Establishing Regulatory Starting Materials & Understanding the ICH

Episode 2

Ed Narke
Welcome to this week's podcast of CMC live. Once again with my co-hosts, Meranda and Brian. I am your host Ed Narke. We are here to educate and oversimplify, and under simplify in some instances, the regulations and expectations out there based on our experiences.

Joining us once again, Dr. Jim Mencel, a colleague of ours who works in API/ Regulatory areas, mostly working with clients in small biotech companies. Typically, with programs that have short timelines, limited budgets, and a board of directors who like to get things done quickly without spending a lot of money.

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Jim, welcome to the show today. Today, we are going to start with a bit from last week. Last week, in podcast part one, we discussed expedited drug development and breakthrough designation therapies. For the folks that have not heard that episode yet, or as a recap, there are a few situations out there where companies can get some expedited approvals based on some trials and data that they get from clinical studies. The problem has always been the acceleration of the CMC program. A lot of the time, those pieces of data and those types of programs still need time, and they cannot be expedited. Thus, the CMC sometimes becomes the bottleneck, or the showstopper, at the end to push programs out too far.

Today we are going to get into some of the more specific areas and items that folks would have to deal with. Jim is a great person to talk to about this. One of the reasons I mentioned he is also sort of an unofficial regulatory expert here, is because he has had a lot of dealings with these types of programs. One of the major discussion points and debates lately, in the last eight years, has been establishing regulatory starting materials and the importance of starting with the ideas around that. Everyone has a bit of a different take on it. In the last eight years, there has been a dramatic increase in process understanding. Now, folks want the story behind the story. For compliance, it is much more frowned upon to commit extraordinarily little data, unless you're holding it in your pocket. Most of the small biotech companies out there have limited data, just because of the funding and they tend not to make a lot of Lots of material.

Most recently, I guess it was 2010 or 2011. The ICH, which is the International Council for Harmonisation, pulled together the ICHQ12, which had a lot more information on establishing drug substance process controls,

and provides a little bit of flexibility in the selection of starting materials, depending upon scenarios. Q11 creates an environment where sponsors can develop a process understanding that accommodates any changes in the future. As well as methods of synthesis and changing your starting materials. All of the data that is generated and required is for patient safety. So, these principles assure that a starting material meets the requisite technical and quality elements to allow for commercialization. Commercialization is, essentially when you submit your marketing application, your NDA, or BLA. This is information that we would provide in there [NDA or BLA], you would be accruing it throughout development.

With that said, drug development has always been forced and companies have always been forced to balance the need to get to safe and efficacious profitable drug products. Not everyone could be a large, vertically integrated, Big Pharma. This is kind of how our group [DSI] comes in to help. So, we invited Jim on here today to talk about some of the issues. Jim, welcome once again, at this point, timing. I think a lot of the questions that we get from clients are, "when do you need to justify or just start thinking about a regulatory starting material?" Any thoughts from your experiences?

James Mencel
Well, my view is that you need to start thinking about it as early as phase two. You could even begin thinking about it earlier. There are several reasons why you're going to get to a point where you've got to decide where things are going to be made. Anything up to the point of the regulatory starting material can be made non-GMP. Anything from the regulatory starting material and onwards is GMP. As you begin to think about the CMO you are going to use, also think about what sites they might have, and even the cost of goods for your material. Knowing your regulatory starting material can have a lot to say about where you might want to run certain parts of the process.

The other part of it, it takes a fair bit of time to develop a package to support a regulatory starting material proposal to an agency. The better packages are supported by data. For example, knowing your process and where impurities purge, knowing the points where you crystallize and knowing the things that could contribute to the quality of the proposed regulatory starting material. The reason this is important is that the stronger your packages, the more likely you are to be successful in your proposal. Now, the FDA will listen to a scientific argument. There are guidances as you said, in ICH Q11, which the FDA truly sees as guidance, and they will listen to a scientifically reasonable proposal, around those guidances. The better your proposal, the more likely they are to respond. Typically, if they do respond in the affirmative, it's more like, "okay, we're agreeable to this. We'll want to see X, Y, and Z going forward."

