HOUSE OF REPRESENTATIVES STAFF ANALYSIS

BILL #: CS/CS/HB 269 Experimental Treatments for Terminal Conditions
SPONSOR(S): Insurance & Banking Subcommittee; Health Innovation Subcommittee; Pilon
TIED BILLS: **IDEN./SIM. BILLS:**

REFERENCE	ACTION	ANALYST	STAFF DIRECTOR or BUDGET/POLICY CHIEF
1) Health Innovation Subcommittee	12 Y, 0 N, As CS	Tuszynski	Poche
2) Insurance & Banking Subcommittee	12 Y, 0 N, As CS	Haston	Cooper
3) Health & Human Services Committee		Tuszynski	Calamas

SUMMARY ANALYSIS

The Food and Drug Administration (FDA) has regulatory authority over what drugs are marketed and sold within the United States. Investigational or experimental drugs are new drugs that are not approved by the FDA and are in the process of being tested for safety and effectiveness. An investigational drug must go through a lengthy and expensive approval process requiring phased clinical trials. Approval of an investigational drug by the FDA can take as long as 11 years.

The FDA has a procedure to gain access to investigational drugs that have not yet been approved by the FDA, known as expanded access. Under the FDA's expanded access scheme, physicians can request an investigational drug for a single patient using an emergency use application. However, this process is considered burdensome, time-consuming, and confusing. In February of 2015, the FDA announced a draft application that removes many of the burdensome and time-consuming requirements of the old procedure.

The bill creates the "Right to Try Act," which establishes a framework in which a manufacturer may provide a post-phase 1 investigational drug, biological product, or device to an eligible patient with a terminal condition, bypassing the FDA's emergency use expanded access program. The bill defines an eligible patient and a terminal condition. The bill also requires certain information and attestations in a written informed consent document, which must be signed by the patient or the patient's parent, guardian, or health care surrogate and provided to the manufacturer, in order to receive a post-phase 1 investigational drug, biological product, or device.

The bill also protects the licenses of physicians who recommend investigational drugs, biological products, or devices from disciplinary action as a result of making the recommendation. The bill permits insurers to pay for investigational drugs, but does not require such payment. Lastly, the bill provides liability protection for manufacturers, persons, and entities involved in the use of the investigational drug, biological product, or device pursuant to the provisions of the bill.

The bill does not appear to have a fiscal impact on state or local governments.

The bill provides an effective date of July 1, 2015.

FULL ANALYSIS

I. SUBSTANTIVE ANALYSIS

A. EFFECT OF PROPOSED CHANGES:

Background

Regulation of Drugs

The U.S. Food and Drug Administration (FDA) has wide regulatory authority over what drugs are marketed and sold within the United States. The Pure Food and Drug Act, passed in 1906, was the genesis of the federal regulation of drugs.[1] The responsibility of enforcing this act was given to the Bureau of Chemistry, later renamed the Food and Drug Administration in 1927.[2] The Federal Food, Drug and Cosmetic Act (FFDCA) was passed in 1938 and gave authority to the FDA to oversee the safety of food, drugs, and cosmetics.[3] In 1962, in the wake of deaths and birth defects from the tranquilizer thalidomide marketed in Europe, Congress passed the Kefauver-Harris Drug Amendments to the FFDCA, increasing safety provisions and requiring that drugs be proven effective as well as safe.[4]

Approval Process

Investigational or experimental drugs are new drugs that have yet to be approved by the FDA, or are approved drugs that have not been approved by the FDA for a new use, and are in the process of being tested for safety and effectiveness. To bring a drug to market, an investigational drug's sponsor, typically a pharmaceutical company or research entity, must go through a lengthy approval process. It can take up to 11 years[5] from the beginning of the FDA's involvement to bring an investigational drug to market; the average time to market is 8 years.[6] The same process applies to new biological products and devices.

The first step in the process, basic laboratory research, can take years and occurs prior to FDA involvement. Basic laboratory research, often funded by the federal government in federal labs or research universities, investigates chemical components and compounds that may have therapeutic efficacy. If research identifies a component that may be promising as an experimental drug, private industry or private research groups continue development of the drug and begin animal testing.

