JOHN A. MERHIGE, CREDENCE MEDSYSTEMS

John A Merhige is Chief Commercial Officer at Credence MedSystems, leading the business development, sales and marketing activities. Previously, he was Vice-President, Market Development at Sanofi BioSurgery. Mr Merhige came to Sanofi upon its acquisition of Pluromed in 2012, which he joined in its early stages. Prior to Pluromed, he founded Prelude Devices and previously he gained general management and commercial leadership experience at Ford Motor Company and Avery Dennison. Mr Merhige graduated from Dartmouth College (Hanover, NH, US) earning a BA, a BE in Mechanical Engineering, and a Masters in Engineering Management from Dartmouth's Thayer School of Engineering and Tuck School of Business.

Here, in conversation with ONdrugDelivery Magazine, Mr Merhige discusses Credence's Companion Safety Syringe System, new advances in the product development pipeline, customer/market driven feedback from user studies and exciting developments planned for 2018 that will take the company on to the next major phase in its growth.

"With our staked syringe, the staked Companion, the drug companies will receive sterile syringes with the needle mounted, just like they do today, in three-inch tubs, just like they do today."

Q It has been a couple of years since we last spoke (see Issue 64 (Feb 2016), pp 34-35) and there are exciting new developments to discuss. But before that, could you bring new readers up to speed? Introduce Credence MedSystems, tell us about the Companion Safety Syringe range, and explain how the Companion enables Innovation Without Change.

A Credence MedSystems was founded in early 2013, so we're into our fifth year. We're located in the San Francisco Bay area, right in the heart of Silicon Valley, which is the home of technical innovation. This location has been a big part of the fabric of who we are as a company. Our mission is to provide innovation in injectable drug delivery to our pharmaceutical manufacturing customers.