During the review period of the NDA, we will then comment finally. But at least having that nod upfront is unbelievably valuable. Also, having them say "no outright" can be very valuable as well. Now, when you deal with the Europeans, it is a different situation, they treat the ICH guidances more like rules. In that instance, it's very important to figure out how closely you fit to what might be a more rule-based approach. For example, is a material

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commercially available as a commodity, as opposed to intermediate. The sooner you begin thinking about this, the better you can begin to formulate a plan for how you are going to support what you want to propose.

The other particularly important thing is to know your fallback position. There might be more than one. The important reason is that you have to start thinking about what the chemistry would look like if you had to fall back. That chemistry that you would have preferred to run non-GMP, would become GMP, which means it needs to be very carefully controlled and needs to be profiled with things like proven acceptable range experiments or normal operating range experiments. I suggest that as soon as people have the process identified, they should identify where their starting material may be, build a case around it, and do their internal test run as to whether they feel that they could support their argument.

Brian Lihou
I have a question for you, Jim, if you don't mind. It's not uncommon for smaller companies to have a division on that position, when to commit this and when not to commit, and there are fixed budgets involved. How do you approach a client that doesn't have that same viewpoint, and you need to explain to them the pitfalls of not following that or not trying to consider FDA and EU expectations for ICH at an early phase? How do you reconcile that with what you know you need to do, and the client may want to dig their heels and go the other way?

James Mencel
It's not uncommon, Brian, what you're asking. Even CMC teams at companies are often reluctant to approach the FDA because they just have this perception that they take a big risk even if you're not prepared to do so. The best way I found to help clients understand the need to approach, is to describe what has to occur as a consequence of knowing or not knowing.

What it comes down to is, when you are having these discussions, you're probably coming somewhere close to the end of phase two. Let's talk about a normal program that's not expedited, right? They're going to be making their pivotal trial materials at the end of phase two. This more or less locks the route in place. It becomes very difficult to change things after that point. If they know where their starting materials are going to be, they can also begin to look at putting that at the site where it should be. There are very few companies that are not aware of the fact that there's going to be a cost of goods element that they're going to have to sell to their investors.

Let's face it, if they can cut out three steps of synthesis and make those non-GMP and run those somewhere that's less expensive, for example, India as opposed to running them in the EU or the US, there can be tremendous cost savings on that program. So, there are several angles. One is the cost angle, the sooner you know, the sooner you can begin to move this to a less expensive place. The other thing is, the sooner you are ready to propose, the sooner you'll hear FDA or EMA response. This can be very telling because if they disagree, you immediately know you're going to your fallback position. So, knowledge is power. And to the extent that you could support a proposal, why would you not put that out there and know where you stand?

I see this as being an advanced scout watching another team play ball. If you could stand on the field and watch how they approach the way they do things, you're prepared when you face that team yourself. I think that if you can approach the FDA and say, “look, here's what we have based upon the guidance, what do you think?” I think you are better off than waiting until when you have to do it because you've run out of time. You really aren't prepared.

Brian Lihou
You said something interesting, it was it was very quick, but you referenced that fallback position. Do you recommend to clients to begin to understand and comprehend that there may need to be a Plan B? And how often or how early do you work with clients to develop that Plan B?

James Mencel
Early, I think that in addition to considering where their starting material would be, they need to figure out that if that is not accepted, what is the fallback? Now, I'll qualify that, Brian, and say if the proposed materials are intermediate in the process, it's more difficult to sell. Not impossible, but more difficult. If you have an intermediate, you're proposing, then you need to think about if this one doesn't get accepted, how far back can I go where I feel I have a more secure position? How far back do I want to go? You might need more than one spot. Now, it's going to be very rare, this will occur if you're proposing a commodity. In a commodity, in that case, it's a material that's already sold in commerce. It's more a situation where you have an advanced intermediate that you're proposing as a starting material, that you know may not get accepted and that is several steps away from something else. You have to deal with what that something else is. I ask people to plan both at the same time so that they are ready to support the primary position and also understand what it would take to support the secondary position.

Ed Narke
So, Jim, that's that was great. I'd like to step back because there may be folks joining us for the first time today, or who may have not had the familiarity or experiences with discussing this. From my angle on the regulatory background, from a regulatory perspective, it sounds like there are no universally right or wrong choices. There is nothing in the guidance that is going to prescribe exactly what to do, each program is different, right?