When the drug is ready for human trials, an investigational new drug application (IND) is submitted to the FDA,[7] which includes details on the appropriateness of human testing.[8] Once the IND is approved, the sponsor may begin testing to gather evidence as to the safety and effectiveness of the drug.[9] Generally, the investigation into experimental drugs, biological products, and devices is divided into three clinical development trials, detailed in the chart below. [10,11]

CLINICAL TRIAL PHASES			
Phase	**Participants**	**Purpose**	**Average Time**

[1] Pure Food and Drug Act of 1906, ch. 3915, 34 Stat. 769 (1906) (Repealed by the Federal Food, Drug, and Cosmetic Act of 1938 [21 U.S.C. Sec 329(a)]), http://www.fda.gov/regulatoryinformation/legislation/ucm148690.htm; The Federal Food and Drugs Act of 1906 is called the "Wiley Act."
[2] Federal Food and Drugs Act of 1906, P.L. 59-384, s. 1.
[3] Food, Drug, and Cosmetic Act of 1938 (21 U.S.C. ch. 9 § 301 et seq.).
[4] Kefaver-Harris Drug Amendments to the FFDCA, P.L. 87-781, (1962).
[5] Christopher P. Adams & Van. V. Brantner, *New Drug Development: Estimating Entry From Human Clinical Trials* 9 (Jul. 7, 2003), available at http://www.ftc.gov/reports/new-drug-development-estimating-entry-human-clinical-trials
[6] *Id.*
[7] 21 U.S.C. § 355(i)(1); *see also* 21 C.F.R. § 312.
[8] 21 C.F.R. § 312.23.
[9] 21 U.S.C. § 355(d)(5).
[10] Adams & Brantner, *supra* note 5.
[11] Phase 4 trials are post-approval clinical trials to test the long term effects of investigational drugs, biological products, and devices.

Phase 1	20-80	This is the initial introduction of a new drug into humans. These studies are typically closely monitored and designed to determine the metabolism and pharmacologic action of the treatment, side effects associated with increased dosage, and if possible, to gain early evidence of effectiveness.	1.7 years
Phase 2	Several Hundred	These are the controlled clinical studies conducted to evaluate the effectiveness of the treatment for a particular indication or indications, and to determine common short-term side effects and risks.	2.4 years
Phase 3	Several Thousand	These are performed after preliminary evidence suggesting effectiveness of the treatment has been obtained from Phase 2. This phase is intended to gather the additional information about effectiveness and safety that is needed to evaluate the overall benefit-risk relationship of the treatment and to provide an adequate basis for physician labeling.	3.7 years

When a sponsor believes there is "substantial evidence" [12] of safety and effectiveness, the sponsor submits a new drug application (NDA) to the FDA for approval.[13] The NDA must contain full reports of the phased clinical trials detailing the safety and effectiveness of the drug.[14] During the NDA review, the FDA evaluates the clinical trial data, analyzes samples, inspects the facilities where the finished product will be made, and checks the proposed labeling for accuracy.[15] Once the FDA determines that there is substantial evidence of safety and effectiveness, the NDA is approved and the sponsor is allowed to bring the drug to market.

Expanded Access

The FDA established regulations allowing expanded access to, or "compassionate use" of, experimental drugs, biological products, and devices in 1987, and individual patient "emergency use" expanded access in 1997. These regulations provide access to:

1. Individuals on a case-by-case basis, known as "individual patient access";[16]
2. Intermediate sized groups of patients with similar treatment needs who otherwise do not qualify to participate in a clinical trial;[17] and
3. Large groups of patients who do not have other treatment options available.[18]

The access routes for intermediate and large groups are essentially expanded clinical trials. If enough patients are outside of the geographical area of a clinical trial, or were unable to meet the criteria of the specific trial, the FDA can approve concurrent trials.

