HSC 335 -- Pharmaceutical Policy (Fall 2020)

Week 2 Questions

<u>Deadline:</u> September 3, 2020 at 2:45pm (submit via Slack DM)

Name:

Expanded Access

While the FDA generally limits patients' access to drugs for which the benefits have not yet been established, the expanded access program allows patients to request access to drugs before they have been approved by the FDA. Though the vast majority of expanded access requests are granted by the FDA, this does not mean that patients will actually be able to access the requested drugs.

- Why does the FDA allow expanded access to unproven drugs?
- What are the requirements of the expanded access program?
- What are the considerations that the FDA must balance related to an expanded access request?
- How long does it take the FDA to make a decision regarding an expanded access request?
- Why doesn't FDA's approval of an expanded access request guarantee a patient access to the drug?

<u>Question 1</u>

What does the FDA's expanded access program do?

☐ Prevents physicians from obtaining experimental drugs.

☐ Distributes drugs specifically to high-risk rural communities.

☐ Distributes drugs to pediatric patients.

☐ Allows physicians to obtain experimental drugs for seriously ill patients outside of clinical trials.

☐ Allows physicians to obtain experimental drugs for seriously ill patients by enrolling them in clinical trials.

Question 2

The outbreak of what disease led the FDA to formalize its expanded access program in 1987?

- [ ] HIV/AIDS
- [ ] Ebola
- [ ] Syphilis
- [ ] Meningitis

Question 3

Which of the following does the FDA require as part of expanded access? Select all that apply.

- [ ] An eligible patient has a serious or life-threatening condition.
- [ ] There is no comparable or satisfactory alternative therapy.
- [ ] The patient's physician obtains the patient's informed consent.
- [ ] The expanded access drug must be administered in a hospital setting with close monitoring.

Question 4

In 2016, the FDA approved what percent of single-patient expanded access requests?

- [ ] Less than 5%
- [ ] About 40%
- [ ] More than 99%

Question 5

Which of the following is a challenge for patients seeking to enroll in expanded access programs? Select all that apply.

- [ ] A manufacturer may not have sufficient drug manufacturing capacity to accommodate its clinical trials and expanded access requests.
- [ ] While the FDA approves the majority of expanded access requests, it takes them 4 months on average to review the requests.
- [ ] Manufacturers may be reluctant to offer expanded access out of fear that adverse events experienced by patients could delay drug approval.
- [ ] There can be substantial risk associated with taking an experimental drug.
- [ ] Patients often will have to pay a lot of money to access the experimental drugs.
- [ ] Some physicians may be unaware of the expanded access program.

Right to Try Laws and Synthesis

What is a "right to try" law? What is the relationship between right to try laws and FDA's expanded access program? In this video, we'll take a look at laws passed at both the state and federal levels that purport to give patients a right to try experimental medications. As you'll see, many have wondered what unanticipated consequences they will have.

Question 6

Which of the following are features of state "right to try laws"? Indicate all that apply.

- [ ] Prohibit state medical licensing boards from revoking a physician's license solely because the physician recommended that a patient try an experimental drug
- [ ] Require physicians to prescribe drugs if patients meet eligibility criteria
- [ ] Prohibit employees of the state from blocking a patient's access to an investigational drug
- [ ] Require drug companies to provide experimental medicines to patients who meet eligibility criteria
- [ ] Require insurers to pay for experimental therapies for patients who meet eligibility criteria

Question 7

Which of these is true about state right-to-try legislation, the 2018 federal right-to-try law, and the FDA's expanded access program?

- [ ] They ensure that patients will receive treatments that will improve their conditions.
- [ ] They allow drug companies to begin to earn profits earlier.
- [ ] They require a federal judge to approve each expanded access request.
- [ ] All of the above
- [ ] None of the above

PDUFA and Pediatric Research

Following passage of the Kefauver-Harris Drug Amendments Act, the FDA was required to carefully evaluate safety and efficacy data related to new drug applications. The time needed to complete this analysis necessarily lengthened the process of drug approval. Additional funding was needed to support the FDA's work, but government officials did not supply sufficient funds via the federal budget. Ultimately, Congress passed the Prescription Drug User Fee Act in 1992. In this video, we will discuss the main provisions and effects of this legislation.