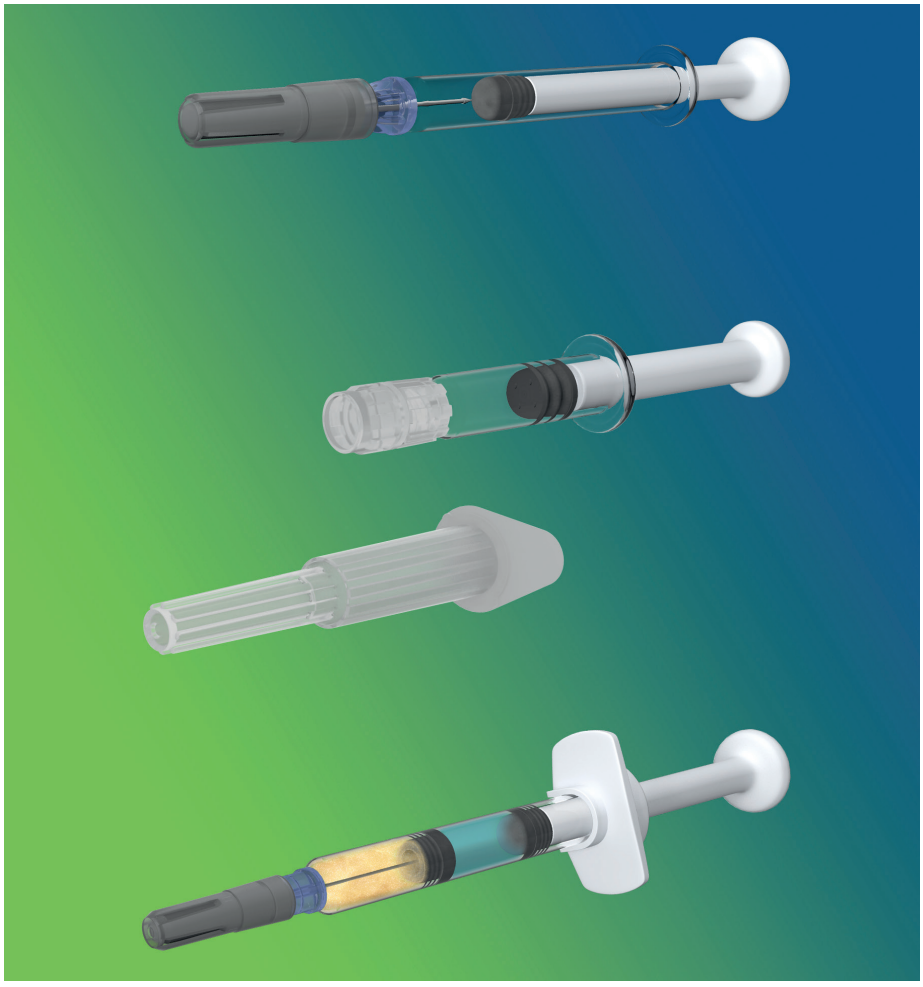

Figure 1: The Companion platform. The Companion staked needle syringe (top), the Companion luer lock syringe (middle), and the dual-chamber device for reconstitution (bottom).

I think one of the points I made last time we spoke, and it is just as important today, is that we have a great team of people. They're experienced, they love what they do, they care deeply about the impact our work has on patients and caregivers in terms of protecting them, enabling successful injections and compliance with prescription regimens. This is the core of what we do. But equally important, we like and trust each other and, when you're in that kind of environment, coming to work is easy because everyone is supportive of the mission and everyone is going in the same direction. It's a special place to work.

You asked about Innovation Without Change and that is our core philosophy. I would expand upon the question a little because Innovation Without Change is not just about our product line. It's also about how our business model achieves Innovation Without Change. We have shaped the business model and the design and development of the products on that core concept of maximising the innovation that is delivered but minimising the disruption to our customers when they implement the technology.

It always makes sense to start with thinking about the end user – whether a healthcare provider or self-injecting patient – and the experience they have when using our devices. Across the Companion platform (see Figure 1) we provide a very consistent experience. At its most basic, the user performs an injection, they hear and feel a click when the dose is fully delivered, and then the needle disappears. It is retracted back into the plunger rod and the barrel of the syringe (Figure 2).

That experience sounds like needlestick safety, and certainly passive and integrated needle safety is an element of it, but the Companion goes well beyond that. The protection element encompasses needlestick safety of course. Reuse prevention, so that needles cannot be shared across users, is also important. But that element of protecting the patient also goes to the integrity of the drug as well. For example, our devices don't use glue to attach the needles. Removing glue from the system removes the risk of unwanted interaction with the drug product. It also enables flexibility in silicone minimising techniques. We also have options that remove any contact with stainless steel or with tungsten.

Beyond protection, with the Companion users have a familiar-looking syringe in their hand. It doesn't look disrupted by the technology because all of the technology is integrated into the syringes. That consistent experience across the product line provides an enhanced user experience that extends further than injection safety into ease of use with the goal of enhancing patient compliance.

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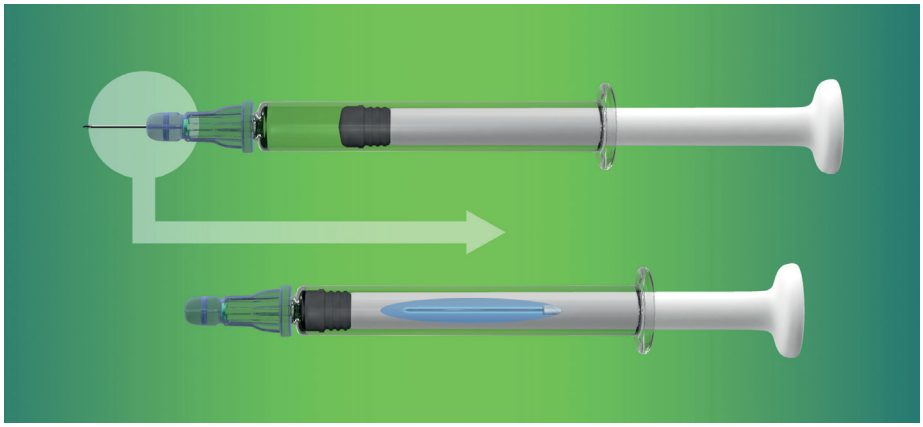

Figure 2: After the user performs an injection, they hear and feel a click when the dose is fully delivered, and then the needle is retracted back into the plunger rod and the barrel of the syringe.

