Welcome to Civil Discourse. This podcast will use government documents to illuminate the workings of the American Government and offer contexts around the effects of government agencies in your everyday life. Now your hosts, Nia Rodgers, Public Affairs Librarian and Dr. John Aughenbaugh, Political Science Professor.

N. Rodgers: Hey, Aughie.

J. Aughenbaugh: Good morning, Nia. How are you?

N. Rodgers: I'm fine. How are you?

J. Aughenbaugh: I'm cold.

N. Rodgers: It is a little chilly. Folks, we're finally getting around to recording more episodes because people have stopped being interesting in the news briefly, which I say briefly because who knows what will happen? We'll probably record this and then we'll both look at the news and go, we have something else to talk about.

J. Aughenbaugh: About, yes.

N. Rodgers: But what I want to talk about is this episode series. We've got three or four that we're going to do here, we're not sure exactly how many it's going to take to get through. Bear with us, folks. We're going to talk about the FDA, the Food and Drug Administration.

J. Aughenbaugh: That's right.

N. Rodgers: You know what it made me think of last night when I was thinking about us recording this? Do you remember Welcome Back, Kotter?

J. Aughenbaugh: Well, yeah.

N. Rodgers: One of the kids got hooked on something and at that point it probably was weed. It was probably a relatively innocuous. It certainly wasn't.

J. Aughenbaugh: Retinol.

N. Rodgers: Retinol or anything, but anyway, John Travolta's character.

J. Aughenbaugh: Vinnie Barberino.

N. Rodgers: Vinnie Barberino came in and he was going, "Give me drugs." He was walking around the room saying that. The guy's like, "I'm not doing that." He's like, "Yeah, you are. Give me drugs." He wasn't technically doing it, but it was funny the way his friends reacted because some of them reacted like it was a joke and some of them reacted like it was really serious and scary.

J. Aughenbaugh: Yes, I remember the episode.

N. Rodgers: But it just made me think about that, "Give me drugs." Isn't that basically what the big pharma does when they go to the FDA, don't they say, "Give me drugs?" Don't they say, "Let me make drugs?"

J. Aughenbaugh: Yeah. Where's our approval?

N. Rodgers: There we go. Give me approval. They could get a note signed Epstein's mother's doctor which would be fabulous. That's enough retroactive for our 50-plus crowd. But in actuality, the FDA does not give you a note. Well, technically, it does give you a note from their doctor saying, but it's not a process of you show up and you say, "I have a drug," and they say, "We love your drug. Here's approval."

J. Aughenbaugh: It is. Yeah.

N. Rodgers: It's not like that.

J. Aughenbaugh: It's not like that at all. It is a very time, labor, expensive process. We should probably provide a little bit of disclosure before we begin this episode. Folks, we are going to have a civil critical discussion about the drug approval process that one must go through to have the FDA, the Food and Drug Administration, approve ones drug. We're going to point out why it takes so long, why it is so expensive. If that sounds like we're being empathetic to drug companies.

N. Rodgers: We are, a little bit.

J. Aughenbaugh: We are, a little bit.

N. Rodgers: We also recognize that big pharma is also big evil.

J. Aughenbaugh: Yes. Because they have made a whole bunch of money producing a whole bunch of drugs.

N. Rodgers: They've made some noted mistakes, which we are going to get to in a later episode where we're going to talk about, oh, that was a choice, that was a bad choice.

J. Aughenbaugh: We're also going to go ahead and talk about the strengths and weaknesses, the pros and cons of the FDA drug approval process, right? Because remember, folks, this is a government process. As we've noted in numerous episodes of this podcast, if you want efficient, effective, and economical work done.

N. Rodgers: Processes.

J. Aughenbaugh: The federal government probably is not for you.

N. Rodgers: Is not your example. There are reasons in some instances for what happens, but let's start with big pharma first. I am working at big pharma. I am working for one of the companies.

J. Aughenbaugh: Yes.

N. Rodgers: I say, I want to have a drug that will lower the rate of sarcasm that college professors engage in their classrooms. I have a targeted audience. Because one of the things you have to have is a problem you're trying to solve. You can't just say, I'm a make a drug that makes people happy. Well, I guess you could, that would probably call that an antidepressant, because there has to be purpose for the drug, there has to be, what target thing am I going after? Am I going after breast cancer? Am I going after brain disease? Am I going after high blood pressure or glaucoma? Usually you start off with a group or a disease that you are trying to mitigate and fix.

J. Aughenbaugh: Medical health problem, yes.

N. Rodgers: My problem is sarcastic professors in college. I'm going to make a pill that they can take every day that is going to make them less sarcastic in the classroom. Not that I know anybody who needs this. She said with side eye that the listeners can't see.