Ultimately, you mentioned sourcing, you mentioned you're aware of several steps. Just for those folks who are not familiar, the term regulatory starting material has been adopted by the agencies out there to indicate the point where regulatory change control happens. Now it's also the point where GMP is expected and introduced into the synthesis of a drug substance. Any changes prior to the regulatory starting material, I wouldn't say they're not important, but that's the reason why we've established that point. That's where any changes before that point, should not affect any of your API or ultimate drug products.

So, going back to there are no universally right choices, that was mentioned earlier. I'd like to focus on some of the strategy areas. Ultimately, in my opinion, the regulatory starting material substance boils down to the issue of impurities if you have a fairly long synthesis system that's very clean at the very last steps. I've always had success making that case versus even a short synthesis where the impurity profile changes, you know, based on what day it is.

So, looking at a few things, can you talk to some of these: lengthening a synthetic route, where that route starts, does it have to be three steps prior does it have to be five steps prior, where does that GMP start? The second thing is limiting the production of the RSM to one or more approved routes. You know, have you had experience or thoughts on having multiple routes that feed into, and then also how that affects GMP and where GMP starts. And then third, limiting the manufacturer to a single supplier, you may also have a similar process, very simple or maybe a little more complex coming from two different routes. Maybe one's coming from Asia, versus one that is coming from Europe. So those three things, can you speak to any of those regarding how the FDA and also sponsors deal with establishing where GMP starts and regulatory starting materials?

> “One of the crux issues with choosing a starting material is the whole case you can make about how you purge the impurities from that point forward.”

James Mencel
Sure, I would say that one of the crux issues with choosing a starting material is the whole case you can make about how you purge the impurities from that point forward. Okay, for example, I like to think of things in terms of flow diagrams, right. If you make a flow diagram from the molecule you're going to choose, and you look where in the process are their points of purification: they could be extractions, could be a crystallization, some processes include chromatography, but what you need to do is to find where the points are from that spot, where impurities can be purged. The more specific you can be, “this specific impurity in this material is purged at this step.” You know, it goes to this level. If you have spike and fate of impurities studies from that point where you know the impurities that are present in that material, and you spiked them and enhance levels and you track their purge and their fate throughout the process, that all strengthens the argument for understanding what kind of controls you need to have on that proposed material and its quality. That's the downstream. That is saying, okay, so you talked about how many steps from the end. You know, I don't know if there's going to be a governing number, but what I would say is clearly more steps, especially steps that include crystallization or purifying events is better. Steps that include bringing impurities into the process are not going to be better. Steps can work for or against you, that is the downstream picture. There's the upstream picture too, and that is, what do you know about what controls the level of impurities in that proposed regulatory starting material? What do you know about how you're going to control its quality so that those impurities are below certain levels? You could set specifications for that material that you know from your spike fate and purge studies, or manufacturing experience will purge so that your API is going to pass specifications.

It's important to look at the starting material that you're proposing in the context of what contributes to impurities. By the way, this includes metals. This can include rogue solvents like benzene or chloroform. You need to think about what's the contributor coming into it. How do you control that? Then the next thing is from that point, how do you understand that material in context to what it contributes downstream and how that purges? You need to look very holistically at that material at a spot in the synthesis and how you're going to control or convince the FDA or the EMA that you control the impurities coming from it. The better the case you make, the more likely they are to say this is an acceptable material. I hope that answers the question.

Ed Narke
It does. I'll move forward here. Just having flashbacks of when I started in manufacturing, I worked at a company called Lonza. A well-known CMO out there that does a lot of chemistry. At that point, I moved into regulatory, I guess that was 20 something years ago. The guidance, the regulations, the exposure, experiences, offshoring, and all these things come into play which almost changed the way we looked at starting materials and where GMP starts. I think it was 1987 the original drug substance guidance, it was pretty clear cut, very prescriptive, you had to incorporate into the drug substance’s structural element, and it has to be commercially available.

I remember talking with different suppliers, most of them selling materials that were going into the tire and automotive industry and we tried to make a case that it was commercially available, and you can see where that goes. It had to be made by common procedures, I think that's where you know, the FDA -- this is before ICH -- started to say it's too prescriptive, not one program can fit into that and be the same. In 2004, they drafted a new guidance that stuck for a while, called the Guidance for Industry Drug Substance. That's the one I remember,

that was my Bible. Same thing though, very prescriptive. Towards the end of when I was working at large pharma, ICH Q11 sort of came out on top of Q7, which sort of defines where GMP.

