Cancer Patient Access to Unapproved New Drugs: From Laetrile to Project Facilitate

David Brushwood, RPh, JD
Senior Lecturer,
University of Wyoming School of Pharmacy

Faculty Disclosure

• David Brushwood declares no existence of a financial interest in any amount related to the content of this activity.

• Advisory Board members and other individuals, not previously disclosed, who may review, propose recommendations, and/or edit the content of PharmCon CE activities declare no existence of a financial interest in any amount related to the content of this activity.
Learning Objectives

At the conclusion of this activity, participants should be better able to:

1. Evaluate legal arguments from the case of Rutherford v. United States, related to the use of unapproved laetrile products by cancer patients.
2. Identify the legal principles applicable to new drug approval and the availability of unapproved new drugs.
3. Compare the “Right to Try” law with the FDA’s “Project Facilitate.”

United States v. Rutherford (SCOTUS-1979)

• “The question presented in this case is whether the Federal Food, Drug, and Cosmetic Act precludes terminally ill cancer patients from obtaining Laetrile, a drug not recognized as safe and effective within the meaning of the Food, Drug, and Cosmetic Act.”
• “Terminally ill patients and their spouses brought this action to enjoin the government from interfering with interstate shipment and sale of Laetrile.”
• “The FDA Commissioner found that Laetrile in its various forms constituted a ‘new drug’ and concluded that there were no adequate well-controlled scientific studies of Laetrile’s safety or effectiveness.”
The Court’s Interpretation of the FDCA

• “The FDCA makes no special provision for drugs used to treat terminally ill patients.”
• “Nothing in the history of the FDCA suggests that Congress intended protection only for persons suffering from curable diseases. To the contrary, Congress expressed concern that individuals with fatal illnesses, such as cancer, should be shielded from fraudulent cures.”
• “For the terminally ill, as for anyone else, a drug is unsafe if its potential for inflicting death or physical injury is not offset by the possibility of therapeutic benefit.”

The Court’s Rationale and Ruling

• “Since the turn of the century, resourceful entrepreneurs have advertised a wide variety of purportedly simple and painless cures for cancer, including liniments of turpentine, mustard oil, eggs, and ammonia; peat moss; arrangements of colored floodlamps; pastes made from glycerin and limburger cheese; mineral tablets; and “Fountain of Youth” mixtures of spices, oil, and suet.”
• “This historical experience suggests why Congress could reasonably have determined to protect the terminally ill, no less than other patients.”
• “Whether, as a matter of policy, an exemption should be created is a question for legislative judgment, not judicial interference.”
The FDCA Approach to New Drugs

• Is the article a drug?
  • Is it a food?
  • What is the labeler’s (distributor’s) intent?
• Must the drug be approved by the FDA?
• Is the drug a new drug?
  • Is the drug GRAS (Generally Recognized as Safe)?
  • Is the drug GRAE (Generally Recognized as Effective)?

What is a “Drug”?  

• “The term “drug” means
  • (B) articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals; and
  • (C) articles (other than food) intended to affect the structure or any function of the body of man or other animals.”
• “The term “food” means (1) articles used for food or drink for man or other animals, (2) chewing gum, and (3) articles used for components of any such article.”
• From case law: A food is an article used for its “taste, aroma, or nutritive value.”
Must the Drug be Approved?

• “No person shall introduce or deliver for introduction into interstate commerce any new drug, unless an approval of an application is effective with respect to such drug.”

• “The term “substantial evidence” means evidence consisting of adequate and well-controlled investigations, including clinical investigations, by experts qualified by scientific training and experience to evaluate the effectiveness of the drug involved, on the basis of which it could fairly and responsibly be concluded by such experts that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling or proposed labeling thereof.”

What is a “New Drug’?  

• “The term “new drug” means

• (1) Any drug the composition of which is such that such drug is not generally recognized, among experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs, as safe and effective for use under the conditions prescribed, recommended, or suggested in the labeling thereof, except that such a drug not so recognized shall not be deemed to be a “new drug” if at any time prior to June 25, 1938, its labeling contained the same representations concerning the conditions of its use; or

• (2) Any drug the composition of which is such that such drug, as a result of investigations to determine its safety and effectiveness for use under such conditions, has become so recognized, but which has not, otherwise than in such investigations, been used to a material extent or for a material time under such conditions.”
Labeling and Misbranding; Definitions

• “The term “labeling” means all labels and other written, printed, or graphic matter (1) upon any article or any of its containers or wrappers, or (2) accompanying such article.”
• “A drug or device shall be deemed to be misbranded—
  • (a) If its labeling is false or misleading in any particular.
  • (f) Unless its labeling bears
    • (1) adequate directions for use; and
    • (2) such adequate warnings against use in those pathological conditions or by children where its use may be dangerous to health, or against unsafe dosage or methods or duration of administration or application, in such manner and form, as are necessary for the protection of users.”