J. Aughenbaugh: I feel also targeted.

N. Rodgers: That's my concept. Then I put some chemicals together and I run over to the FDA and I say this works a charm. It doesn't work like that. There's way more steps in-between.

J. Aughenbaugh: Yeah. Nia, with the hypothetical you just described, a pharmaceutical company first, and this is basically the first step in the drug approval process, this is known as discovery and concept. You have identified a particular medical health problem or issue, and now you're a pharmaceutical company and you are employing hundreds, perhaps thousands of really smart researchers, scientists who are trying to come up with a drug that will reduce sarcasm.

N. Rodgers: Do I have to tell the FDA about that stage?

J. Aughenbaugh: Not necessarily.

N. Rodgers: I might be doing that in house without mentioning it yet.

J. Aughenbaugh: Yeah. In part because pharmaceutical companies don't necessarily want to go ahead and tell their rivals what they're working on.

N. Rodgers: Because then they might all come out with an anti-sarcasm drug all at once, or whoever gets to market gets the patent, which we will get to later.

J. Aughenbaugh: Yeah. Also, in the lab during the discovery and concept process, you may think that you're working on a particular drug to address a particular problem, but in the process, accidentally, you end up finding that you created a drug that perhaps may work on a different medical health problem.

N. Rodgers: Instead of an anti-sarcasm drug, maybe you have an anti-cat drug. Now, everybody who takes it doesn't like cats anymore. That is not a side effect that you are willing to live with.

J. Aughenbaugh: Yeah, because you don't want to be going ahead and upsetting a whole bunch of cat lovers.

N. Rodgers: Yeah. That's for the librarians among us.

J. Aughenbaugh: You're working on this, and contrary to what most people believe, and there have been some survey results of recent vintage that I got to admit when I read them, I just started smiling. There was a survey done by the Harris Poll in spring of 2021 where they surveyed over 1,500 adults. Thirty-five percent of the respondents thought that it takes only 4-10 years to develop a drug, typically. Four to ten years.

N. Rodgers: What's the actual timeline?

J. Aughenbaugh: It's typically somewhere between 15-20 years.

N. Rodgers: Really?

J. Aughenbaugh: Yes, 15-20 years.

N. Rodgers: So big pharma is just banging away at this anti-sarcasm drug for 15 years with no payback, no guarantee?

J. Aughenbaugh: Yes. They're investing in a whole bunch of their money, their shareholders money with no guarantee.

N. Rodgers: But that includes not only that concept part, but don't they call it the pre-clinical research part where you're, you're actually researching the chemicals and you're looking at what other people have done and you're trying to do a big, what we would call in academia, a literature review where you're looking at every single piece of literature and by the way, that means in other countries and other languages, you're having to get all that translated so that you can understand what's being done in this area and we're being silly with an anti-sarcasm because that's not a legit thing obviously.

J. Aughenbaugh: Yes.

N. Rodgers: But if you're looking at cancer drugs, you need to look at every study that's ever been done about every combination of drugs or combination of chemicals to see.

J. Aughenbaugh: Because you're not only looking at the compounds that make the drugs, but you're also looking at all the research that explains the health problem. When you're talking about cancer, are you talking about lung cancer?

N. Rodgers: Right. You're picking a specific cancer usually because there's no such thing as a drug that would cure all the cancers.

J. Aughenbaugh: You have to be very familiar with the medical health problem. It would not be unusual for a pharmaceutical company to have two or three teams working on a particular drug, but from different perspectives.

N. Rodgers: Because you'd have doctors on one team who actually understand what the working of the lungs is supposed to be, but then you'd have chemists on a team that would be looking at what chemicals affect the uptake of blood in the lungs or whatever. Okay, I can see where they wouldn't necessarily be working on the same thing because they wouldn't have the same background. But that's all before you get to anything where you get to a test.

J. Aughenbaugh: Nia, that's typically the second step, pre-clinical research.

N. Rodgers: I'm sure that's years long. It's not the night before literature review that many of our listeners do right before they turn in a paper. We're not not trying to be ugly, but that would not cut it in this particular instance because one, you don't have enough familiarity with the topic, but also argues a softer or greater than the FDA.

J. Aughenbaugh: Yes. I know many of my students are just like.

N. Rodgers: I don't believe that.

J. Aughenbaugh: Really? [inaudible] comparatively is an easier or greater. The third step is the clinical research step. Now, Nia, what do you think goes into clinical research?

N. Rodgers: Great, [inaudible] . Well, the first thing you have to do is, I'm sure you have to test it on non-living things first to see if it explodes or blows up or does whatever. Then you test it on living things that are not humans, so you test on animals, and for the folks here who believed that that is cruel, that is not a debate we can have on this podcast because there are many sides to that question. Whether you believe or not that's cruel, it is one of the functions of medical science, is that they test on animals whose reactions would be similar to humans.