Protecting the caregiver and patient, protecting the integrity of the drug and improving compliance are a big part of what we do. And this is all wrapped up into the Innovation part of Innovation Without Change.

So, turning to the Without Change part of Innovation Without Change; this is about product design and business model as I mentioned earlier. Using existing primary package components, existing syringe barrels, stoppers and other closure components, from trusted suppliers to the industry, preserves the prior work that the drug companies have done in validating their products and primary packaging components. It preserves their sourcing strategy. It preserves their processes and filling procedures. Because we've designed the product line in a certain way, and because our business model is one of assimilation into the supply chain as opposed to disruption to the supply chain, it allows our pharma partners minimised disruption to, and preservation of, their existing processes.

We have a grand vision to set a new standard for syringe-based drug delivery that includes, but goes well beyond, needlestick prevention.

Q When pharma manufacturers are presented with the concept of Innovation Without Change, how do they react?

A It's a really good question. Naturally, we talk to a lot of people – inside and outside the industry. Those outside the industry often ask why "without change"? Don't you want to change things? Don't you want to disrupt with this technology. And of course we do in that sense. Disruptive technology is wonderful. But if you cannot implement that technology then it is just left on the shelf. So people within the industry truly appreciate the idea of minimising disruption to existing processes.

Another thing that really hits home is that different companies have different drivers that lead them to our platform. For some it's needlestick safety legislation and reuse prevention guidance from the WHO. For others it's more of a classic marketing driver – it's the ability to differentiate their drug-device combination products using a device, to earn loyalty from their users and to promote compliance.

We're working with the syringe manufacturers so that, for example, with our staked Companion, the drug companies will receive sterile syringes with the needle mounted, just like they do today, in three-inch tubs, just like they do today. We're also working with some of the leading contract manufacturers and that provides a further risk reduction for pharma. Why

rebuild a manufacturing footprint when there are experts who can do the manufacturing? They produce the Companion products under our design controls and under our lot release but they are perfectly suited to build our products because while the design is innovative, the manufacture is pretty straightforward. So the ability to readily outsource production of the Companion to contract manufacturers is another risk reduction for pharma, because they can trust the supply chain.

Overall, when we explain the concept of Innovation Without Change it really does resonate with people in the industry.

Q The parenteral delivery devices field is both growing and changing very rapidly. Things are moving forward apace. Can you talk about how demands from the market, first specifically the market in terms of the industry and regulators, are changing and how those changing demands are driving the development of Credence's Companion products?

A We try hard to make sure the market is guiding our product development. Let me make a couple of points on this. First, as the molecules coming through pharma pipelines become more complicated it has a trickle down all the way through to the delivery device and the manufacturing of the delivery device. Take molecules that are sensitive to glue, or to tungsten, or aggregate when in contact with too much silicone oil. We touched on how we address that – we remove glue from the system and there are benefits there.

Another consequence of these complex molecules coming through development is that many of them either cannot be formulated to be stable in a ready-to-inject solution over the shelf-life of the product or, if they can, it is very time consuming and costly to achieve. This gives rise to the need for point-of-care reconstitution, of a lyophilised/freeze-dried drug powder with a diluent. You've got to have an easy-to-use device to enable these products to be administered at the correct dose, without contamination, without exposure to needles. So we've put a lot of work and made a lot of progress with a dual chamber reconstitution system that is removing user steps. You don't have to twist and turn and purge an air bubble. The user picks it up, pushes on the thumb-pad, the drug is mixed, they perform the injection, and the needle retracts (Figure 3). We have a version where there is no needle, so it's suitable for IV administration.