Individual patient access includes "emergency use." Emergency use requests can be made by phone or other means of electronic communication. A patient may start using the investigational drug, biological product, or device immediately upon FDA authorization of the request.[19] The written emergency use request must be received by the FDA within 15 business days of the telephone

[12] 21 U.S.C. § 355(d)(5).
[13] 21 U.S.C. § 355(a).
[14] 21 U.S.C. § 355(b)(1)(a).
[15] Adams & Brantner, *supra* note 5.
[16] U.S. Food and Drug Administration, *Expanded Access Categories for Drugs*, http://www.fda.gov/NewsEvents/PublicHealthFocus/ExpandedAccessCompassionateUse/ucm431774.htm. (last visited March 4, 2015).
[17] 21 U.S.C. § 312.315.
[18] 21 U.S.C. § 312.320.
[19] Peter D. Jacobson, J.D., M.P.H. & Wendy E. Parmet, J.D., *A New Era of Unapproved Drugs: The Case of Abigail Alliance v. Von Eschenbach*, 297 JAMA 205 (2007).

authorization.[20] The written emergency use request requires physicians to submit 26 distinct fields of information and seven attachments.[21] This process can take up to 100 hours to gather and submit the required information.[22]

The FDA reviews emergency use requests and makes the determination of whether to approve the request based on the following factors:

- The patient has a serious or immediately life-threatening disease or condition, and there is no comparable or satisfactory alternative therapy.[23]
- The potential benefit justifies the potential risks, and that those risks are not unreasonable.[24]
- Provision of the treatment will not interfere with the initiation, conduct, or completion of clinical investigations that could support marketing approval of the expanded access use or otherwise compromise the development of the expanded access use.[25]
- A determination by the patient's physician that the probable risk to the person is not greater than the risk of the disease or condition.[26]
- A determination by the FDA that the patient cannot obtain the treatment under another IND or protocol.[27]

Between October 1, 2013 and September 30, 2014, the FDA approved 1,066 of the 1,069 emergency use requests it received. [28]

"Right to Try" Laws and FDA Response

Five states have passed laws in the past 12 months providing terminally ill patients access to experimental drugs outside of the FDA's normal regulatory scheme: Colorado,[29] Louisiana,[30] Missouri,[31] Arizona,[32] and Michigan.[33]

These state laws allow, but do not require, manufacturers of experimental treatments to make these treatments available to eligible patients with terminal illnesses. The laws also require written informed consent from patients stating that they are aware of the dangers associated with the experimental treatment. The laws also include provisions that protect the licenses of physicians who recommend or prescribe experimental treatments; exempt insurers from having to pay for experimental treatment; and provide liability protection to manufacturers and distributors of experimental treatments.

On February 4, 2015, the FDA issued new draft guidance for Individual Patient Expanded Access, or "compassionate use," applications. The draft guidance addresses a new "compassionate use" form, a streamlined alternative for submitting an IND application for use in cases requesting individual patient expanded access to an investigational drug, biological product, or device. The old form, FDA 1571, was designed for large experimental drug sponsors and manufacturers to apply for expanded access, not physicians.[34] The new form, FDA 3926, is designed for physicians seeking authorization on behalf

[20] *Id.*
[21] Peter Lurie, M.D., M.P.H., *A Big step to help the patients most in need*, FDA Voice, February 4, 2015, *available at* http://blogs.fda.gov/fdavoice/index.php/tag/individual-patient-expanded-access-applications-form-fda-3926/. (last visited February 17, 2015).
[22] *Id.*
[23] 21 U.S.C. § 312.305(a)(1)
[24] 21 U.S.C. § 312.305(a)(2)
[25] 21 U.S.C. § 312.305(a)(3)
[26] 21 U.S.C. § 312.310(a)(1)
[27] 21 U.S.C. § 312.310(a)(2)
[28] Expanded Access Submission Receipts Report: Oct 1, 2013 - Sep 30, 2014, http://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/DrugandBiologicApprovalReports/INDActivityReports/UCM430188.pdf (last visited February 10, 2015).
[29] Colo. R.S.A. §§ 25-45-101 to -108
[30] La. R.S. § 1300.381-386
[31] V.A. Mo. S. § 191.480
[32] Ariz. R.S.A. §36-1311 to -1314
[33] Mich. C.L.A. §§ 16221, 26451
[34] Supra. at FN 21.

of an individual patient. The new form requires only eight distinct fields of information and one attachment.[35] The FDA estimates that it will take approximately 45 minutes to complete the new form.[36]

