Taking Medicines Back to The Future – A Discussion on Value Chain vs. Supply Chain: What's the Difference?

Episode 12

Ed Narke
Welcome to CMC Live! Today, we have another very special, excellent guest. We'll be talking about some very important things. Hedley Rees is on the show. During his 40-year stint working in the pharma industry, Hedley realized that there was, and continues to be, something seriously wrong with how medicines come to market. Globally, drug prices are rising, clinical trial failures are more common than successes, and large sums of money are spent on patent litigation. To correct this and approach the modernization in the industry, Hedley has written a book titled *Taming the Big Pharma Monster* and has used his consultancy, Pharma Flow, as well as Welsh led initiative, Friends of Medicines Modernization (FOMM), to organize medicines for the 21st-century conference. Hedley is joining us today from Wales in the UK and will be sharing some of his thoughts on a few things: *Taking Medicines Back to the Future, Cutting Through the QbD* Foliage (yes, we can revisit QbD 10 years later), and something I think is very special and the reason we started talking ten years ago- I'm talking with Hedley about how your supply chain is your value chain. So, Hedley, let's get this episode started by going into some of your background, how you got started, and getting your thoughts on a few things. Perhaps, let's start with why you describe the pharma industry as a monster in the title of your new book.

> "If they all beat together at the same time, instead of taking sixteen years for penicillin to come to market it would take maybe four years."

Hedley Rees
Thanks, Ed. I am trained as a production engineer. So, I've learned how to make things to start with the end-users of your product and then construct something that creates value for them. I learned that outside of pharma. In 1988, I joined Bayer in the UK, a manufacturing plant. I cut my teeth on Alka Seltzer, sterile injectables, the whole range of products that were standard for the industry. I spent 16 years there and then did about 12 years going through various biotech companies; these were the larger biotechs. In 2004/2005, I worked with Genentech launching Tarceva, a drug for non-small cell lung cancer, which successfully launched and became a blockbuster. Because it launched in the US and I was based in Oxford, they made me redundant. They were very kind to me. They sent me off with a piece of money to set up a business of my own. At the time, I thought it could be difficult, and it was quite difficult because selling supply chain management skills to biotech companies who wanted to make an exit was a bit of a difficult sell. I talked to a CEO of a small biotech, and I said, "Look, we could do this for your supply chain. We could make it more effective," and they say, "Well, I'm hoping to make an exit next year. So that'll be somebody else's problem. Hence, we don't need your skills". So that's what made me start to write because I realized I have to build an understanding in the industry that it's the supply chain that

delivers the product to the patients, the people who pay for it. So without a supply chain, you haven't got the business.

In 2008/2009, the editor of Wiley Pharmaceutical Sciences in Hoboken, Jonathan Rose, sent me an email saying, "I've seen the training you do on your website, and that format would suit the book quite well. So would you like to write a book?" Published in 2011, you kindly contributed a large section on QbD, Ed, which I'm still very grateful for. The final chapter explained how disconnected the industry had become, how it's full of handovers, discovery research handovers to development, and development handovers to commercial. No one can question whether a molecule is suitable for manufacture or not. I put in several suggestions about reintegrating, reducing the amount of outsourcing, linking discovery research up with development, so it becomes one design function. The book sold in 70 odd countries, but only as a sort of a niche application. So only people who are really interested bought it. I thought maybe people were changed, but not a lot happened. So I thought I would have to write something that's more accessible to the man in the street or easy to understand, and that was *Taming the Big Pharma Monster*. I explained how the whole dynamic over the last 40 years has been based on patents and how searching for a patented molecule has been completely unhelpful. You put that in with a degree of outsourcing and what I call outthrowing, which is dropping out to patent products when they've enjoyed their patent protection for all those years. I've become passionate about the whole thing, about change.

