

Final Paper Proposal

Overview: I plan on writing my final paper in the format of a scholarly article. I will be doing a legal analysis on why compassionate use/expanded access policies are underutilized by pharmaceutical companies, despite FDA approval of such policies (in limited scopes). The paper will outline the legislative and litigation background of compassionate use/expanded access programs, and what steps would need to be taken if a sick individual were to request access to a pre-market drug through a compassionate use/expanded access program. The paper will explore the different types of concerns a pharmaceutical company might have about enacting a compassionate use/expanded access policy, thereby causing them to underuse it, including: public relations, cost to the company, liability to the company, affect on getting the drug to market and FDA compliance (outlined in Title 21, Chapter 9, §360bb). I want to explore how this underuse may impact various stakeholders: drug companies, consumers, third party payers, and regulatory agencies. Finally, I will conclude with some regulatory and industry-level proposals that might be able to encourage pharmaceutical companies to more actively pursue a compassionate use/expanded access program for a pre-market drug they are developing when such a program serves the public interest.

Key Questions:

- Why is the compassionate use/expanded access framework so underutilized? Is it in the public's interest to make the mechanism more active?
- What is the current state of FDA regulations focused on compassionate use/expanded access policies?
- Why should a pharmaceutical company pursue a compassionate use policy?
 - Will it provide for good public relations?
 - Will it allow for additional data about the effectiveness/side effects of the drug?
- Why should a pharmaceutical company *not* pursue a compassionate use policy?
 - What is the potential cost to the company?
 - Does it impose any liability on the company?
 - Will it hinder or delay getting the pending IND application to market?
- What are possible options for the industry, for the FDA, or for other stakeholders to change policies or regulations that would incentivize pharmaceutical companies to more often offer compassionate use/expanded access?

Proposed Outline:

- I. Executive Summary
- II. Introduction:
 - a. Despite many theoretically available mechanisms, expanded access/compassionate use programs are often completely inactive or severely under-utilized.
 - b. Is making this mechanism more active in the public interest/interest of consumers?
 - c. Roadmap: In this paper I will provide the overview of the current regulatory and legal regime, map out the incentives created by that regime,

and propose how the system can be reformed either through regulation or other means to make it work better for all the key stakeholders.

- III. Background**
 - A. Overview of the evidence on expanded access/compassionate use overtime
 - B. Regulatory setting
 - 1. Food, Drug and Cosmetics Act (1938), Kefauver-Harris Amendments (1962)
 - 2. Food and Drug Modernization Act (1997)
 - C. Litigation setting
 - 1. *United States v. Rutherford* (1975)
 - 2. *Abigail Alliance v. von Eschenbach* (D.C. Cir. 2007) (en banc) (cert. den'd)
 - D. Recent/Proposed Changes to Regulations
 - 1. Expanded Access to Investigational Drugs for Treatment Use
 - 2. Charging for Investigational Drugs
 - 3. ACCESS Act
- IV. Current Compassionate Use/Expanded Access Process**
 - A. Physician Consultation
 - B. Filing an Access IND to the FDA
 - 1. Individual patient IND (also referred to as a single patient IND)
 - 2. Individual patient protocol (also referred to as a single patient protocol)
 - 3. Emergency IND
 - 4. Emergency protocol
 - 5. Intermediate-size patient population IND
 - 6. Intermediate-size patient population protocol
 - 7. Treatment IND
 - 8. Treatment protocol
 - C. Pharmaceutical Company Approval
 - 1. IRB
 - 2. Informed consent
 - D. FDA Compliance
 - 1. Post-use written report
 - 2. Reporting requirements for adverse events
- V. Risks and Benefits of a Compassionate Use/Expanded Access Program for a Particular Drug**
 - A. Overview of how the current system impacts different stakeholders
 - B. Past experiences
 - C. Public relations considerations
 - D. Building a Consumer Base Among Physicians and Patients
 - E. Potential for Liability
 - F. Institutional Hurdles
 - 1. IRB approval
 - 2. FDA
 - a. Information needed to comply
 - b. Effect on FDA approval- delays, etc.

- VI. Towards New Incentives
 - a. Weighing of the Risks and Benefits Causing Companies to Underuse Compassionate Use/Expanded Access Programs
 - b. Possibility for Company/Regulatory Proposals to Increase its Utilization by Pharmaceutical Companies
- VII. Conclusion

Preliminary Sources/Key Informants:

- Companies with compassionate use/expanded access programs
 - Pfizer
 - Genentech
 - BioMarin
 - Novartis
 - AstraZeneca
- Companies without compassionate use/expanded access programs
 - Cytokinetics
- Professor Wendy Parmet- “A New Era of Unapproved Drugs” (contact established)
- Justine C. Guccia- “Compassionate Use: Balancing Compassion and Risk in Clinical Trials”
- Patricia J. Zettler- “The Implications of Post-Phase 1 and “Off-Label” Treatment Use of Experimental Drugs: How Expansive Should Expanded Access Be?”
- Meghan K. Talbott- “The Implications of Expanding Access to Unapproved Drugs”
- Dr. Robert Temple, Center for Drug Evaluation and Research- Deputy Director for Clinical Science and Acting Deputy Director of the Office of Drug Evaluation-I
- Abigail Alliance for Better Access to Developmental Drugs (contact established)

Note: I plan on using this paper to satisfy the upper-level writing requirement.