Abigail Alliance Case

In 1999, Abigail Burroughs, a 19-year-old college student, was diagnosed with head and neck cancer. Despite undergoing chemotherapy and radiation therapy, her tumor showed increased expression of the cell surface membrane receptor EGFR.[37] She did not meet the inclusion criteria for either of the two clinical trials targeting EGFR at the time. Shortly after her death in 2001, her father formed the Abigail Alliance for Better Access to Developmental Drugs[38] and, in 2003, sued the FDA. The Abigail Alliance argued that terminal cancer patients have a constitutional right to experimental drugs, positing self-defense theories as well as 5th amendment substantive due process claims, and that the FDA should grant access to experimental drugs for use by terminally ill patients.

In 2007, after years of protracted litigation, the U.S. Court of Appeals for the District of Columbia, sitting *en banc*, upheld the previous trial court decision finding no constitutional right to unapproved drugs by terminally ill patients.[39] The Supreme Court of the United States declined to review the case.

Dispensing

Chapter 465, F.S., limits the dispensing of medicinal drugs to licensed pharmacists and licensed physicians.[40] The Board of Pharmacy[41] regulates the practice of pharmacy and the licensure of pharmacists. Currently, manufacturers of medicinal drugs are not authorized by Florida law to dispense directly to patients.

Effect of Proposed Changes

The bill creates the "Right to Try Act" (Act), establishing a framework in which a manufacturer may provide an investigational drug, biological product, or device to an eligible patient without utilizing the FDA's emergency use expanded access program. The bill allows manufacturers to contract with and dispense investigational drugs directly to patients, without licensure or regulation under chapter 465, F.S., by the Board of Pharmacy.

To be eligible to access such drugs, a patient must have a terminal condition that will result in death within one year of diagnosis if the condition runs its normal course. The patient's treating physician must attest to the terminal condition, it must be confirmed by a second evaluation by a board-certified physician in an appropriate specialty, and the patient must have considered all other approved treatments. Under the bill, a terminal condition is a progressive disease or medical condition that causes significant functional impairment, is not considered reversible with available treatments, and will result in death within a year without the administration of life-sustaining procedures.

The bill requires the patient, a parent of a minor patient, a court-appointed guardian for the patient, or a health care surrogate designated by the patient to provide written informed consent prior to accessing an investigational drug, biological product, or device under the Act. The written informed consent must include:

- An explanation of the currently approved products and treatments for the patient's terminal condition;
- An attestation that the patient agrees with his or her physician in believing that all currently approved products and treatments are unlikely to prolong the patient's life;

[35] Id.
[36] Id.
[37] Jacobson & Parnet, *supra* note 19.
[38] Id.
[39] *Abigail Alliance for Better Access to Developmental Drugs v. Eschenbach,* 495 F.3d 695 (D.C. Cir. 2007).
[40] S. 465.0276, F.S.
[41] S. 465.004, F.S.

- The specific name of the investigational drug, biological product, or device;
- A realistic description of the most likely outcome, detailing the possibility of unanticipated or worse symptoms.
- A statement that death could be hastened by use of the investigational drug, biologic product, or device.
- A statement that the patient's health plan or third-party administrator and physician are not obligated to pay for treatment consequent to the use of the investigational drug, biological product, or device, unless required to do so by law;
- A statement that the patient's eligibility for hospice care may be withdrawn if the patient begins treatment, and reinstated if curative treatment ends and the patient meets hospice eligibility requirements; and
- A statement that the patient understands he or she is liable for all expenses consequent to the use of the investigational drug, biological product, or device and that liability extends to the patient's estate, unless negotiated otherwise.

The bill provides that there is no obligation on the part of any manufacturer to provide a requested investigational drug, biologic product, or device under the Act, but that a manufacturer may do so with or without compensation. The eligible patient may be required to pay the costs of, or associated with, the manufacture of the investigational drug, biological product, or device. The bill allows a health plan, third-party administrator, or governmental agency to cover the cost of an investigational drug, biological product, or device. The bill does not mandate insurance coverage for an investigational drug, biological product, or device, nor does it affect any mandatory coverage for participation in clinical trials. The bill exempts a patient's heirs from any outstanding debt associated with the patient's use of the investigational drug, biological product, or device.

