CLINICAL INNOVATION: Fair & Effective Incentives for New Uses of Established Drugs

A critical review of the current landscape - Discussion

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Presenters:

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Panellists:

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Private and Public Approaches to New Uses

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Rescuing failures

- Life on composition of matter patent
- Use patent that cannot carved out
- No concern about discovering negative information on marketed drug
- Some de-risking
- Use patent may be vulnerable

Private rescue does happen (though public role can be useful)

Repurposing generics

- No life on composition of matter patent
- Skinny labeling
- Hard to win indirect infringement theories
- Significant de-risking

Generic repurposing rare, usually involves public funds – can private incentives work?

Historical Data on Rescue

- 12/170 new molecules approved between 1996-2004 relied solely on use patents (Rai and Rice (2014))

"Contracting for Rescue"

NIH National Center for Advancing Translational Sciences

Discovering New Therapeutic Uses for Existing Diseases

Goal:
To identify new therapeutic uses of proprietary compounds and biologics across a broad range of human diseases in areas of medical need.

- Match candidate Agents from pharmaceutical partners with innovative ideas for new indications from the biomedical research community.
  - **NIH provides:** template Collaborative Research Agreements (CRAs) and Confidential Disclosure Agreements (CDAs), FOAs, review, funding, and oversight
  - **Pharmaceutical partners provide:** compounds, biologics, in kind support, and pertinent data
  - **Academic researchers provide:** deep understanding of disease biology, new concepts to test, and access to appropriate patient populations

[Adapted from Presentation by Christine Colvis PhD]

NIH National Center for Advancing Translational Sciences NCATS

Repurposing generics

- Historically, public/non-profit funds
- Stevens et al. (2011): in period from 1990-2007, only 10/1541 new drug approvals for new uses
  - 9 of 10 involved public funding

Potential private incentives

- Mechanisms for preventing generic substitution
  - Regulatory
  - Formulation patents
- *Ex ante* commitments by buyers' side?
- How much off-label is okay?

Clinical Trial Data Infrastructure

ClinicalStudy DataRequest.com

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

References

- Arti K. Rai and Grant Rice, Use patents can be useful: The case of rescued drugs. *Sci. Transl. Med.* 6, 248fs30 (2014)).
- Ashley Stevens et al., The Role of Public Sector Research in the Discovery of Drugs and Vaccines. *N Engl J Med* 2011; 364:535-541.

Second Medical Use Patents in the US

Todd Volyn

February, 2018

Standard Regime

- Use Claims: Use of Composition X to treat Disease A
- Method of Treating: Administering an effective amount of X to treat A
- Determining the concentration of Y [some diagnostic marker] and administering an effective amount of X to treat patients with more than A concentration of Y [the diagnostic marker]
- Combination products: Treating a patient with an effective amount of composition X and effective amount of composition Y to treat B

Regulatory Exclusivity

- Not a property right but…
  - Three years of market exclusivity may be available for a new indication.
  - The exclusivity is limited to the new indication
  - Skinny labeling

Enforcement

- Generally, induced infringement requires "Active encouragement of infringement"
- *Takeda v. West-Ward*, 785 F.3d 625 (Fed. Cir. 2015):
  - "The label must encourage, recommend, or promote infringement." 631.
  - "But we need not decide whether evidence as to the invariable response could ever transform a vague label into active encouragement." 632.
- Eli Lilly v. Teva, 845 F.3d 845 (Fed. Cir. 2017):
  - "The product labeling here is not so tenuously related to the use covered…and Eli Lilly does not need to rely on speculation about physician behavior." 1369
  - "…evidence that the product labeling…would inevitably lead some physicians to infringe establishes the requisite intent…" 1369.
- Can a skinny label avoid induced infringement? Sometimes, always, or never?

A Critical Review of The Current Landscape - Discussion

8 February 2018

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Where do we stand on the law in Europe?

a) German Federal Court of Justice *Carvedilol II* requires wording on label that would infringe claim.

b) Two Supreme Court decisions in NL.

- MSD v Teva ribavirin case. Went to a hearing (about 6 a year). Complex claim but Teva made a very imperfect carve-out of their label.
- Having lost at first and second instance MSD won at Supreme Court.
- SMU claims are no different to any other patent claim. They can be infringed directly and indirectly.
- Direct infringement when manufacturer foresees or ought to foresee an infringement. Has to take all effective measures that can reasonably be required of him to avoid this.
- Earlier Novartis v Sun zoledronate case (which did not have a hearing) reached similar conclusions.

15

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Where do we stand on the law in Europe?

c) Warner-Lambert before the UK Supreme Court.

- Court of Appeal decision upholds its earlier objective view of infringement from its decision on summary proceedings. Intention negative when manufacturer taken all reasonable steps in his power to prevent the consequences occurring.
- Indirect infringement requires supply of means for putting the invention into effect. Does not need downstream manufacture. Can include packaging/labelling by pharmacist.

16

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What do I think will happen?

- Assuming Warner-Lambert's patent survives on insufficiency then hope Supreme Court will follow CA on infringement. Position similar to NL.
- The question that arises is what reasonable steps must a generic take? May be different answers in different countries due to differences in prescribing, dispensing and reimbursement laws.

17

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