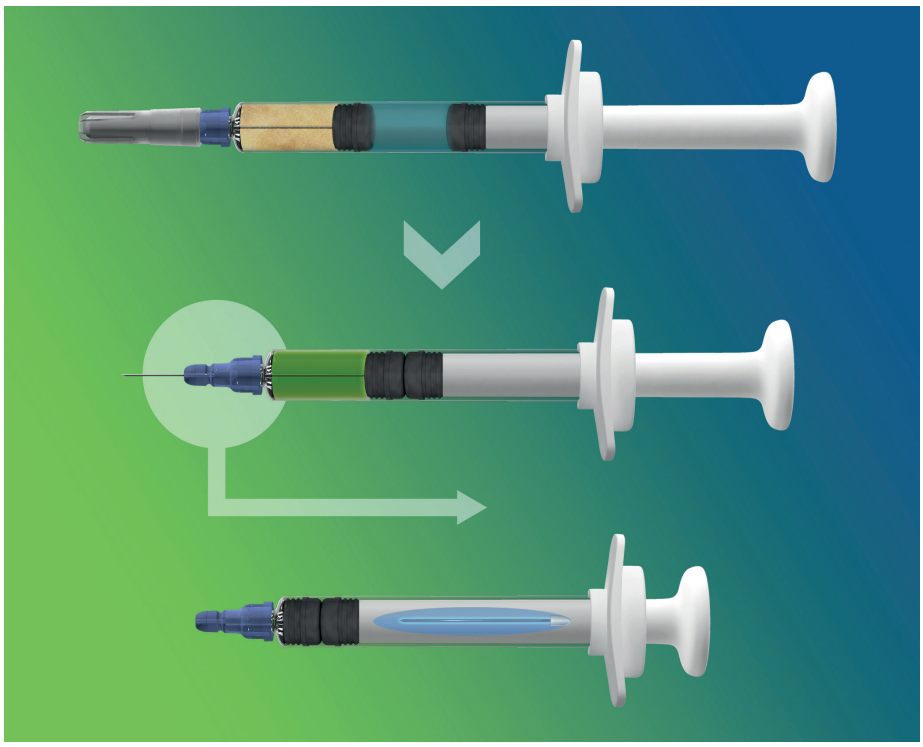

Figure 3: Steps of the Companion dual chamber device for reconstituting lyophilised products.

Because we have simplified, and simplified and simplified, we're getting to a point where this dual chamber system can be housed in an autoinjector. So we're reaching a stage where the user experience of injecting a lyophilised product is largely the same as injecting a stable solution. The implications of this are tremendous. The reliability of delivering a fixed dose by a trained professional or a self-injector is there. Now pharma can say "well maybe we don't have to get this stable in liquid formulation before we go to market and deliver a therapeutic benefit to the patient and gain market share. Maybe we can go to market sooner with a viable product, and spend fewer development dollars." As we look at the transfer of healthcare from a formal setting to the home, this becomes even more important. So our dual chamber system is an area of intense focus for us, and it has achieved really fantastic traction and made substantial progress. You can't just have a "cool device" – you need a device and robust process that go together. We have formed some really valuable partnerships with contract fillers and lyophilisers and this is helping us bring a complete solution to the market. Again, it goes back to assimilating with the existing supply chain, and using the expertise that already exists out there. Innovation Without Change is not just some marketing line. It really runs deep and informs everything we do.

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Let me tell you about another thing we've been working hard on. Compliance is a major problem. It's very much in the news and we are talking about a problem of the order of economic magnitude of US$300 billion in the US, twice that globally. It's a cascading effect. The patient doesn't take their drug according to the prescription regimen, they get sick and end up having to go into a clinic, a hospital or emergency room, which is expensive, to recover from what was a wholly preventable situation.

So we have been working hard on developing a smart syringe. A lot of people are working on connected health but we feel we have a pathway to a product that works in the economic range that makes a connected single-use prefilled syringe possible. So we're working on a device that collects the right data, improves compliance, but is also addressing the economic challenges out there.