In 2017, I read an article by a gentleman called Bob Gaines, Robert Gaines. He wrote germ theory. He also wrote an article titled something like *75 Years After Penicillin,* and he explained penicillin, the whole end-to-end lifecycle of penicillin. Although Alexander Fleming discovered the mold, it took him 12 years to understand the active ingredient. It was Oxford University that helped him do that. They could make enough small quantities for clinical trials. They proved that this Penicillium, or penicillin, was working in animal models, and it helped a few soldiers in the war to survive. But they couldn't make any more of this gram quantity, so they flew to the forerunner to the FDA, the US Department of Agriculture. There was a guy there called Andrew J. Moyer. He was an expert and, wait for it, manufacturer. He knew how to touch a mold so that he could exponentially increase the yield. It was that process used then by the big pharma companies- Pfizer, Merck, etc., to bring penicillin to market. Moyer held the patent, and he was inducted into the US Hall of Fame in 1987, I think it was. So actually, it was a huge collaborative effort between the scientists who made the discovery, the chemists, and whoever isolated the API and ran the clinical trials and the preclinical work, but also the manufacturing guy. If they'd all been together simultaneously, instead of taking 16 years for penicillin to come to market, it would take maybe four years because they would have been looking at where we need to get to with this penicillin. It's a mold, and you would engage with a mold expert. That was a huge finding for me as part of the research I've been doing because Fleming was a doctor. He was a physician; Jonas Salk was a physician who invented the polio vaccine, or developed the polio vaccine, who never patented it. His researchers, the three who sold the patent for penicillin for $3, were physicians. In those days, doctors and physicians led the charge in developing drugs, and some of them even injected themselves with their compounds to prove that they worked. Manufacture then was regarded as an important part of the end product because they weren't committed to manufacture until you had the evidence that the drug was working. That's where I got *Taking Medicines Back to the Future*. If you could go back to Fleming's day and say, "Let's capture this, let's cut to the model that you've got there. And let's get everyone together at the start with healthcare professionals." First of all, we decide if we need a medicine. Is there some other preventative or some other way of dealing with this condition? If you need a medicine, then you bring all the right people together, and

> "The main point between strategic supply team management is you actually engage with the end user of your product the same way as Apple would or any company who really builds value into their products."

you plan the whole thing as one discrete development program the same way as you develop a plane, car, or anything else. So that's it. Not quite in a nutshell, but that's what I am today.

Ed Narke
Okay, Hedley, that's great. We'll come back to *Taming the Big Pharma Monster* shortly. So back to *Taking Medicines Back to the Future*. This is available on your blog site, Pharma Flow, if you Google that. I had a couple of questions, and you listed the underpinning principles for this concept. One of them that's interesting to me, and probably our group here and some of your clients, is when you talk about supply chains and how they should be designed strategically and make them simple and streamlined. Can you flush this out and talk a little bit?

Hedley Rees
I mean, I talk to excipient suppliers sometimes, and they say the guys who were developing that product didn't consult us. They didn't try and understand what's going to work, what isn't going to work. The main point between strategic supply chain management is that you engage with your product's end-user, the same way as Apple would or any company, which builds value into its products. You develop the product with your end-users, build the value, and then build your supply chain. You include your suppliers when you design the product. You don't specify that so and so will be the supplier of that excipient or so and so will be the supplier of that. You look for broader relationships with companies who are bringing expertise, so you're not buying products; you're buying knowledge from these companies.

There's one guy, Brian Carlin. He is well known. He's an excipient icon, kind of a classic. I had this conversation years ago. There's so much knowledge, yet they don't really get engaged in optimizing the process. As you go through drug product, then finding packaging…why do we have five or six stages? Why don't we make the whole thing under one roof? When I was a Bayer in 1980, we used to bring raw materials in the back door, and we'd ship our finished product out the front door to hospitals and clinics around the UK. We'd ship overseas to other Bayer entities, and they would do the same thing. So there was a direct connection with the business, and patients, hospitals, and clinics. It was so much more efficient having one quality system. The only sort of movements are the in the plant movements. You look at where we are now, and this is one reason why quality by design isn't working because it's going to cost you a fortune. If you're a clinical trial sponsor, you will have to buy that from the service providers. It's all in the supply base, and it's all fee-for-service stuff. I'm not saying there's not good quality service, but people think, "I'll do it the old way. I'll just pick the materials, and I'll do the minimum."

> "The value that you add – the money you bring in – has got to be less than the cost that you incur in the business and then you obviously make a profit grow."

Ed Narke
Right. So one thing that resonated, probably when we first started talking, I think I saw it was either a blog or a book, but it was called something like *How Your Supply Chain is Your Value Chain*. I think that was your concept, right? Whosever's it was, I use it all the time now to try to explain kind of what you're setting up here. Building a value chain there- from our end, if you have a good supply chain value chain, it could come back to you through the price of your product, meaning someone was licensing your product. There's more value created by a compliant process that's consistent in those types of things. Did you want to say anything more about the value chain?