The bill states that health care facilities are not required to provide new or additional services associated with a patient's use of an investigational drug, biologic product, or device under the Act, unless it is approved by the health care facility.

The bill prohibits the Board of Medicine or Board of Osteopathic Medicine from revoking, suspending, or denying renewal of a physician's license based solely on the physician's recommendation to an eligible patient regarding access to or treatment with an investigational drug, biological product, or device. The bill also prohibits action against a physician's Medicare certification for the same reason.

The bill provides liability protection for a manufacturer, person, or entity involved in the use of an investigational drug, biological product, or device in good faith compliance with the provisions of the bill and exercising reasonable care.

The bill provides an effective date of July 1, 2015

B. SECTION DIRECTORY:

Section 1: Creates s. 499.0295, F.S., relating to experimental treatments for terminal conditions.
Section 2: Provides for an effective date.

II. FISCAL ANALYSIS & ECONOMIC IMPACT STATEMENT

A. FISCAL IMPACT ON STATE GOVERNMENT:

1. Revenues:

   None.

2. Expenditures:

   None.

B. FISCAL IMPACT ON LOCAL GOVERNMENTS:

1. Revenues:

   None.

2. Expenditures:

   None.

C. DIRECT ECONOMIC IMPACT ON PRIVATE SECTOR:

The bill permits manufacturers of investigational drugs, biologic products, and devices to provide such drugs, products, and devices to patients with a terminal condition without the approval of the FDA. A manufacturer can track the safety and effectiveness of the drug, biological product, or device on a human subject much earlier than through the traditional FDA approval process, which may quicken the development process and the shorten the amount of time it takes for a drug, biological product, or device to get to market.

The bill also permits a manufacturer to charge an eligible patient for use of the investigational drug, biological product, or device.

The bill provides liability protection to manufacturers, persons, and entities involved with the use of an investigational drug, biological product, or device in good faith compliance with the provisions of the bill and exercising reasonable care.

D. FISCAL COMMENTS:

None.

III. COMMENTS

A. CONSTITUTIONAL ISSUES:

1. Applicability of Municipality/County Mandates Provision:

   Not applicable. This bill does not appear to affect county or municipal governments.

2. Other:

   Access to and the use of investigational drugs is controlled by the FDA through the “expanded access” provisions of 21 U.S.C. § 360bbb and 21 C.F.R. § 312. The language of this bill creates a framework that bypasses this federal regulatory scheme.

B. RULE-MAKING AUTHORITY:

Not applicable.

C. DRAFTING ISSUES OR OTHER COMMENTS:

The bill language protects a physician’s license and Medicare certification from action for recommending an investigational drug, biological product, or device, but not for administering the same investigational drug, biological product, or device.

IV. AMENDMENTS/ COMMITTEE SUBSTITUTE CHANGES

On March 10, 2015, the Health Innovation Subcommittee adopted a strike-all amendment and reported the bill favorable as a committee substitute. The amendment made the following changes:

- Changed “terminal illness” to “terminal condition.”
- Required confirmation of a patient's terminal condition by a second, board-certified physician in an appropriate specialty for that condition.

- Clarified that a terminal condition is a condition that will result in death within one year of diagnosis if the condition runs its normal course.
- Replaced “health care provider” with “physician.”
- Removed the explicit exemption for a governmental agency from paying the costs associated with providing an investigational drug, biological product or device.
- Removed the section that prohibited an official, employee, or agent of the state from blocking or attempting to block an eligible patient’s access to an investigational drug, biological product, or device.
- Strengthened the liability protection for a manufacturer, person, and entity involved in the use of the investigational drug, biological product, or device, except for willful torts.

On March 25, 2015, the Insurance & Banking Subcommittee adopted one amendment and reported the bill favorable as a committee substitute. The amendment returned the language from the original filed version of the bill relating to liability protection for a manufacturer, person, and entity involved in the use of the investigational drug, biological product, or device. The amendment requires a manufacturer, person, and entity involved in the use of the investigational drug, biological product, or device to comply in good faith with the terms of the section and to exercise reasonable care.

The analysis is drafted to the committee substitute as passed by the Insurance & Banking Subcommittee.