J. Aughenbaugh: That's correct.

N. Rodgers: Sometimes that's a rabbit, sometimes that's a monkey, sometimes that's a rat.

J. Aughenbaugh: Yes. It's going to vary.

N. Rodgers: But they are required by regulation in the United States to do that on animals before they do that on people.

J. Aughenbaugh: Yes.

N. Rodgers: Because whether [inaudible] levers and whether animal lovers around the world agree or not, the US government perceives that human life is more important than animal life.

J. Aughenbaugh: That's correct.

N. Rodgers: That it's staged in that way, and so before you get to experiment on humans. I imagine that probably big pharma would love to go straight to human trial because it would probably save them a lot of money and a lot of time.

J. Aughenbaugh: It would.

N. Rodgers: Except that experimenting on humans is just roundly seen as not a good idea.

J. Aughenbaugh: Well, particularly if you at some point in time want to market your drug, you don't want your drug company to have the reputation.

N. Rodgers: We killed a bunch of humans trying to get to this drug.

J. Aughenbaugh: I'm unaware of any company's business strategy.

N. Rodgers: Ones that don't die will be stronger. No, that's a terrible strategy. I can give an example of when it does not work out. There is a reason why we do it, the order that we do it. The anti-nausea medication, thalidomide, was tested on animals, and then it was tested on humans.

J. Aughenbaugh: Yes.

N. Rodgers: Then doctor started saying, you know who gets really sick are women who are pregnant, so we should give it to them. The trials, I believe, had not been tested on infants. They didn't know what they were doing essentially when they gave it to pregnant women was testing it on unborn humans, fetus, and what it turned out to do to fetuses was terrible. It stopped your development, it stopped development in limbs, it stopped development and all kinds of things. They didn't know that until baby started being born.

J. Aughenbaugh: With all kind of of deformities.

N. Rodgers: Then all of a sudden, they were like, oh. That's one of the reasons that we have clinical trials in the order that we have them. First on non-living things, then on animals, then on adult humans, and then if it's going to interact with children, eventually on children. That's why you saw the COVID vaccine

go through those steps. Because they didn't want to give the COVID vaccine to five-year-olds before they knew whether it could hurt five-year-olds or not.

J. Aughenbaugh: That order is designed as accountability check because you hope that you figure out what are the side effects before we actually get to trying it out on human beings. For good or bad, Nia, as you just pointed out, in the United States, the priority is children must be protected first. Because the logic is children have the potential of a very long life whereas many of us adults, we've already had our shot.

N. Rodgers: Some of us have thrown it away, so we might as well.

J. Aughenbaugh: Again, we could debate this.

N. Rodgers: It's consent, right? When you go to be in a clinical trial, you sign 464 pieces of paper that say that you will not hold pharma responsible for what happens to you during this trial and they explain every piece of paper to you.

J. Aughenbaugh: Nia, I have a good anecdote from my life when I was a much younger person, I participated in a drug trial, it was an antidepression medication. I volunteered, of course I was getting paid, was one of the reasons why I participated. I needed the money.

N. Rodgers: That is an ethical question about research clinical trials is, are starving college students really your best audience?

J. Aughenbaugh: But I do remember, it took nearly an afternoon.

N. Rodgers: To go through the paperwork.

J. Aughenbaugh: To go through the paperwork. I got to admit, when they got to the section about potential side effects, I almost said, thank you, no.

N. Rodgers: They have to disclose everything that has happened in earlier trial.

J. Aughenbaugh: Before they get to the human trials, the clinical trials.

N. Rodgers: When given to this in human doses, rats fell over dead. That probably won't happen to you. Here, sign here.

J. Aughenbaugh: But there was a lot of paperwork in a talk all afternoon. In one of the things they disclose is that, this is a controlled experiment, listeners. That means one group of the volunteers are going to receive the drug, and then there's one group that isn't, they're going to get a placebo. Because they're trying to figure out whether or not whether the drug works.

N. Rodgers: Or better than a sugar pill. If the drugs shows no more effectiveness than a sugar pill, then there's absolutely no point in taking the drug.

J. Aughenbaugh: They also went ahead and screen for, have you been diagnosed as suffering from depression? Or in the case of our hypothetical sarcasm reduction drug.

N. Rodgers: Have you been witness to be sarcastic?

J. Aughenbaugh: Sarcastic.

N. Rodgers: On a scale of 1-10, where would you put your normal sarcasm level? What's interesting is sometimes you'll see in the newspaper or, newspaper is not anymore, but in online and in media, you'll see a request for people to be part of a trial and it will say, are you between the ages of 18 and 34 and suffer from extreme sarcasm? We'd like to talk to you. It's that kind of thing.