Hedley Rees
Yeah, well, it's strange because it's still called the supply chain even in the more advanced sectors. But, again, as I've researched various books and things, Professor Michael Porter at Harvard is probably the world's best authority on supply chain management. He doesn't know it. But if you look at the Porter value chain model, he talks about the difference. Competitive advantage is a mix of value-adding activities. A value-add is not just some theory, but it's when people pay you money for what you're doing to that product when they come in and buy it and give you the money. So sometimes people say I'm adding value here because I'm doing something good. Well, if a customer is not going to pay you for it, it's not valuable. It's the same way all the activities you've got in the business, their cost, and the value that you add. The money you bring in has to be less than the cost you incur. Then, you make a profit grow.

Competitive advantage is created both by the value-added activities and the cost of activities, and they both work together. Porter talks about linkages about how primary and secondary activities link together. If I'm buying raw materials, the production line is having difficulties because maybe the supplier wasn't the right supplier to be with, so I can do my job in procurement. I can buy better quality materials, which improves the yield on the line or improves the performance of the production input equipment. In that sense, the secondary procurement activity creates a competitive advantage by improving the product. Every stage of manufacture is a value-added stage. If each stage does not create value, then it shouldn't be there. For some reason, even supply people don't like using the term 'value chain'. I think it's because it's seen as a business term. In contrast, it's a term that should emphasize that every stage of what I make has got to have more value than the one before.

Ed Narke
That's right. I don't know why they don't use it either. I just thought about it, and I think using it probably would create more value for their organization. To talk a little bit about Janet Woodcock, I know you have a lot of respect, and you followed some of her initiatives. For those who don't know, she was the former director of CDER, FDA; she had a lot of the QbD light and QbD big pharma type of initiatives that kind of transpired and went to someplace. What you said earlier was kind of interesting, the idea of having everything under one house and one roof. There's a dock at the back where it goes out in the bus or a truck or something.

> "In terms of procurement, the industry has outsourced this critical asset."

I think that we talked to a guy named Dave Adams who works for us; he's worked at Lonza as an API guy. He has a podcast coming, or it came out earlier this month. He talked to Meranda and I about how he started manufacturing in the late '70s when there was no GMP, no regulatory, and no QA. Everyone was called the manufacturer. It was a bunch of folks, from what I understood, that sort of learned on the job. They went in, and they got a job, there was equipment, they worked there for 20 years, they made things, they got better at it. Then suddenly, there were these concerns about safety and compliance. Folks start to know that safety issues are certainly a concern from things that happen when a product was shipped. So they standardized things, and then subsequently QA and regulatory came. That was an interesting progression at that time. I wasn't working at that time; I think I was watching cartoons or something like that, probably at that stage. I learned that there was an evolution, and I certainly see it now; I could see how they've transitioned some of the rules that they respect and hold up now versus when some of those that I worked with 15-20 years ago were different. They were just getting started, and they didn't know the system and the process.

Back to the main question. In the modern world and the days of Amazon and Zoom video, when you talk about putting everything under one roof and having stuff come in and go out, and everything's controlled, is that a possibility or reality, everything seems to be outsourced to make them, bottom line, look a little bit better without

trying to compromise quality. I agree with you to try to do QbD when there are seven or eight parts, machines in different areas with different management and cultures: it's not going to be possible. Is that possible to ever happen again, where everything happens under one roof? If you look at Big Pharma now, as most know, they're doing not as much manufacturing; it's outsourced. There's large CMOs, like Patheon and Catalent, who have absorbed that as sort of the outsource ease, and they've made giant, great businesses out of it. Barring, just going back to the '70s or '80s, is it possible moving forward? Are there any trends that you see that lead us to believe that we could get there again?

Hedley Rees
Yeah, a couple of things just to say about the supply chain in the drug industry. In 2015, I had an email from Regulatory Affairs Department at the Cuban Regulatory Authority, saying, "Would you kindly send us a complimentary copy of your book?" I would have thought they could have afforded one. So I sent him a copy. Someone I know at Lonza, someone I respect a lot, said, "I've just been to Cuba. They are doing all the things in your book. They're making everything under one roof. They're integrated." I suddenly thought, by golly, they've probably done it. You've got to do cultural and organizational things where you have to make R&D work as one unit, not as two separate units.

