - Court Decisions triggering Failure to Market provisions
 - General questions related to certifications, notice, timing of approval, etc.

Happy Halloween!



