Yes, You *Can* Teach an Old Drug New Tricks: *Regulatory Pathway for Repurposed Drugs*

ASENT
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Agenda

- **Drug Repurposing – What is it? And why do it?**
- **Regulatory Pathways for Repurposed Drugs**
- **Legislative Attempts to Address Repurposing**
- **The Current Environment Surrounding Orphan Drugs & Drug Repurposing**

Drug Repurposing – What is it? And why do it?

What is Repurposing?

- **Drug repurposing is the application of known drugs and compounds to treat new indications (i.e., new diseases or conditions).**
  - **Also known as drug repositioning, re-profiling, re-tasking, or therapeutic switching**
- **"Repurposing generally refers to studying drugs that are already approved to treat one disease or condition to see if they are safe and effective for treating other diseases." (NCATS)**
- **Many products are repurposed (Sildenafil, Aspirin, Thalidomide).**

Why Repurpose?

Risk

Speed

Cost

Why Repurpose?

Patients!

Especially patients with rare (orphan) and neglected diseases or conditions.

II

Regulatory Pathways for Repurposed Drugs

505(b)(2) Application

- **A 505(b)(2) application is an application containing "investigations . . . relied upon by the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted."**

- **"Paper NDA" as antecedent; Originated in the late 1970s (Dr. M. Finkel, FDA).**

  – **Permitted the sponsor of a "duplicate drug" (i.e., Post-1962 drug) to submit published studies in support of its NDA.**

505(b)(2) Application

- **Permits the sponsor of a drug to rely on published studies and/or the FDA's safety and effectiveness findings from studies contained in another NDA to satisfy the "full reports" requirement of the FDC Act.**

- **There needs to be a scientific or medical "bridge" between the product that is the subject of the 505(b)(2) application and the product that was the subject of the previously-approved related NDA or was the subject of the studies in the public domain. Often this "bridge" is built by comparative bioavailability information.**

505(b)(2) FDA Guidance

- **Some types of changes to approved drugs for which a 505(b)(2) application may be submitted:**
  - **Formulation**
  - **Dosing regimen**
  - **Active ingredient**
  - **New molecular entity**
  - **Combination product**
  - **Indication**
  - **Rx/OTC switch**
  - **Naturally derived or recombinant active ingredient**
  - **New Device in a combination product**

Patent & Exclusivity

- **A 505(b)(2) application may be granted . . .**
  - **3 years of new clinical investigation exclusivity**
  - **5 years for a new chemical entity exclusivity**
  - **7 years of orphan drug exclusivity**
  - **6 months pediatric exclusivity (add-on)**
  - **5 years Generating Antibiotic Incentives Now (add-on)**
- **Patent certification to Orange Book listed drug patents.**
  - **30-month stay, but no 180-day exclusivity.**
- **Orange Book patent listing available.**

Orphan Drug Exclusivity

- **Seven Years of Marketing Exclusivity**
  - **The FDC Act provides a seven-year period of exclusive marketing to the first sponsor who obtains marketing approval for a designated orphan drug.**
  - **The scope of orphan drug exclusivity is broad; it prevents FDA approval of ANDAs, "full" 505(b)(1) NDAs, and 505(b)(2) applications.**
  - **Orphan drug exclusivity begins on the date that a marketing application is first approved for the designated orphan drug.**

Orphan Drug Exclusivity

- **Once FDA approves a marketing application for a designated drug, the Agency may not approve another firm's version of the "same drug" for the same disease or condition for seven years, *unless* . . . .**
  - **The subsequent drug is "different" from the approved orphan drug (chemically or "clinically superior"), or**
  - **Because the sponsor of the first approved product either cannot assure the availability of sufficient quantities of the drug or consents to the approval of other applications.**

III

Legislative Attempts to Address Repurposing

MODDERN Cures Act (2011/2013)

- **Modernizing Our Drug & Diagnostics Evaluation and Regulatory Network Cures Act**
  - **“Dormant Therapies” – A medicine that is being investigated or is intended to be investigated for an indication to address one or more unmet medical needs.**
  - **Patent and exclusivity protection enhancements.**
  - **Directed HHS and IOM to “conduct a study on intellectual property laws and their impact on therapy and diagnostic development in order to formulate recommendations on how to facilitate the clinical evaluation and development of therapies currently available on the market for new potential indications.”**

Dormant Therapies Act (2014/2015)

- **Dormant Therapies Act**
  - **A "redo" of the MODDERN Cures Act.**
  - **A drug determined to have insufficient patent protection and that shows promise for treating diseases for which there are limited or no treatments.**
  - **create a new guaranteed 15-year "protection period" for certain drug and biological products designated and approved as dormant therapies. As part of the deal, however, companies must agree to waive patent rights.**

OPEN ACT (2014/2017)

- **Orphan Product Extensions Now Accelerating Cures & Treatments**
  - **According to Rep. Bilirakis, "The OPEN ACT will incentivize drug makers and innovators to 'repurpose' major market drugs for life-threatening rare diseases and pediatric cancers, which opens the door to the development of hundreds of safe, effective, and affordable treatments for rare disease patients."**

OPEN ACT (2014/2017)

- **The OPEN ACT would authorize FDA to designate a drug (including a biological product) "as a drug approved for a new indication to prevent, diagnose, or treat a rare disease or condition," provided, among other things, that "prior to approval of an application or supplemental application for the new indication, the drug was approved or licensed for marketing, . . . but was not so approved or licensed for the new indication."**

OPEN ACT (2014/2017)

- **The designation of a drug approved for a new indication for a rare disease or condition would result in a 6-month extension of various exclusivities provided for under both the FDC Act and the PHS Act.**

- **In addition, certain patents would get a 6-month exclusivity extension.**

IV

The Current Environment Surrounding Orphan Drugs & Drug Repurposing

- **“Critics in Congress and in the pharmaceutical industry and patient groups say that while the [Orphan Drug Act] has generally worked, it has proved to be a bonanza for the makers of some very big drugs, allowing them to charge higher prices than there would have been with competition.”**

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  - **The New York Times, “Orphan Drug Law Spurs Debate” (April 30, 1990).**

Congressional Inquiry

- **March 3, 2017 letter from Sens. Grassley, Hatch, and Cotton to the Government Accountability Office.**
- **“While few will argue against the importance of the development of [orphan] drugs, several recent press reports suggest that some pharmaceutical manufacturers might be taking advantage of the multiple designation allowance in the orphan drug approval process.”**

Fallout for Drug Repurposing?

- **OPEN ACT – A future in doubt?**
- **Will the Orphan Drug Act be revised or retooled? And, in doing so, will repurposing be negatively affected?**
- **FDA's Rare Disease Repurposing Database is no longer operational.**
  - **Table 1. Orphan-designated products with at least one marketing approval for a common disease indication**
  - **Table 2. Orphan-designated products with at least one marketing approval for a rare disease indication**
  - **Table 3. Orphan-designated products with marketing approvals for both common and rare disease indication**

THANK YOU!!

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