J. Aughenbaugh: Yes.

N. Rodgers: You see a lot of those where they already tell people to sort of weed themselves out.

J. Aughenbaugh: Yes.

N. Rodgers: A lot of times you'll see are you a smoker between these ages or are you obese between these ages, and can we get you into our trial? And then, like I said, there is some question about paying people to be in trial. That's a little sketchy, maybe, would be a good way to [inaudible]. What you may get are people who skewed too certain socioeconomic groups. Like you, college students, who are, man, I sure could use some pizza and beer money, right? It may skew away from wealthy people, it may skew away from people who are more established in a different way in life and are not interested in being experimented on. It may also skew more towards people who accept risk in a different way than people who don't.

J. Aughenbaugh: It's harder to control for intervening variables if the only ones who are participating are poor people with little education, who grew up with poor diets, poor living in housing conditions. Again, there might be other factors that are affecting a particular medical health condition.

N. Rodgers: Which is why they don't just run one trial.

J. Aughenbaugh: Yeah, that's right.

N. Rodgers: That's why when they say they've done clinical trials, it's always plural.

J. Aughenbaugh: Yes.

N. Rodgers: They usually start with a small group in case it turns out to be something that kills people and they don't want to kill 500 people at a time, that's terrible.

J. Aughenbaugh: Yes.

N. Rodgers: They start off with a small group then they usually expand to a bigger group. One of the problems that Aughie and I want to mention here, as a problem with the FDA's requirements for clinical research is that, back in the day, they did research on men. They didn't do research on women.

J. Aughenbaugh: Yes.

N. Rodgers: They had no idea whether medication would work for women are not, right?

J. Aughenbaugh: Correct.

N. Rodgers: They didn't experiment on women. Part of that has to do with who has the reproductive burden in our society, which generally speaking is women.

J. Aughenbaugh: Yes.

N. Rodgers: Women carry children two term and so they didn't want to experiment on women, but part of it was that scientists were experimenting on people who looked like them. You had male scientists experimenting on males, generally, white males experimenting on white males.

J. Aughenbaugh: Or conversely.

N. Rodgers: Or white males experimenting on black males.

J. Aughenbaugh: Black males because the assumption was black males were inferior and their lives mattered less, so if there was harm or danger, it would be less of a cost to society.

N. Rodgers: Which is where you get Tuskegee.

J. Aughenbaugh: Yes.

N. Rodgers: The horrific Tuskegee experiments like just let people have syphilis, even though we know that that's a deadly disease.

J. Aughenbaugh: Some of those paternalism in regards to gender, right?

N. Rodgers: Right.

J. Aughenbaugh: We want to protect women because they have this vital role in society of having our babies and maintaining the home.

N. Rodgers: But what that has done over the years has pushed back our knowledge of those groups.

J. Aughenbaugh: How drugs affect them because there are physiological differences.

N. Rodgers: Between males and females.

J. Aughenbaugh: Males and females.

N. Rodgers: In some instances in the races, it took us forever to start studying sickle-cell anemia.

J. Aughenbaugh: Yes, which has a [inaudible] that overwhelmingly affects African Americans more than Caucasians.

N. Rodgers: Right. It just didn't get studying. The FDA's got some stains on it in terms of not requiring trials where you have equal numbers of men and women, where you have it across races, where you have it across ethnicities, and religious groups, and socioeconomic classes, you were saying, right? All of that needs to be taken into account and the trials. So now they're much better about saying no, one trial is not going to cut it.

J. Aughenbaugh: Yes.

N. Rodgers: I'm going to need to see a spread across a variety of folk.

J. Aughenbaugh: Particularly because pharmaceutical companies, if they're driven by profit. I read the literature from pharmaceutical companies.

N. Rodgers: We want to help people.

J. Aughenbaugh: Yeah.

N. Rodgers: But it's still a business. Let's be honest, it's still a business.

J. Aughenbaugh: But if you're a business and you're trying to market a drug that is taken you 15 years to develop and you have invested in some instances billions of dollars.

N. Rodgers: I want to ask you about that in a minute, how much it actually costs.

J. Aughenbaugh: Just roll with me on this. Fifteen years, billions of dollars, and you want to get a return on your investment. You want to know that you can market this to as many people as possible.

N. Rodgers: Right. That's why they don't do niche drugs for the most part.

J. Aughenbaugh: You're going to want to do multiple clinical trials with the greatest, if you will, number of people so you can control, so for a whole bunch of variables.

N. Rodgers: Right. Because the more people will buy your drug, the more you will sell, obviously.

J. Aughenbaugh: Yes.

N. Rodgers: You want your pain medication to fix everybody's pain, not just a certain group's pain. This is made for, I mean, I'm not picking on Pacific Islanders, but in the United States, that's a relatively small population. If you said this works exceptionally well for Pacific Islanders who have knee pain, well, after you've sold it to those 400 people, what do you do then?

