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ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

Bottles of Lies: The Inside Story of the Generic Drug Boom

Dr. Pickard:
Globally, patients are looking ways to control rising healthcare costs. They are now using generic drugs in ever-increasing amounts. But are we aware of the risk in this practice? I'm your host, Dr. Maurice Pickard, and you're listening to Book Club on Reach MD. And today, our guest is Katherine Eban. She is the recent author of the well-received book Bottles of Lies: The Inside Story of the Generic Drug Boom. Katherine Eban is also an Andrew Carnegie Fellow, and also the author of Dangerous Doses: A True Story of Cops, Counterfeiters, and the Contamination of America's Drug Supply. Thank you very much for joining us today.

Katherine Eban:
Thank you for having me.

Dr. Pickard:
To begin with, what events drew you to this topic as an investigative journalist?

Katherine Eban:
Well, it was 2008, and I got a phone call from actually a radio show host named Joe Graydon, who hosts a program called The People's Pharmacy. I have been on his program before. He had interviewed me about my work. But this time, he called to say that patients were calling in to his show, complaining about side effects from generic drugs, and he had taken their complaints to the FDA, and the FDA's response was basically, 'well, it's in their heads, it's psychosomatic.' And he did not believe that, so he urged me to investigate. And that is really where I began, about 10 years ago.

Dr. Pickard:
Was there any particular lead that really made you say, 'Hey, wait a minute, this is really a story that may be threatening on a global level many patients?'

Katherine Eban:
Well, yes. It wasn't hard to find U.S. patients who were having the complaints about these generics, and also doctors who were struggling to stabilize patients after they were switched to certain generics. But what really led me in a different direction was my contact with the whistleblower who urged me to look at the manufacturing plants overseas, largely in India and China, that are making the majority of our low-cost generics.

Dr. Pickard:
I believe his name was Dinesh Thakur. He is really almost a hero if you read your book. You can't help but admire him for his courage. Can you tell me, what were the things that he was exposed to? He had worked, I think, in the pharmaceutical industry in the United States before he began to be employed in India.

Katherine Eban:
That's right. He was a young engineer at Bristol-Myers-Squibb in New Jersey when he was recruited to go to Ranbaxy, which at the time around 2003, was India's largest drug company. And while he was there, his boss became suspicious about the company's data, and asked him to do a research product, and to investigate the company's worldwide regulatory filings. In other words, what did they claim to regulators? And what kind of clinical and test data did they submit to regulators in order to get approval to market their drugs? And what Dinesh uncovered was really harrowing; that over 200 drug products in more than 40 countries were filed with manipulated or fabricated data. And this was – his findings were then reported to a subcommittee of the board of directors, and their proposal was to bury this

information. And basically, Dinesh was forced out of the company, and he ended up approaching the FDA with his information, and that sparked an 8-year investigation that sort of forms the narrative thread of the book.

Dr. Pickard:
We can't forget that the Hatch Bill also laid the groundwork for this rush to manufacture drugs overseas. It really laid the groundwork for this new kind of industry that became really the pride of India. Could you tell us a little bit – remind us a little bit about what the Hatch Bill was?

Katherine Eban:
Sure. So the Hatch-Waxman Act was passed in 1984, and it really created the modern-day drug industry in this country. Because what it did, it created a unique pathway for generic companies to apply to the FDA to market their drugs. Basically, it said look, the molecule has already been approved, we know it's safe and effective, so what we're asking you companies to do is just to prove that your version of it is bioequivalent; that it acts similarly in the body, and has roughly the same absorption into the blood. But it also had a deal sweetener for the generics, and it really sort of sparked a frenzy. The deal sweetener was called "First to File" and it said if you are the first through the door to apply for a generic and you get approved, you will have six months of exclusivity on the market where you can sell your drug without other generic competitors at roughly 80% of the brand name price. So that incentive was so big for generic companies, that many of them wanted to be first even if they didn't yet know how to make the drug. And, in fact, it did give rise to falsification of data in order to lay down a marker as first to file.

Dr. Pickard:
You know, one of the things that amazes me is how the manipulated the data. And one of the things that really surprised me was the key executives all the way at the top – you have to remember that this is something that begins in the culture of the company at the very top, that executives came to the United States, loaded their suitcases with brand-name drugs, brought them back to India, and used those brand-name drugs from the United States to do their data, so of course the drugs would look right. But some of the other things are really surprising; that it tells you how deep-seated this was. But I have to ask you – you know, we're very quick to blame the FDA – how is the FDA supposed to manage or investigate various plants often in remote areas of India? They have to give them two and three and four months notice. Some of the plants that you described hadn't even been visited in over a decade. You can't read the language, you're ushered in by executives, you're wheeled around, and you have two to three days to look at a plant that often covers miles. What's the answer to this?

Katherine Eban:
You lay it out very well. It's essentially an impossible task. You know, the FDA is a domestic agency. Almost overnight on this wave of globalization, it was required to become a global agency, and you know, is required to inspect plants that are 7,000 miles away. But let's remember, the FDA is not required to give companies advanced notice that they are coming to the plants. The FDA has chosen to do that. I mean, it has not dramatically thought through how to effectively regulate these plants. It has reassured Congress and the American people that it has everything under control. We basically believed them. But the problem is, they give eight weeks of advanced notice they're coming. They ask these plants to manage domestic travel in India for their investigators, they're providing translators in China – you know, and the end result is that investigators are not getting a true picture of what is going on in the plants. And in some cases, as I exposed, you know, they're being wined and dined by these manufacturing plants and taken on trips to the Taj Mahal. So the question is, where does that leave the American consumer?