I think we talked about this once or it might have been someone else that works here at DSI, how we ourselves could have written ICH Q11 based on our experiences at toll CMOs, toll manufacturers, because we would just watch what they would do, and we would write down everything. Essentially, it's good drug development, its sound drug development process, understanding, finding your sweet spot, knowing about your operating parameters, knowing what's critical in the process steps, and then just generating data, even on the scale, if you can. Would you like to share a few of your thoughts on ICH Q11?

James Mencel
Well, I think it's a great document, Ed. Here's what I would say, I'll go back to the sports analogy. If you were going to show up for the Super Bowl, and the other team was going to give you their playbook and say "here, here's our playbook, here are the plays we're going to run for every one of these downs and every one of these quarters", you'd be crazy not to take that. The FDA essentially has given you, their playbook. They are saying, "look, we've been through a lot of games here. We've played a lot of games, with a lot of people, here are all the things we've seen that they didn't do that they should have done, okay?" I think if you're in this business, and you're an API guy, or a drug product person, and you want to be a good scientist in the business, you cannot - not read those guidances. The FDA is opening their playbook and they're saying, here's what we want to see, here's how we suggest you think about this. I feel that the later Q guidance's, the 8, 9, 10, 11, and now 12 (the one that's in draft about post-approval change), I think they're fantastic. I feel like I could have written ICH Q11, myself. Anybody that did process chemistry, that has paid attention to what they've done, that has suffered things that didn't go well, could write that document. I think it's a great document from the context of the regulatory standard materials, of course, there is a component in there that speaks to them. Then there's the ICH Q&A, which is a document sent out to clarify points in ICH Q11, that even goes further into the starting material piece. Yeah, I think it's a great document. I think that any process chemist should read it and understand what's being looked for.

Ed Narke
Okay, you set me up for this one, I have to say it, it's a sports analogy again, it's kind of like the Patriots. Right? They have the other team's playbook, though, so they kind of know what's coming [laughter].

James Mencel
That, or a deflated football, one or the other.

Ed Narke
Oh, that's a different topic for another podcast. To carry on, the ICH had an evolution of guidances and regulations, the 87 just did not work for 90% of the folks. Very manipulable to get what you want but did not help with the quality portion. In 2004, you know, the evolution of the FDA. Then you mentioned the ICH guidance's harmonized, discussed, and evolved There was a point where there was a lot of discussion about QBD, if anyone remembers, Quality by Design, and I think that was kind of in the midst of when those two ICH 11 and 10 – actually 9, 10, and 11 were written. I still sometimes get questions about QBD, and for those that don't remember QBD, or have never heard of it, it is something called Quality by Design, it was an initiative by the FDA. Essentially, if you did a little bit of this and a little bit of that and generated some data and got to understand your process, you would be provided with regulatory relief, meaning that you could make some changes without oversight, just have them slip through.

Unfortunately, it didn't work out as planned. It sort of fell by the wayside and I could probably express this, it was a large pharma initiative, a lot of high volume products, as well as, storage, and cost, and those things came

into it. However, we work with a lot of small emerging biotech's, and we still see the traditional approach, three batches, Certificate of Analysis batch records, but there's not a lot of process understanding. We do see though, you know, working with the vendors and the CMOS, some of the enhanced approaches. There's a lot more collaboration these days with small biotech companies working with their CMO. In some cases, when they use consultants, and we've had the pleasure and luxury to do this, we can help guide the CMOS based on the fact that we know a little bit more about the business model, and what the end game is for the sponsor. Meaning they might want to license it out, they might want to know a little bit more about their supply chain to make it a value chain versus in the past. The question is the traditional approach, providing minimal starting material information about the impurities, for example, defining and maintaining tight specs for starting material. That is the way, it's quality by chance. We have no information and we'll set tight specs and we can make it. Now large companies can do that if you're going to dump a few batches, but we know from some of our clients and some of our experiences, that's not the right thing to do. You don't want to set a spec too tight, not knowing a lot about the process.