J. Aughenbaugh: With our hypothetical of reducing sarcasm.

N. Rodgers: Yeah, it needs to be all professors, not just political science professors.

J. Aughenbaugh: Ideally, it wouldn't just be college professors, right?

N. Rodgers: That's true.

J. Aughenbaugh: Okay.

N. Rodgers: That is a niche group.

J. Aughenbaugh: That is a niche group, right?

N. Rodgers: That's true. One that doesn't make a huge amount of money. We have to rethink our concept.

J. Aughenbaugh: But now, we're talking about reducing sarcasm for all middle managers because most college professors in the bureaucracy of universities are middle managers. Now we want to go ahead and see if this actually works on middle managers in all private and public sector bureaucracies.

N. Rodgers: We would make a fortune. If we can force-feed these to Elon Musk, can you imagine? I'm just saying. Anyway, but as part of the review process, which is the fourth step, is the FDA saying, how many people did you test it on? How widely does it work?

J. Aughenbaugh: Here's a key point, because Nia is now just moved us to the fourth step of the process, which is the actual new drug application stage.

N. Rodgers: Wait. I want to ask you a question first. How much money does it cost me to get to the FDA review stage?

J. Aughenbaugh: I've read a lot of studies, but on average, it typically costs over one billion dollars to create a brand new drug. That's b.

N. Rodgers: Be as in babillion?

J. Aughenbaugh: Yes, right?

N. Rodgers: The Aughenbaugh and Rodgers Pharmaceutical Company, made of two people mixing stuff in Aughie's kitchen, is not going to be able to compete with Pfizer, and Johnson & Johnson, GSK, and all the other.

J. Aughenbaugh: Yes.

N. Rodgers: It's really interesting when a relatively small pharmaceutical comes up with something they've clearly done a lot of fundraising. They've got a lot of investment from people who believed that they really are. Which is where you get stuff like Theranos, where you get that woman who, what is her name? Elizabeth something? Who fashioned herself after Steve Jobs, but she got people to invest.

J. Aughenbaugh: Yes.

N. Rodgers: She had a relatively small company and she got people to invest zillions of dollars. I know it's not a real word, but work with me. It's a larger number than billion and she got them to invest in that. You're talking about a lot of money.

J. Aughenbaugh: Yes.

N. Rodgers: Didn't your poll say that people thought it was?

J. Aughenbaugh: Yes, the Harris Poll. This is great. Seventy-six percent thought it costs less than $100 million to develop a brand-new drug.

N. Rodgers: It costs at least 10 times that.

J. Aughenbaugh: Yes.

N. Rodgers: So it's not cheap?

J. Aughenbaugh: Yes.

N. Rodgers: Now, there's a form I got to fill out. Because of course, there's a form because it's the government. Have you ever applied to the government for anything and not had to fill out a form?

J. Aughenbaugh: Yeah, because let's face it.

N. Rodgers: The government does love a form.

J. Aughenbaugh: Yes, for no other reason, government agencies have learned over the years one of the most important acronyms you'll ever hear on this podcast, CYA.

N. Rodgers: Part of you that could commonly also be referred to as butt.

J. Aughenbaugh: Butt. Tush.

N. Rodgers: Your tush, your tuchus. I liked that. That reminds me of her [inaudible] , cover your tuchus. But you've got to cover yourself with your liability. I'm going to need you to fill out this form. Actually, I'm going to need your fleet of lawyers.

J. Aughenbaugh: Yes.

N. Rodgers: You fill up this form that swears that you were telling us everything that happened in the trials, including how many people died, how many times it didn't work. You can't just turn in all the good data and say, man, this is fabulous. You just have to.

N. Rodgers: You know our pharmaceutical company, the Rogers Aughenbaugh Pharmaceutical Company, reaches out to the FDA.

J. Aughenbaugh: That would be RAP, Rodgers Aughenbaugh Pharmaceutical, RAP. A RAP company.

J. Aughenbaugh: Hey, [inaudible] , that's a new idea for the podcast of merch.

N. Rodgers: I like it. Anyway, RAP, who do we know that's a lawyer? [inaudible] paperwork.

J. Aughenbaugh: Or some of our former students who we know are gone to law school, right? Or [inaudible] , we know her. She's a Boston. Will get somebody to fill out our paperwork and there'll be like, are you kidding me? Do you know how many pages there are on this form? This is [inaudible] .

N. Rodgers: Yes, so know we got [inaudible].

N. Rodgers: I bet the part of that billions is paying the lawyers.

J. Aughenbaugh: Yeah, thy have a lawyers, right? What we're going to fill out is known as an NDA, of course.

N. Rodgers: This has an acronym, of course.

J. Aughenbaugh: A New Drug Application.

N. Rodgers: New Drug Application, NDA.

J. Aughenbaugh: What we have to include?

N. Rodgers: Oh, as opposed to non-disclosure agreement. Funny that they have the same acronym. Not that I'm a conspiracy theorist or anything.