So that's one thing. The other thing, another seminar I've got a lot of respect for, is Professor Andrew Cox. He set up the first MBA in Strategic Procurement in the world at Birmingham University. He probably is the world's leading academic in procurement. He's got this concept of critical assets, deciding what you are going to make versus buy. You keep your critical assets in-house, you make them yourself, and you buy what's not critical. Now, product development has got to be critical. That is where competitive advantage is. I would say for small molecules; pharma has probably outsourced 95% of its development capability. Notice 10 years ago, they were called CMOs. Now they're called CDMOs, Contract Development and Manufacturing Organization. Pharma cannot develop a drug without the contract base, and there's no skin in the game. In the '80s and '90s, this is what pharma did to itself. It gave its old employees, set them out into the unknown, and gave them contracts for five years where they have to succeed. This is all written in *Taming the Big Pharma Monster*, so I'm not making this up as I go along. These companies have grown into mega-corporations that have become very, very successful. And why wouldn't they because they were just spun out? This is why there are so many field reps getting to market these days because the sponsors of the clinical trials don't have the capability. Between CMOs and CDMOs, it's all in the hands of third parties.

So in terms of procurement, the industry has outsourced this critical asset. Boeing tried that in the '90s. They outsourced, for the Dreamliner, a much higher proportion of their components, and they suffered an 18-month delay, a huge cost overrun, and they had to bring it all back in-house. Their strategy was to move the risk into the supply base rather than their own suppliers. But when you do that, you almost increase your risk because the people you're working with have the same level of communication and level of commitment. So the whole outsourcing thing, I would like to see a big pharma buy a CDMO and a CRO and say, "Okay, guys, let's put all this combined knowledge together, and let's make drugs for patients. Let's engage with hospitals, let's engage with the experts/physicians in these various indications, sepsis, Alzheimer's, blood cancers, and let's all use the skills that we've got." There are things you need to outsource if you can specify it, quite simply, like third party logistics is logical for outsourcing because you can say, "I want this to get from here to there. I want to use that motor transport. I would do this and that." You can define it so you can measure it. But with development, you can't be prescriptive. You have to sort of work with it as you go along. If the people you're working with don't have skill in the game because you chose that, you can't say anything when you don't get the drugs to market.

Ed Narke
Hedley, that's a great explanation. I'm looking at a picture of your *Taking Medicines Back to the Future* blog article on your Pharma Flow website here. I had some questions about it, but now it makes sense. It would be interesting if a sponsor bought a CRO and a CMO and, somehow, turned that into something unique. I think that's where you were going with that.

So getting on to some of the QbD actions, I know Meranda has a lot of questions about QbD. She's very knowledgeable but still learning. *Cutting Through the QbD Foliage: Aiming for the Roots First*, that's an excellent title there. I couldn't have come up with one better myself. It actually does explain it. The quality by design initiative, I think that's kind of how our group started. I worked in manufacturing for a couple of years, and then I worked in Big Pharma, and I had exposure to this, and this is when it was beginning, probably in the early 2000s.

> "The problem with pharma is that there is no competition because once you've got a patented molecule approved, the most that's gonna happen is you get an oligopoly where two or three companies make blockbuster revenue."

There was the intention to do real-time release and make changes without supplements, change control, and things like that. It all sounded great because it's like a modernization of what we used to do, which was having to maintain filings with all this data and how much would you put in. There's a give and take. It sounded like it was going to be a great thing. In my opinion, what happened was that the big pharma folks got tied up into it too much- high volume products, things like that. It became more of a theoretical thing. You had conferences based on QbD, and I think what everyone missed was that not everyone worked in manufacturing, like myself, and then went to regulatory and saw these buzzwords. At the same time, I was interested, and I said, "This is probably what I need to do and start talking about and embrace." I thought it was a great concept too. But what no one ever said, no one ever wrote anything about this, at least I haven't seen anything well written about it, was, QbD is just good scientific-based research and development- doing the things that you're supposed to do, laying out the plans before you execute, looking at what could potentially happen down the road, seeing things that come up and addressing them. I think that happens.