Some of the enhanced approaches that we've seen, - and this is where you might talk to them - selecting materials based on scientific understanding, looking at pilot scale, and some scale-up study, some of the factorial design work that might be done in development to draw some conclusions to make some more intelligent decisions on setting specs. Providing some of this information in the conformance sections of an NDA, some of the manufacturing process development to help the reviewer understand that you are controlling understanding your process. Then, of course, the big one, you mentioned earlier, understanding the source. Certain parts of the globe have some higher standards or different practices. Ultimately, you mentioned, and I'll leave it at that, the formation and the fate of purge of impurities. Two or three of the programs that I worked on, sort of saved the day just to have all that information on the fate of the purge of impurities. So, talking about the enhanced approaches, which is kind of an offshoot of the QBD. For those who are out there who are interested, where is QBD today? Versus the traditional approach where some companies still employ, can you talk to some of those different approaches to follow?

James Mencel
Sure. By the way, I was a big believer in QBD, it came out when I was still very involved with generics. The idea behind QBD was that you built the quality into the process. There was a train of thought that you would release the material, and that was the controlled quality with an option to reprocess it. In other words, a lot of time, the FDA would go in and everything was based upon whether the material passed or failed its final release specifications. So that was where you figured out what you had.

Now, I have to say some companies were not very good, but some ran just like that. QBD was designed or intended to do, was to force scientists to think about what things you need to control, as the process is going forward, that eliminates a problem upfront, so you don't have it later on.

> "I think it's [the ICH Q11] is a great document. And I think that any process chemist should read it and understand what's being looked for."

Let's look, for example, at a class three solvent, suppose early in the process, you use butanol for crystallization, right? In a Quality by Design program, if you test the crystallized material for butanol and it passes, you will never have to test for butanol again, if you don't use it in the process. The same is true for a potentially genotoxic impurity. Suppose you have one early in the process. If you validate a method to test for it at step two, in an eight-step process, and it passes at step two, it's not going to grow. You don't need to pass a test for it in the API. The idea is that when you do a quality by design approach or an enhanced development approach, you want to know as much as you can about your process, and where the things that you need to control are and how do you

control them. The whole idea is to put the controls into the process you're talking about setting specifications. Your spike, fate, and purge data are very important. Instead of setting specifications that are tightknit because you're afraid of anything, you spike a certain amount of an impurity, you have to have the impurities or find a dirty batch. You spike them in, and you run the chemistry downstream. What do you see? Do they go away? Also, you should do a paper exercise, what could they turn into in the chemistry? All of this is understanding your process, what it will do, and what you need to control. You could talk about enhanced development, but really what it is, is people paying attention.

I have a colleague from Sandoz, and he talks without end, about how well they develop processes there because their scientists used TLC plates in the 70s and 80s. They understood every impurity in that process of where it went, what it turned into, and how they got rid of it. He said that when he looks at these guidances he feels like he's being told something that he learned early in his career, that people just seem to have forgotten. I kind of agree with him. He's one of our DSI colleagues, a very good friend of mine, but I think he's 100% right. He sees the statistics as going overboard. A lot of people license statistics. When you design experiments, where you change multiple variables to see what affects, you need the statistics. What it comes down to is, you want to try to understand what is making your process tick. If you get some new impurity, the process is telling you something. Where is it coming from? Sometimes you get impurities, you can't get rid of. How do you deal with an impurity that does not go away? Part of your planning approach would be “well, maybe we need to spike that into a toxic batch.” It comes down to thinking ahead of time. What do I need to do at step A? Have a process that goes out to step G, every step along the way. So, if I have things that form, I know how to get rid of them, or I don't form them. I hope that hope helps answer your question.

Ed Narke
Yeah, that is great. I think these tie together. Just thinking about ICH Q11, again, for those who are not familiar with it, check it out. I think I asked Jim, where he kind of explained it along the way, how to conduct an assessment. You are trying to establish your regulatory starting materials, any changes that you foresee or data that you have operating conditional changes near the beginning of the process have a lower probability potential to impact the quality. Having a strong impurity profile, knowing what is in there, having the right methods in place, the qualified method set the time earlier on, especially if you have a risky synthesis. We also talked about some of the analytical, we will leave it at that though.