- What challenges was PDUFA intended to address?
- What has been the effect of user fee funding on drug and medical device review times?
- What concerns have arisen about user fee funding?

Question 8

What were two motivations for Congress to pass the 1992 Prescription Drug User Fee Act?

☐ Concern that prescription drug user fees were excessive

☐ Lack of safety and efficacy standards for approving new drugs

☐ Insufficient staffing for FDA review of new drug applications

☐ Significant delays in the FDA new drug approval process

Question 9

What is "regulatory capture"?

☐ When government regulators absorb market share from individual companies that they regulate

☐ When government regulators hold manufacturers captive with strict standards

☐ When a government agency is perceived to align its policies with the goals of the regulated industry, rather than the public

☐ When government regulators capture the hearts and minds of those they regulate

Interview with Dr. Margaret Hamburg

We are pleased to be joined by former FDA commissioner Dr. Margaret Hamburg to discuss her experience leading the agency during the Obama administration. In the videos below, she shares her insights on the FDA's role in the US and the world.

Our conversation with Dr. Hamburg addressed many other FDA and drug regulation topics that we cover in this course, so you will find additional excerpts of her comments on such issues as drug advertising and post-market surveillance in future modules.

Question 10

Identify three things you learned about the FDA from Commissioner Hamburg:

1.

2.

3.

Think Like the Commissioner

In the capstone activity for this module, you will put yourself into the role of FDA commissioner, and consider how you would respond to some real-world scenarios. You will compare your evaluation of each situation to those of your peers, as well as what Commissioner Hamburg would do.

A. Watch the "Ask the Commissioner: Funding the FDA" video and then hit pause to answer the next two questions

Question 11

Do you think that moving to a model of 100% user fee funding of the FDA is a good idea?

☐ Yes

☐ No

Explain your answer:

Question 12

Do you think that moving to a model of 100% federal funding of the FDA is a good idea?

☐ Yes

☐ No

Explain your answer:

Please also cut and paste your answer to these questions into the appropriate section of the #discussion channel on Slack and comment on at least two other student responses.

☐ Click the checkbox to confirm you've posted and commented on Slack.

Now watch "Commissioner's Response: Funding the FDA"

B. Watch the "Ask the Commissioner: Right-to-Try" video and then hit pause to answer the next question

Question 13

Put yourself in the shoes of a policymaker trying to design a drug regulatory program that balances some patients' understandable desire to try unproven drugs that may help their medical condition with the increased risks that the drugs may cause harm and the potential for such a program to cause delays in clinical trials and the generation of knowledge that benefits all patients. What do you think the main features of such a program should be? Briefly describe what features you would include in your proposed program below.

Please also cut and paste your answer to this question into the appropriate section of the #discussion channel on Slack and comment on at least two other student responses.

☐ Click the checkbox to confirm you've posted and commented on Slack.

Now watch "Commissioner's Response: Right-to-Try"

C. Watch the "Ask the Commissioner: Safety and Efficacy" video and then hit pause to answer the next question

Question 14

What do you think about returning to the pre-1962 drug approval standard, requiring some demonstration of safety before a new drug is released into the market, and leaving determination of its efficacy to after it is in widespread use?

☐ This seems like a good idea.

☐ I am unsure whether or not this is a good idea.

☐ This seems like a bad idea.