Our location in Silicon Valley is a factor. We're in the middle of everything going on here and we are bringing a Silicon Valley approach to the pharma industry. It is this approach that has allowed us to do things that others have not thought of despite the fact they've been in the market for decades.

As I said, we let the market guide our development. We work hard to stay focused on advancing our products – in particular our staked Companion and other Companion products – but we also continue to build a platform with the breadth required to respond to market needs.

Q Continuing on the theme of the rapidly evolving market, but this time the market in terms of the end-users – patients and healthcare professionals – again how is the development of Credence Companion products responding to and being driven by these changing demands?

A All of us involved in developing delivery devices have multiple masters. There is of course the primary customer – the pharmaceutical company. There are the regulators. But it is all ultimately guided by the user.

We perform extensive user studies, our customers perform extensive user studies. First users guide development, then they verify that we're going in the right direction and then they also inform our lifecycle strategies. So it is about the user, always.

A critical point that we've digested is that we cannot rely on training. Training is important and there are companies out there that do a great job on training tools, such as Noble. Training is critical but you cannot rely on the user being trained the way you envision them to be trained. The goal has to be that proper use of the device occurs on the first untrained attempt. We talk about ensuring the proper use by design. It's a high standard but it is the standard.

How are we achieving this? There are fundamental, technical things we've worked on such as the force profile of the injection. We've made amazing headway in smoothing out the force profile and reducing the force of activation when the needle retracts. We've reduced that peak force by almost 50% in the last few months and that is a real feather in the cap of our design team.

Additionally, we realise that we have a small device – the Companion looks like a normal syringe and therefore doesn't have much surface area for on-device guidance, but there are other things you can do. We've made a version of the Companion where the plunger rod is transparent so you see the inner workings of the plunger rod that house a portion of the retraction mechanism. This cues the use that there is something else going on. Then we've coloured certain components. Green means "go" so we have a pre- and post-injection guidance depending on the different positions of a green component before and after injection. We've also incorporated clicks. These approaches combine to motivate proper use the first time the device is used, and then reinforce it on the second and third use, and so on. I would say that if we're thinking about what the greatest user input has been, the most significant user impact on the device design in the past 12 months or so, then it has been on this topic.

Q What is the latest news from Credence? What have you been up to and, in particular, what are the latest insights from Credence's interaction with users? How do they like the Companion products?

A So I've touched on the dual chamber syringe for reconstitution, and its progress towards a size where it can be incorporated within an autoinjector. And I've also mentioned the work on a smart, connected Companion. But there's a lot more!

I wish I could share some of the user studies that our customers have performed but, of course, that is confidential. What I can say is that we hear consistently an overwhelming user preference for our technology over both existing solutions out there in the market today as well as solutions in development. That is something we are very proud of and has helped lead to the traction we have with our pharma customers.

What is driving this positive response from users? Well certainly the passive safety and the "cool" and "wow" factor of the needle retracting at the end of the injection. But equally it's the end-of-dose cues, it's the familiarity of using a device that looks like a "normal" syringe and is comfortable. The use steps are the same as the steps users have used in the past.

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Also, the consistent experience across the platform comes up as a positive. There are different drugs, different routes of administration, different requirements, different user populations. Getting this consistent user experience allows the drug companies to have and provide that to their users. Familiarity.

You also asked what we have been up to. So, after a lot of hard work over a long period, we are on the verge of having great news to report regarding a major deal with a top pharma company. It's very slightly premature right now to talk about it in detail. But it's a great accomplishment for the company. We're very excited. It's a point of inflection for the business where we will move to the next stage. While we've had many collaborations at various stages, this is the first one that really moves us on to the next level.

Q As 2018 starts to really get underway and gather momentum, what does Credence have planned for the year ahead in terms of milestones for the company and Companion product development?