I worked at Lonza on a small product back in the late '90s, and they had rooms of notebooks and data and everything. It was for a big pharma product, and none of that information translated into anything until a submission was, I think, 30 pages, the latest phase three. There were tons of information, where the sweet spot was in the process, where the edge of failures was, whatever you wanted to know about the formulation, you had this, you change an excipient here. None of that was ever conveyed. The fact that they generate that much information was impressive. In my mind, when I saw that and experienced that, that was quality by design. That was kind of what you would say if we wanted to make an airplane the same way each time. We know if we use this metal, if we use this person, or if we build it here, you're going to know what you're going to get, you're going to be able to tweak this or that to make sure that the end product looks like what it's supposed to look like every time.

I think somehow some of the politics of QbD came in. I guess many individuals put it up there, and that was their claim to fame. It never really translated into anything. Now, not to keep going on here, but small, emerging biotechs, even back then, and of course, today, have very limited budgets. If they have a budget, it's about time as well. They don't have the time to put in all this money and generate all this data. They're racing to the market

because there's a limited window of time versus their competitors. A lot of them have an exit strategy. It's either the partner with a large company or to license the product out and pick up another product and start developing it. That was my opinion on QbD. I think it's still out there. It's always been. It's called great drug development, smart drug development, doing it the right way, not cutting corners, and stuff where you can't. Talk to us about that. I mean, *Cutting Through the QbD Foliage*- again, this is a blog on your website. You mentioned gifted scientists. From what I just mentioned, I believe this is for people that know how to develop a drug properly and appropriately. Can you explain what you were talking about there?

Hedley Rees
Going back to Janet Woodcock, she famously said in 2002, with GMP in the 21st century, she said, "Look, we don't want to regulate you, we want pharma companies to actually adopt best practices, and make their products to the highest quality levels." I'll give you an example. If you think of semiconductors, you think of a cleanroom; you think that the quality levels for these wafers. Now, I'm not an expert on this, but I know people who work in the cleanrooms in semiconductors. They are not working to those six sigma quality levels because someone's told them to do that. They work into those because they know if they don't, the competition will probably hit on any quality issues they've got, and they're going to lose business. So the problem in pharma is that there is no competition because once you've got a patented molecule approved, the most that's going to happen is you get an oligopoly where two or three companies make blockbuster revenue. The conclusion that I've come to is that unless there are changes to compound claims, patent law, where you can claim a molecule as your own, even though you've got no evidence, it could ever be a drug. It's incentivized the industry to turn away from the quality of the finished product, towards let's just get an approval.

If you've got a choice between solving a difficult problem or doing something that will get approval, very often, the wrong course is chosen. You can't do that in industries where it's competitive. The independent thing is that people think making medicines is different from anything else, and it's not. With a medicine, you would never predict what anything goes into a person's body, what that's going to do to the body. The body is the most complex, connected thing in the world. So when you talk about Alzheimer's, and people say, "Look, there's this amyloid-beta that wraps itself around people's brains. If we dissolve that, then we've got a drug." That's a theory. More than 30 late-stage trials in Alzheimer's have gone down, based on a theory. Like what happened with penicillin, with all those drugs. Those guys were building strong evidence that the molecule they had was working, strong evidence of efficacy to the point where Salk injected his family with the polio vaccine. Until they had that evidence, the drug didn't go forward.

Now, these days, predictive technologies have come on an order of magnitude than they were 40-50 years ago. You've got things like organ-on-a-chip, where you can predict what effect a drug will have on a heart, liver, kidneys, or whatever. There's been a lot of work done on that in universities, but the industry is not really harnessing it. We're sticking to the old let's test an animal model, throw as many molecules as we can. What is going to come through in the end? I think people are going to say this isn't good enough. Surgeons and doctors are starting to say that these latest CAR T therapies for blood cancers are patient specific. They have to take cells from the patient, and they go through a process called apheresis where they spin out the cells. That goes off to a manufacturing plant, maybe 300 miles down the road, stays there for two to six weeks, and by the time it gets back to the hospital, very often the patient's passed away because they were very ill anyway. The chances of that material being directed on those journeys, it's got to be cryogenically frozen. So the logic says, we have got to start to manufacture in hospitals. We have got to help build a cadre of skilled manufacturing people who are half-physician, half-manufacturer. I'm not saying all of it but using postponement strategies where you can discuss some of the operations so that the person is the person who actually treated them, the patient, their healthcare professional, they are the pilots of aviation. You wouldn't design a plane without talking to a pilot and engaging deeply with them. The passengers assume that they've spoken to the pilots, so this plane is safe. The number of patients now who want to get involved in the drug development process is incredible. If they could be confident

that these drugs will be safe and effective, they wouldn't particularly want to get involved. Still, the health care professional always has to be involved because he's the person who translated a disease into a medical intervention.