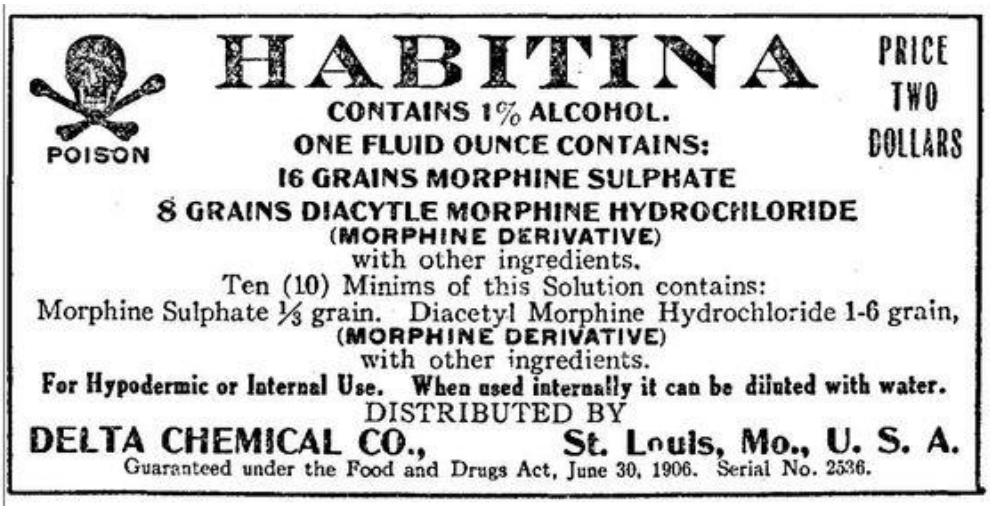
☐ I have a different response.

Explain why you chose this answer:

Please also cut and paste your answer to this question into the appropriate section of the #discussion channel on Slack and comment on at least two other student responses.

☐ Click the checkbox to confirm you've posted and commented on Slack.

Case Study 1: Habitina



In the late 1800s and early 1900s, a wide range of elixirs, tonics, and other pharmaceutical preparations of varying quality and usefulness were sold in the United States. One of these was Habitina, a treatment for those addicted to morphine. As the product's name suggested, the drug was intended to help addicted individuals break the morphine habit.

The government brought suit against Ryland C. Bruce and R.C. Prewitt for selling Habitina, arguing that its sale represented "a scheme and artifice to defraud" the public by false and fraudulent representations. Notably, the government did not bring suit under the Pure Food and Drug Act, but under a postal fraud law. Evidence was introduced, including the label depicted above, showing that Habitina was composed almost entirely of morphine, and that it was unlikely that Habitina could successfully cure a patient of morphine addiction. Bruce and Prewitt were tried, convicted, and sentenced. Bruce v. United States, 202 F. 98 (8th Cir. 1912).

Question 15

It is now the 1940s and the Delta Chemical Company—led by Bruce and Prewitt's children—decide to change the constitution of Habitina and reformulate it using a non-opiate chemical that they synthesize in their laboratories. Which of the trials below would be most likely to satisfy the legal standard for FDA approval under the 1938 Food Drug and Cosmetic Act?

- ☐ A comparison of reformulated Habitina with original Habitina to demonstrate which is more likely to work in treating morphine addiction.
- ☐ A chemical purity study showing that there is 20 mg of reformulated Habitina in each fluid ounce, as the new drug label suggests.
- ☐ A month-long study of regular dosing of Habitina in 10 healthy volunteers, showing that only minor adverse events occurred.
- ☐ A survey of US patients identifying a substantial and widespread unmet medical need for reformulated Habitina.

Question 16

It is 1965. After the passage of the Kefauver-Harris Amendments, the FDA retroactively applied the new standard to all drugs marketed under New Drug Applications that were approved between 1938 and 1962, and Habitina's reformulated active ingredient comes up for review. Which of these trials would be most likely to be accepted by the FDA as suitable to allow the reformulated version of Habitina to remain on the market?

- [ ] A month-long study of 800 subjects, half receiving regular doses of Habitina and half receiving placebo, showing substantial evidence of efficacy.
- [ ] A comparison of reformulated Habitina with original Habitina to demonstrate which is more likely to work in treating morphine addiction.
- [ ] A chemical purity study showing that there is 20 mg of reformulated Habitina in each fluid ounce, as the new drug label suggests.
- [ ] A survey of US patients identifying a substantial and widespread unmet medical need for reformulated Habitina.

Question 17

What standard would the FDA apply to the re-review of Habitina?

- [ ] Whether the benefits appear to outweigh the risks.
- [ ] Whether there is any evidence of effectiveness.
- [ ] Whether Habitina appears to have clear and convincing evidence of effectiveness.
- [ ] Whether Habitina appears to have clinical value.