Options for Access to Unapproved New Drugs

• Marketed Unapproved Drug—FDA Low Priority for Enforcement
• Granting of Grandfather Status
• Granting of GRASE Petition
• NDA Approval
  • 505(b)(2)
  • ANDA
• Expanded Access program for Investigational New Drugs (IND)
  • Compassionate Use
  • Treatment IND (Group C)
  • Parallel Track
**Brief Outline History of Drug Regulation In the US**

- Early Decades—Self Regulation by Word of Mouth.
- Starting in 1700s—Colony/State Regulation of Pharmacists/Pharmacies.
- 1906—Pure Food and Drugs Act.
- 1951—Durham-Humphrey Amendment.
- 1962—Kefauver-Harris Amendment.

---

**Abigail Alliance v. Von Eschenbach (DC Cir 2007)**

- “This case presents the question whether the Constitution provides terminally ill patients a right of access to experimental drugs that have passed limited safety trials but have not been proven safe and effective.”
- “The Alliance requested that the FDA promulgate new regulations that would allow sponsors to market experimental drugs, under some circumstances, after the completion of Phase I trials.”
- “Terminally ill patients, in the Alliance’s view, are typically willing to assume risks.”
Abigail Alliance and Due Process

• “We must determine whether terminally ill patients have a fundamental right to experimental drugs that have passed Phase I clinical testing.”
• “The Due Process Clause provides that no person shall be deprived of life, liberty, or property, without due process of law.”
• “The Due Process Clause specially protects those fundamental rights and liberties which are, objectively, deeply rooted in this Nation’s history and tradition and implicit in the concept of ordered liberty, such that neither liberty nor justice would exist if they were sacrificed.”

Abigail Alliance Arguments

• “The Alliance argues that its right can be found in our history and legal traditions because the government never interfered with the judgment of individual doctors about efficacy of drugs until 1962”
• “The Alliance’s effort to focus on efficacy regulation ignores one simple fact: It is unlawful for the Alliance to procure experimental drugs not only because they have not been proven effective, but because they have not been proven safe.”
• “The Alliance must show not only that there is a tradition of access to drugs that have not yet been proven effective, but also a tradition of access to drugs that have not yet been proven safe.”
Abigail Alliance The Court Examines History

• “In the early history of our Nation, we observe not a tradition of protecting a right of access to drugs, but rather governments responding to the risks of new compounds as they become aware of and able to address those risks.”

• “The Alliance’s argument ignores our Nation’s history of drug safety regulation.”

• “The fact that a drug has emerged from Phase I with a determination that it is safe for limited clinical testing in a controlled and closely-monitored environment after detailed scrutiny of each trial participant does not mean that a drug is safe for use beyond supervised trials.”

Abigail Alliance The Court’s Conclusions

• “We conclude that the Alliance has not provided evidence of a right to procure and use experimental drugs that is deeply rooted in our Nation’s history and traditions.”

• “Although terminally ill patients desperately need curative treatments, their deaths can certainly be hastened by the use of potentially toxic drugs with no proven therapeutic benefit. Thus, we must conclude that, prior to distribution of a drug outside of controlled studies, the Government has a rational basis for ensuring that there is a scientifically and medically acceptable level of knowledge about the risks and benefits of such a drug.”
Right to Try Laws

- Passed in 41 states. But still problems with federal violations.
- Federal act passed in 2018; no firm opposition.
  - Patient conditions
    - Must have life-threatening illness.
    - Must have exhausted all approved treatment options.
    - Unable to participate in clinical trial.
    - Written informed consent.
  - Drug conditions
    - Phase I trial has been completed.
    - Not approved by FDA for any use.
    - Subject of an IND Exemption.
- Very few current users. Sponsor reporting to FDA has not been released.

Issues with Right to Try

- It is a right to request; not a right to receive.
- Risk/benefit may be difficult to explain.
- Supported by interests that oppose big government and FDA paternalism.
- Criticized by interests that call it a cruel hoax.
- Possible interference with the results of a clinical trial.
- Sponsor reluctance to participate.
- Patients have financial exposure due to insurance refusal of coverage.
- No liability exposure for manufacturer, institution, physician, or pharmacist.
FDA’s Project Facilitate (2019) Nothing New Just Better Supported for Compassionate Use

- Investigational therapies for patients with cancer.
- Broadened eligibility criteria.
- Single point of contact at FDA from submission through follow-up.
- Assistance in selection of drug(s) for patient.
- Assistance with paperwork.
- Referral to IRB, if necessary.
- Referral to a contact at the sponsor drug company.
- Data maintained on outcomes.
- Perhaps a means to improve reputation and retain power.
  - Daniel Carpenter, Reputation and Power: Organizational Image and Pharmaceutical Regulation at the FDA.

Key Takeaways

- FDA authority over new drug approval has been upheld as being in the public interest, despite challenges over the years.
- The FDA has taken the position that all drugs are new drugs, even though the FDCA clearly suggests otherwise.
- Challenging the FDA is a poor choice.
- Among federal agencies, the FDA has a very high profile and is very highly regarded for their work.
- The FDA is aware that they serve the public, and they find ways to enhance that public service to preserve/expand agency authority.
Thank You