Ed Narke
That was fascinating, Hedley. It sounds like you have pretty good knowledge of the cell therapy space these days. We'll have to save that for the next podcast. However, maybe QbD can be implemented in that setting, in the hospital. That would be interesting. So, Meranda, you had a few questions about QbD?

Meranda Parascandola
Yeah, I was reading your article, and QbD is something that I've come across in my past. But unfortunately, I wasn't fully able to grasp it, and this conversation has been very enlightening. In your opinion, what needs to change? You mentioned the doctors being part of that change. Do you have any other insights on what might need to change to bring that back?

Hedley Rees
I think we have to reverse the system dynamic that has happened over 40-50 years. When the patent's awarded, and we ask for more evidence that that compound will get to market, it can be made in the sort of quantities it has to be made. Numbers of clients I've worked with, they've had tox failures in phase two. They say phase one, phase two, when that should never happen. We say you're not going to get a patent until you've exhausted the big prototype technology that we now have to prove that the compound has a future. Not beyond all doubt, but to a certain level of proof because that's what's happened. They always built the evidence that was going to work before actually scaling up in manufacture. One way would be to involve regulators in the patent approval process. In Brazil, they started to do that. It's still sort of a work in progress. Still, because you need people who understand science technology in the patent award process. I use the example that if I walked into the patent office and said, "I've got this molecule here, it's going to help the car tires hold the road more effectively." They say, "Okay, how do you know that?" Well, it was my molecule. "Well, yeah, but we're not going to give you a patent if you don't have any evidence it's going to work. We will reward you for putting in the work to prove that this will be a commercial success. So if you can't prove this is going to be a commercial success, you're not going to have a patent." In every other sector, you have to prove it's commercial. That's what the paper is about so that other people can't take commercial, intellectual property. In almost most of the molecules in pharma, there is no IP in there because they probably aren't going to fit the mix of safety, efficacy, and quality that the filing requires. Once you start to ask for more evidence, people developing drugs have to start talking to doctors to say, "Can we do a bit more testing on this compound with the patient, or can we try to understand a bit more." They start to build a knowledge of the compound. That's what QbD is about. It's about building knowledge and understanding of the compound you're developing, not just in the test tube but as you go in to make it.

That starts a dynamic because when doctors get involved the regulators get more involved. There's more pre-competitive collaboration. Again, it's a case in point with the COVID vaccine. Thirty sets in clinical trials, 200 in total with preclinical. Where's the value in all those companies all competing against each other in a race? No one's going to win that, certainly not the patient. We've got to get back to the days when Fleming had his Penicillium, and he was going around to people saying, "I found this. Can anyone help me find out what's inside it?" Once you start to do that, you get more drugs coming to market because people start to learn how to do it. The other thing that people have noticed is that you could develop a drug now without being a pharma company. If you're a rare disease organization, or there's one person I know, he's Chair of the Kidney Association, his wife sadly died of a kidney condition. He speaks in Parliament about it. He knows more about medicines and side effects and how different drugs interact with a condition more than anyone in the pharma industry. Now with what we know here about the drug development process, he could come to us if we had enough money; it wouldn't have to be the sort of money it cost to develop the moment and say, "Look, this is what you've got to do.

You need access to patients." Well, you've got that because of your charity; all the people in there have similar conditions. So it's quite possible now to develop a drug. I wrote an article two years ago, for the Catapult Medicines Discovery called *Patients Band Together to Develop Their Own Drugs*. This wasn't quite developing drugs because it was for diabetics, type one diabetics. They've got this hashtag #wearenotwaiting because the pharma companies aren't developing the technologies they want. They hack in, put in their own solutions together, and have quite a lot of success. They learn as they go along. You could argue they may well be more compliant than some companies who claim to be compliant. I don't know, but that could be the case.