Case Study 2: Brincidofovir

In 2014, news reports described a 7-year old boy, Joshua Hardy, who was afflicted with a life-threatening adenovirus infection following treatment for kidney cancer that left his immune system weakened. One report noted the tireless efforts of advocates to help Joshua obtain a drug that could save his life. Unfortunately, the drug in question, brincidofovir, had not yet been approved by the FDA.

Brincidofovir is a prodrug of cidofovir (Vistide), which was approved in 1996 for the treatment of cytomegalovirus retinitis. Cidofovir can be used to treat five different types of virus, including adenovirus and cytomegalovirus, which are common in those with compromised immune systems (such as those with cancer, AIDS, or who have undergone a stem cell or organ transplant). A prodrug is a substance that is converted into the active form of the drug once it enters the body, although the two forms do not necessarily have identical effects. In the case of brincidofovir, the prodrug is better able to enter a patient's cells, has a stronger antiviral effect, and is less likely to cause kidney damage than cidofovir. Joshua had already been treated with cidofovir, but it was impacting his kidney function and so his parents requested access to brincidofovir.

Although the FDA had previously approved requests for expanded access to brindcidofovir, by 2012 brincidofovir's manufacturer, Chimerix, had determined that the number of expanded access requests that it was receiving and granting was interfering with the drug development and approval process and stopped offering such an option. After a social media "firestorm" raised both awareness and public pressure, Chimerix provided Josh Hardy with access to the drug. Josh's parents reported that he responded well to the drug and he was discharged from the hospital 1 month after receiving brincidofovir.

In 2015, Chimerix's stock fell 80% after brincidofovir failed to demonstrate a statistically significant reduction in cytomegalovirus infection after stem cell transplantation, which was the indication for which Chimerix had been seeking FDA approval. Similar trials in patients after kidney transplants were also unsuccessful. As of early 2019, the drug has yet to obtain FDA approval for any indication, although it has received an Orphan Drug Act designation for the treatment of smallpox, and fast-track designation for the treatment of adenovirus, cytomegalovirus, and smallpox. Clinical trials to test brincidofovir for other indications are ongoing.

Question 18

Under the expanded access program administered by the FDA since 1987, Josh's physician could have asked the FDA to allow access to the investigational drug, and Josh could have obtained access, only if:

- [ ] the manufacturer agreed to provide the drug to Josh.
- [ ] Josh had a serious or life-threatening condition.
- [ ] access would not have interfered with ongoing clinical trials.
- [ ] Josh had a serious or life-threatening condition and the manufacturer agreed to provide the drug.
- [ ] All of the above

Question 19

Suppose the 2018 federal Right to Try law had been available for Josh Hardy in 2014. How might this law have altered his options?

- [ ] It would have allowed Josh to access brincidofovir, even if his disease had been non-serious.
- [ ] It would have allowed doctors to administer brincidofovir, even without Josh's (or, since he was a minor, his parents' or legal guardians') consent.
- [ ] It would have allowed Josh to obtain access to the experimental treatment over the objections of the manufacturer.
- [ ] All of the above
- [ ] None of the above

Question 20

Based on the information provided about brincidofovir above, which of the following conclusions is valid?

- [ ] Allowing expanded access to investigational drugs can impose time and cost burdens on manufacturers.
- [ ] The FDA is generally permissive when it comes to handling expanded access requests.
- [ ] Allowing expanded access to investigational drugs can increase availability to those able to obtain expanded access, but decrease availability to the broader population if FDA approval of the drug is delayed.
- [ ] All of the above
- [ ] None of the above

Question 21

Based on your knowledge of expanded access regulations, which group is most likely to oppose expanded access?

- [ ] Patients, who do not want to serve as guinea pigs for experimental therapies of unknown value
- [ ] Physicians, who do not want to subject their patients to experimental therapies of unknown value
- [ ] Manufacturers, which may not have the capacity to handle such requests and are focused on ensuring that their pivotal trials be completed in a timely fashion
- [ ] The FDA, which seeks to prevent all patients from handling investigational drugs