J. Aughenbaugh: That dawned on me as I was doing research for this particular podcast episode. I'm like, wow, hey, that's really similar. Don't go [inaudible].

N. Rodgers: You get conspiracy and then you'll just end up down a rabbit hole, and they will never see you again. What are the parts of the NDA?

J. Aughenbaugh: As you mentioned, we have to include our clinical test results.

N. Rodgers: All of them.

J. Aughenbaugh: Yeah, it can't just be the good ones.

N. Rodgers: On 80% of the people, this works really well. What about the other 20? Oh, we don't talk.

J. Aughenbaugh: We don't talk about them. It's like when I asked my daughter to clean her bedroom. She only shows me the parts of the bedroom that she's cleaned. Then I get near her closet door and about ready to open it, and Mackenzie steps in front of me, "Okay, don't look here." Why don't you want me to look there, little girl?

N. Rodgers: Nothing, answer to that, right? What every kids always says. Nothing, there's nothing to see

J. Aughenbaugh: Okay. Yeah. There's nothing. Seconds, you have to then provide, and this is really important, the manufacturing information to demonstrate that the company can properly manufacturer the drug. There are a lot of parts for this. What do you think RAP, the Rogers Aughenbaugh Pharmaceutical Company, has to go ahead and demonstrate in regards to manufacturing?

N. Rodgers: Well, my guess is that if we are going to manufacture in your kitchen, we have to show that the kitchen is clean, and meet standards.

J. Aughenbaugh: Yeah, a sterile, clean lab, manufacturing plant.

N. Rodgers: We have to show that you and I have some chemical ability to mix things without blowing things up or destroying the world.

J. Aughenbaugh: We're going to give the FDA a whole bunch of resumes and curriculum vitaes showing the bona fides and credentials of the people who are going to be working there.

N. Rodgers: Well that short since there's two of us. I'm assuming that we have to show that we could make it in mass.

J. Aughenbaugh: Yes, because the FDA is going to [inaudible].

N. Rodgers: What if it's really popular?

J. Aughenbaugh: There you go. Listeners, a really good example why this is a big, if you will, consideration for the FDA. We saw this in the early part of COVID-19 when they were coming out with the vaccines. I'm not going to throw them under the bus, but one of the drug companies that produce a vaccine had a problem with one of their manufacturing plants, that made a mistake mixing the batches of the vaccine.

N. Rodgers: So they had to throw all those away.

J. Aughenbaugh: Yes. Then they had to go ahead and see if any of the vaccine doses from that plant actually got sent out to hospitals, emergency room.

N. Rodgers: Recalled.

J. Aughenbaugh: Recalled, okay

N. Rodgers: Also, didn't they shut that facility down because the process was messed up? Like, they had to investigate the process.

J. Aughenbaugh: We also saw a more recent example in regards to the production of baby formula. Now, this gets to the other side of the FDA.

N. Rodgers: Which is the food.

J. Aughenbaugh: Food part. But listeners, were recording in early 2023. In spring, summer of 2022, the United States had a severe shortage of baby formula in the United States.

N. Rodgers: Yeah, we had to hit up other countries. Had to be like, "Hey, Ireland, you got any baby food laying around?" They're like, "Maybe. Well, why are you asking?" "No reason. We were just thinking you might be able to send us some."

J. Aughenbaugh: Which by the way, required the Biden's administration to loosen the regulations because [inaudible].

N. Rodgers: The whole separate issue which we will discuss in another podcast is the regulations of things coming into the country in terms of food and drug and what's allowed and how that is regulated. He actually had to loosen the baby formula regulations to allow a plane full of baby food to come, not just one plane full. Anyway, that's partly because we were down to a really small number of manufacturers. Two, I imagined that that also has an effect.

J. Aughenbaugh: Yes.

N. Rodgers: Like your capacity.

J. Aughenbaugh: We've gone ahead and discussed. You have to disclose the drug test results, all the data that are gathered on the human studies, in the animal studies, you got to demonstrate your manufacturing, then you have to go ahead and explain to the FDA your proposed label for the drug. I know many of us hate looking at the labels on drug bottles.

N. Rodgers: Oh my great googly-moogly, it's not just the label, but that horrible piece of paper that comes with it that's folded is 700 times like origami. When you unfolded the print is like 0.6 font, and you're holding it up to your face saying, what does this say, and it's just amazing amount of information.

J. Aughenbaugh: For our younger listeners who have really good eyesight.

N. Rodgers: Yeah, you're fine. We don't want to hear you complaining. But Aughie and I, we already wear glasses, I'm just saying.