Dr. Pickard:
I'm glad you touched on that. The other hero that I was impressed with in your book was a man named Peter Baker.

DR. Maurice Pickard:
He is an FDA investigator. And it sounds like, within a very short time, he has uncovered, shall we say, all the dirt that exists. What makes this man so special? Why aren't we having more of them?

Katherine Eban:
The FDA has this pretty credulous foreign inspection system, right? They give advanced notice to the plants. They reviewed the data that the plans submit. Then they go and visit. And a lot of the investigators sit in the conference room and ask for documents to be brought to them. Peter Baker said, 'I'm not doing any of that.' He is young, he's energetic, he's smart about computers. And instead what he did was started looking in the plant's computer systems. And once he did that, he was a total game-changer. So he was able to literally track down the metadata from deleted tests. The companies were pretesting drugs to see if they would pass so that they would know how to manipulate the testing parameters once they moved it to the FDA's official system. And basically he uncovered all of that through his inspections. So in the course of approximately five years, in 86 foreign inspections in India and China, he uncovered some type of data manipulation or data fraud in 4/5th of the plants he inspected, which really tells you something about how the industry

works, and also why his inspectional approach is so unique.

Dr. Pickard:
If you're just tuning in, you're listening to Book Club on Reach MD. And I'm your host, Dr. Maurice Pickard. And joining me today is Katherine Eban. We're discussing her very thought-provoking, and almost frightening book, Bottle of Lies: The Inside Story of the Generic Drug Boom. There also appears to be a local pressure on the FDA that voters are calling their representatives, saying, you know, 'My drugs are expensive. I am either going to buy my drugs, or I'm not going to eat. I have a choice of one or the other.' And we see actually in various meetings that when this company you're talking about, Ranbaxy, that when they had really very good evidence to shut them down, they said, 'You know, if we shut them down, they won't be able to pay the settlements to people that they've already lost to our investigative or our attorneys.' There really seems to be an ax there or a tension between the political pressures, say in our country, and what's happening to the FDA as far as how aggressive they are in dealing with companies like Ranbaxy.

Katherine Eban:
Right. So there's this fundamental tension in this question of: What is the FDA's role in all of this? Is it to facilitate the approval of more low-cost generics? And the benefit of that is that it can go to Congress and say, 'Look what we've accomplished for the American people.' Or is it to protect our public health? One really remarkable thing is that I uncovered how frequently the FDA is downgrading the recommended sanctions of foreign plants by its own investigators. In other words, the FDA investigators are going in and finding terrible conditions; bird infestations, faked sterility data, hidden laboratories. And they are, in many cases, recommending that the plant receive a designation of official action indicated, which means they have to fix the conditions immediately or face further sanctions. And in many, many cases, the FDA has said, 'No, they provided further documents, and it's all fine, so we'll downgrade that recommended sanction.' And in some cases, these plants have proved even months later to turn into sort of ground zero for real public health crises. One example of that was a Chinese plant, Zhejiang Huahai. An FDA investigator went in there and found, 'Hey, this plant is not investigating the impurity spikes in its own drugs.' Official action indicated. The FDA said, 'No, it's okay.' Voluntary action indicated, not as serious. And within a year, it turned out that plant was producing active ingredient for Valsartan, the blood pressure medication, that was contaminated with a carcinogen and had to be recalled. So there was a question about really how aggressive and vigilant the FDA is being in response to these findings.

Dr. Pickard:
You know, as a doctor, I've had patients who didn't respond to medications that I thought should be working and we switched from one antibiotic to another. What is the takeaway for our audience, which are mainly doctors and nurses; are we to begin to really be anxious about the drugs? I take generics. And what should our patients do who are on generics?

Katherine Eban:
Let's start with doctors. So, first of all, I think if a drug is not effective or a patient is not responding or if a patient was stable and then becomes unstable after a medication switch, it needs to be a category of thought for a doctor that it's not just to change to a different therapy, but some of the doctors who I feature in my book are changing to different manufacturers of the same drug. They're unfortunately having to diagnose the drug supply, as well as their own patients. But the takeaway is that not all generic versions are identical or interchangeable with one another. And not all generic versions are interchangeable with the brand despite the FDA's claim that it is true. So that is something that doctor's need to consider before they just say, 'Well, that whole line of therapy is not effective, so I'm going to change the entire treatment program for this patient.'

Dr. Pickard:
And what should the patient do?

Katherine Eban:
As you can imagine, I have been besieged by patients who are writing, and my inbox is full of patients asking me this question. So what I did, was I created a guide to investigating your own drugs, which is on my website now. First, and most important, is if you take a maintenance drug, you should pay attention to who manufactures it. You know, most patients don't really pay attention to that. So, after that, there are a number of steps patients can take. So, first of all, there's something called an authorized generic. And that is a generic that is often licensed by the brand-name company, maybe formulated more closely to the brand than other generics. So that's one option. Another option is to research the company. I mean, is this a company that has had numerous recalls? Are they under a warning letter or import alert from the FDA? Have they been caught faking data? These are all questions that patients need to ask and talk about with their doctors.

Dr. Pickard:
So, you know, we've been talking about a lot of different subjects, but you know, it made me think about shared decision-making. We talked about it when people make decisions about diagnostic tests and whether they want to have operations or not, and I think you

really opened my thought process to patients begin to have to protect themselves; they have to take on a certain responsibility even when it comes to the drugs that are being prescribed to them. I can't thank you enough for being with us today. And I'd like to ask our audience that, if they missed any of this discussion, please visit ReachMD.com/bookclub to download this podcast and many others in this series. Thank you for listening, and thank you very much. I encourage everyone to read this book – it may save your life.