I guess it is open for discussion here. I think Brian is more of a drug product guy, but he may have a few questions. Kind of getting close to the end here, I would like to talk about where do we go from here? We talked about some good science, not necessarily exhaustive science, that's imperative. Small biotech’s are spending a lot of money on their clinical studies. As everyone knows in the audience, if they have done this, you know that a lot of the budgets are postponed or withheld from CMC until the very end and that is where a lot of the concerns come up. Sometimes, unfortunately, products that are delayed because of that, there is not a lot of leniency or relief for not having compliance data. Essentially, you are held to the same standard and a breakthrough designated program expedited, there might be some ways to discuss things early on or commit to certain things but, you control the process, and the product is still there from the substance to the product. There is no single template that drives these decisions. Every sponsor program is different, every sponsor has a different mindset, sometimes culturally. Also, an end game, do they want to commercialize this find second sourcing? Take it to a certain point and let the next investor buy it. The justification of regulatory starting materials and any choice of the synthesis, I would say is a balance between appropriate regulatory control and adhering to the guidances and sustainable manufacturability. - That's another thing. You can't make batches and just discard them, right? You want to kind of use them. - Then, a variety of factors can impact that practicality based on each company.

Any other thoughts? I think this is a topic that continues to be hot in the news. As we know, Jim, every day we get questions around this topic, regulatory starting materials, especially in light of a program that is an expedited program.

James Mencel
I could add some thoughts, Ed. One of my favorite quotes is from Yogi Berra, "you could observe a lot by watching," right? There is an awful lot that you could do that does not cost anything, a lot of the time people miss this. I think you guys have heard me say this. When the process is being run, puts your ear to the ground as a chemist. Be a chemist. We are not in the plant, okay. We are consulting, but we have been in the plant. We studied chemistry. I have more textbooks on the wall than I can remember. Let the process talk to you. It tells you things, okay? The phases do not split.

My belief is to pay attention when the processes beings to run, make a process flow diagram for yourself. What goes in? What comes out? What are your in-process controls? What are your specifications? Does it all make sense? You could do this with a piece of paper. It doesn't cost anything. Pencils are cheap, paper is cheap. You could use Chem draw as I do. The way I often do it is in my backyard on a nice day with a pencil and paper. I do the process out of my head. What's going on with this process? You observe a lot by watching, just watch what the process is doing. Write it on paper, compare what you see happening in the plant or the Kilo lab or the research lab with what you have on that paper. You will be so educated by what the process is doing, and that will guide what you do going forward and save money because you will focus on the things that make a difference and know which ones don't. When you do not have a lot of time to develop a product that matters a lot.

> "What it really comes down to is you want to try to understand what's making your process tick. If you get some new impurity, the process is telling you something. Where is it coming from? Sometimes you get impurities you can't get rid of. How do you deal with an impurity that does not go away?"

Ed Narke
Okay, so again, back to the process understanding, right. It is not that difficult, and I don't know when the last you open those textbooks, but I have a couple over here. I don't think I opened them the first time. I was in the process of fix, process development, and transfer, so a lot of the stuff was already known. I just pulled a couple of those leavers and valves.

Anything else, Meranda? Meranda is our Head of Business Development here at DSI. She talks to a lot of these small emerging biotech's out there and gets a lot of questions. I think I just saw one come across my email about an early-stage program and an IND, not to put you on the spot here, but if you have any questions for Jim, right now?

Meranda Parascandola
Not necessarily, not for regulatory starting materials, it is kind of something that I never dug into.

Ed Narke
Right, right.

Ed Narke
As a cheap shameless plug, I will throw it in there, on our DSI website, dsinpharmatics.com, we have an "Ask the Experts" page, and we open this up to anyone around the world globally to send us a question. For the most part, we can address the question high level but without facts and details and some of those things, we would prefer to have a discussion. We have done this for 14 plus years, with about 200 different programs. We have seen a lot of atypical situations

and a lot of missing data, a lot of very aggressive very short syntheses, and things like that. On that note, maybe Brian, anything in closing here, and then we can wrap?

Brian Lihou
I have learned not to go past a Yogi Berra quote. So, I think, Jim, you summed it up perfectly. Really, honestly.

Ed Narke
Well, I think Bill Belichick is going to be sending you the playbook next week. I will make note of it and tag him on Twitter with this podcast. Anyway, on that note, stay tuned for new future episodes on this, maybe developing in different areas.

With that said, I am Ed Narke hosting CMC live with Meranda and Brian. Once again, thanks to Jim Mencel, Dr. James Mencel of DSI, here for his experiences for the last 35 years.

James Mencel
My absolute pleasure.

Ed Narke
Thank you.

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 AN 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.