J. Aughenbaugh: When we see that small print, we have to reach for the magnifying glass. When you unfold that piece of paper, it's not an 8.5 by 11?

N. Rodgers: Oh, no.

J. Aughenbaugh: Okay?

N. Rodgers: I don't know how they get that piece of paper into that bottle, because that piece of paper is the size of my apartment, it's enormous. That's where you get the origami folding thing that you get in there that they put in the side of the box. By the way, that is in aspirin, it's in cold medicine, like all the normal stuff that you take over the counter. There's one of those in there too. Because what it talks to you about is bad reactions and what to do if these things happen and what the possibilities are, what could possibly go wrong. They have to disclose, its disclosure agreement. I mean, a statement.

J. Aughenbaugh: Yeah. It even has instructions on how to use it.

N. Rodgers: Which nobody reads. Everybody wadded up that piece of paper and they go, ha, and then they open the bottle and take however many they were going to take to start with.

J. Aughenbaugh: But this becomes really important. In the example I'm going to give arose when we finally found a good drug treatment for AIDS. The initial drug treatments was, how many drug cocktail was it, near three, four?

N. Rodgers: It was seven drugs taken three times a day, I think.

J. Aughenbaugh: Okay.

N. Rodgers: I think it was seven drugs taken three times a day, but they had to be taken very specific amounts of time apart, like this two has to be taken eight hours apart, and it was very regimented.

J. Aughenbaugh: Yes. I know Nia and I reference the TV show West Wing, but there's a really good West Wing episode.

N. Rodgers: That talks about that.

J. Aughenbaugh: Bartlet Administration was trying to convince the American pharmaceutical companies they had to come up with these AIDS drugs to make them available in African nations either cheaply or at no cost. In one of the issues that arose was that the pharmaceutical companies said, "Even if we do this, they may not be effective." The various Bartlet Administration officials were like, "Well, why won't they be effective?" Because they thought the pharmaceutical companies were being racist. The pharmaceutical company said, "Because it requires a particular regimen taken at particular times of the day, and many people in those countries don't have clocks or wear watches."

N. Rodgers: While that is probably less true now, it's still true in rural areas in many parts of the world. A regimented thing would be really hard to do.

J. Aughenbaugh: But for some of these drugs, for them to actually be effective and or not cause harm or death.

N. Rodgers: They have to be taken that way.

J. Aughenbaugh: Or you have to avoid taking the drug and eating certain foods or drinking certain beverages. There are blood pressure medicines that you have to avoid certain foods because if you take that medicine and eat certain foods.

N. Rodgers: It negates the medicine.

J. Aughenbaugh: It the negates the medicine or may actually cause you to have a stroke.

N. Rodgers: Well, and we saw that with COVID vaccines. The first ones had to be kept at a certain temperature which made them very hard to deliver to hot parts of the world. Because how do you keep something refrigerated when you're driving it out.

J. Aughenbaugh: Before we conclude this particular episode, Nia, I want to mention one thing about the FDA's approval process.

N. Rodgers: Wait, can I mention one thing about labels first?

J. Aughenbaugh: Yeah. Go ahead.

N. Rodgers: That's where you get people who say it's an on label use or an off-label use. What they're referring to is that label where it says, "This drug is to be used for high blood pressure." Aughie's like, "Yeah, but it also helps me lift weights in the morning so I'm going to take it as an off-label drug." His doctor may say, "Aughie, you can take this as an off-label thing once in awhile to help you get a boost of energy or whatever." I know blood pressure medication doesn't work that way, but you know what I mean.

J. Aughenbaugh: Hypothetically, yes

N. Rodgers: But that off-label use is not protected so if something happens to Aughie while he's taking it off-label, he's on his own.

J. Aughenbaugh: He's on his own.

N. Rodgers: He can't sue the pharmaceutical company because they're like, dude, we told you it wasn't for that and you decided you were going to take this as you thought it was some form of steroid and it turns out to give you a heart attack, that's not our problem.

J. Aughenbaugh: This is a really good example of why there are so many lawyers that are involved in the NDA.

N. Rodgers: Because that language is parsed within an inch of its existence.

J. Aughenbaugh: It's not just to cover CYA for the pharmaceutical companies, it's CYA for the federal government.

N. Rodgers: You approved this drug for this thing and they say, no, we didn't, and then it looks in the paperwork and like, oh maybe we did, oh crap.

J. Aughenbaugh: They got, oh crap moment. But here's a really important thing for listeners to know about the FDA's approval process. The FDA doesn't do its own testing.

N. Rodgers: They don't actually test this drug.

J. Aughenbaugh: They review the test results, the manufacturing information, the drug label. They review it, but they don't do the testing themselves.