Ed Narke
Hedley, this is always thought-provoking. As I listened to you, I'm looking at this title, *Taking Medicines Back to the Future,* and it makes perfect sense. I think you're starting another trend here. We're going to wrap it up a little bit here. Is there anything that you wanted to get out there, any promotional stuff for your books, any two-minute topics that you just want to touch on? Then we'll come back to that maybe in another podcast.

> "The body is the most complex, connected thing in the world."

Hedley Rees
Last year, I hosted a conference in Cardiff called *Medicines for The 21st century: Safe, Better, Cheaper*. Janet Woodcock recorded a 12-minute video for that, which I still have. I don't know that she has done anything like that for anyone outside of the US. Still, they also have the critical path initiative and GMPs for the 21st century, which to my mind is a roadmap for actually getting engaged with doctors, biomarkers, clinical trials, but that hasn't gone anywhere, either. But from that conference, there were about 60 of us there. We identified seven areas for improvement around the supply chain, intellectual property, education, and those sorts of things. I wrote a white paper from that, and that's gone to UK Parliament. It's where the health and social care committee asked them to hold the inquiry into patent law. Now, it's politics, nothing may come of it, but the key factor from that was education. So my next project is building digital education in the sort of things we're talking about now: strategic supply chain management, quality by design, basically describing this concept of where healthcare professionals are a part of the drug development process and integrated part of it, and helping them to understand the things that they need to know, simple GMP, simple GDP. I've got 10 to 12 people from the olden days; I shouldn't say olden days, but the people who were there when the World Cup was first started, like Emil Kozik and Brian Carlin. So there's a range of those people, and I'm asking them for feedback on what they think we should be doing to move this forward to have more involvement in drug development. So I'll be keeping you up to date on that as well.

Ed Narke
We'll certainly add a link to that video. That was impressive. I think we've all been fired by Janet Woodcock and some of the things she started to bring about at the FDA. You could certainly see some of the changes that have come into effect, especially with some new technology.

Hedley, it's always great talking to you. I just noticed how much you recognize individuals out there and empower people and recognize them for what they've done. I heard many names. Brian Carlin, I think I've met, and Janet Woodcock, through guidance and initiatives and those things like that. You mentioned Jonas Salk. You can't see this out there in the podcast, but I have the University of Pittsburgh flag behind me. That's where I went to college. That's where the famous Salk vaccine was invented, 1957. So, Hedley, you're a famous author; you don't know it for our industry. You're a pioneer for value chains. You're still a leader in these initiatives, so keep it up. *Taming the Big Pharma Monster by Speaking Truth to Power*, we can find that, I guess, on Amazon these days, or you can Google it, right?

> "The other thing that people have noticed is that you can develop a drug now without being a pharma company."

Hedley Rees
Yes, it's on Amazon and also on the eBook platforms. It's difficult getting the platforms to say these sorts of things. I remembered in 2011, you put an endorsement on my LinkedIn profile, which encouraged me because, in those days people saw me as a bit of a heretic and a bit of a sort of left-field player. So I do thank you for that, and I'm sure we'll do more together and help drive change in this industry.

Ed Narke
Right. Also, finally, I learned it all from you, and I'm not complaining about it. So thanks so much. Talk to you soon.

Hedley Rees
Okay, you take care over there. Cheers!

Ed Narke
On our next podcast, Meranda, Brian, and I will be talking about the CTD Module Three. Though the content of these modules is generally well defined, considerable latitude for assimilating, discussing, comparing, and contrasting the data is allowed, even encouraged. There will be opportunities to get creative, tell a story, and craft cohesive arguments. Join us then for an in-depth discussion.

FDA CMC regulations and guidance simplified through examination, real life experiences and risk-based advice. This podcast hopes to educate sponsors and individuals on agency-related regulatory CMC matters. We will focus on the critical CMC issues and build programs that enhance drug development. CMC topics will include Regulatory Starting Materials, API and Drug Product Process, Formulation Development, Supply Chains, Analytical Controls. Advocating and interpreting CMC Strategy, directing CMC Operations and Quality Assurance oversight in conjunction with developing CMC submission content that represents the best interests of emerging biotech. NOT INTENDED TO BE PRESCRIPTIVE ADVICE BUT RATHER INTERPRETATION THAT IS RIGHT FOR YOU. Since 2007 we have provided our partners with innovative strategies and exceptional advice intended to enhance program development, product approval, and marketing presence.