N. Rodgers: Which is why watchdog groups sometimes have a love-hate relationship with the, with the FDA, because they're like, "Really? You're taking the word of the pharmaceutical that it does what they say it's going to do and doesn't do the harm that they say it's not going to do without any testing?" The answer from the FDA is, "Do you have any idea how many drugs could get submitted for approval? It's like a kazillion. Do you know how many we approve?" How many do we approve, Aughie?

J. Aughenbaugh: What is it, less?

N. Rodgers: It's 0.02% they approve. They turn away 99% of the drugs that asked to be and they're like, "What else do you want us to do? We're trying to regulate." But what happens is that when a drug goes bad, it usually hurts a lot of people and we're going to get to that in another episode.

J. Aughenbaugh: Let's be clear about the percentage. It's not that the FDA turns away over 99 percent. It's that of all the drugs that are attempted, of those in development, only 0.02 percent make it to market.

N. Rodgers: Oh, I'm sorry. You're talking about the failure rate all the way through.

J. Aughenbaugh: But nevertheless, that's still means that the FDA is rejecting a whole bunch of drugs.

N. Rodgers: Like your trials, we don't believe your data, we don't like your label, where we're not a fan of what you've said it will work for and not work for, but it's not bureaucrats making those decisions.

J. Aughenbaugh: No, they have scientists, they have some of the smartest people in the world. We're talking about PhDs, MDs.

N. Rodgers: Going through those NDAs, it's not like me and you going through this NDAs and reading the science and saying, "I don't know, it looks good to me." They're not just having what I think of as middle managers or like regular folk, they're having scientists read through all that material. Can you imagine how much longer it would take if they have to test everything?

J. Aughenbaugh: Again, I've tried to explain this to my students. I'm like, "Hey, if you want the FDA to have a larger role."

N. Rodgers: Then you need to be prepared for a slowdown. We have only to point to the IRS to show how bigger backlog can get.

J. Aughenbaugh: Or you want to go ahead and see a huge increase in your taxes.

N. Rodgers: Or the cost of the drug. If they say, but the manufacturers are going to have to pay for that, then the manufacturers are like, but every pill is going to cost $9,000.

J. Aughenbaugh: Because some watchdog groups have gone ahead and said, well, we should just have.

N. Rodgers: Pharma pay for it.

J. Aughenbaugh: Yeah.

N. Rodgers: Pharmas like, really? Because we didn't put in enough to start with. The billion that we threw in before, that's not enough, we got to now throw in and need to have it tested by the government.

J. Aughenbaugh: At some point in time, accounts, not a lawyers, accounts for the pharmaceutical companies are going to go ahead and say, cost-benefit analysis, this just does not make sense.

N. Rodgers: But what it shows, which I think is interesting, is that the process is byzantine and complicated and so it really is an expensive venture for companies to get into to try to make drugs. It's easy for us to villainize big pharma because they are so villainous in some ways, but also they've done stuff and we're going to get to that where we talk about them and we we hold nothing back. But then also in fairness to them, that's a lot of money to put out to fail. If you think billions per drug and you're not making it to the end process 99% of the time, you're losing a lot of money. But by the same token, we also have to mention before we go, and we're going to say this in every episode so you I'll just get ready for it, the FDA has competing interests. Like every agency for the government, it both regulates a thing and encourages a thing, and that is inherently attention.

J. Aughenbaugh: At times, it causes problems. Because on one hand, we created the Food and Drug Administration to make sure that our foodstuffs and our drugs were safer and we're not harming American people. On the other hand, we don't want that review process, that protection to be so burdensome that it provides a disincentive for the private sector to step up and give us new drugs.

N. Rodgers: Thank you. That's succinctly put, thank you. They have to walk that line. They could regulatory enough that people don't just put snake oil up for sale like they used to or cocaine in Coca-Cola, which is the rumor, but I don't know whether that's ever true or not, but that's the rumor so Coke don't sue me. But between that, and this is so regulated that it takes a drug 50 years to come to market, and by the time we get it to market, a lot of the folks who had whatever it is are dead. Cool, Aughie, thanks so much.

J. Aughenbaugh: Listeners, a little bit of foreshadowing, trailer, if you will. Our next episode talking about cost, Nia. Our next episode is going to look at one of the more controversial issues related to the FDA approval process, generics.

N. Rodgers: I have a friend who works in the pharmaceutical industry and he said, "Generics of a dark hole into which all things go." Because regulation becomes complicated, the law becomes complicated, all of it. I'm looking forward to that.

J. Aughenbaugh: Because what we're thrown on top of this drug approval process is one of me and Nia's favorite topics, patents.

N. Rodgers: It all goes to hell when a patent is involved.

J. Aughenbaugh: All right, Nia. Sounds good.

N. Rodgers: Thanks, Aughie.

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