A We constantly preach to ourselves that we have to maintain depth and focus, but also we have to be broad enough. By this I mean that, for example, you cannot develop a syringe that only works for a product demonstration, or works when you're making a thousand units per month. It's got to work when you're making a hundred million units or more per year. That depth of design, that prerequisite, is a very important priority. This ties-in with the news about a partnership that

> "The news is, we are scaling. We are going from making products on a pilot manufacturing line and moving toward commercial industrialisation of our Companion syringe product. For the business, it becomes a jumping-off point, an inflection point, to build that capability. That is our focus for 2018, by a mile!"

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Fortunately from day one we have been designing a product that is able to be scaled, both in terms of reliability at full-scale manufacturing volumes, and in terms of the economic considerations and challenges in the market. From the outset we've been eliminating components, reducing parts and fine-tuning so that we have a manufacturable product at high volumes at a cost point that meets the pricing needs of the market and still returns to the company a profit margin that the company and our investors need to see. This is going to be a busy year but a very fulfilling year. We're ready for it!

ABOUT THE COMPANY

Credence MedSystems is an innovator in injectable drug delivery devices, offering its pharma partners a simplified path to commercialisation of best-in-class delivery systems. The Companion Safety Syringe System was born from Credence's philosophy of Innovation Without Change, allowing customers to impress and protect end-users while preserving it's existing processes, sourcing strategies and preferred primary package components. The Companion is available in luer needle, staked needle and dual chamber reconstitution configurations. Across the platform, the user performs the injection, receives end-of-dose cues and then the needle automatically retracts into the syringe, preventing reuse.

CREDENCE MEDSYSTEMS

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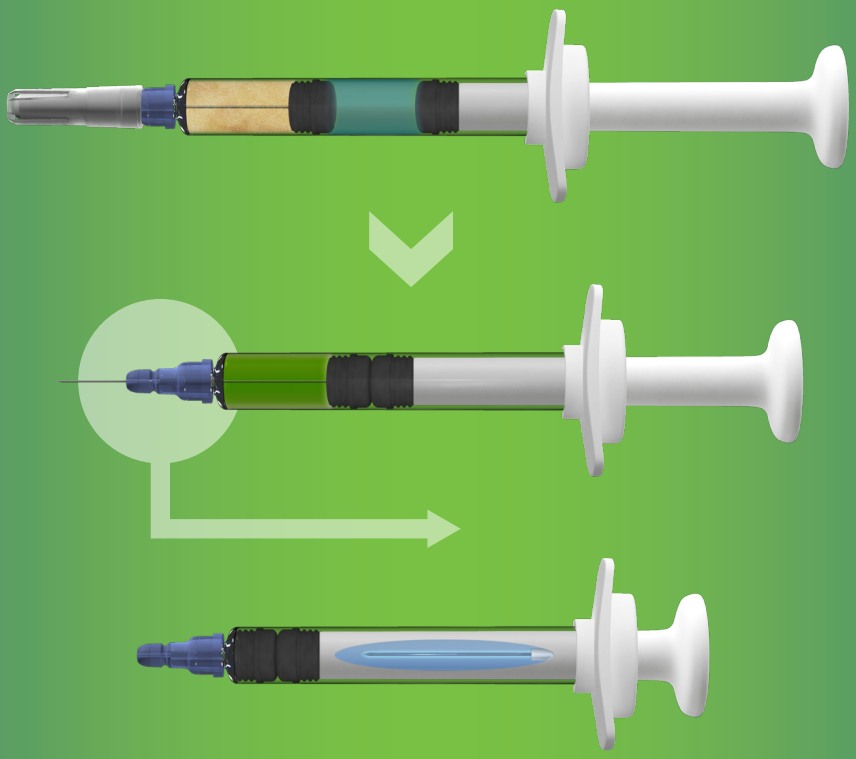
THE CREDENCE COMPANION

IMPRESS | PRESERVE | PROTECT

DUAL CHAMBER



IMPRESS

ENHANCED user experience
FAMILIAR syringe techniques
CONSISTENT platform-wide experience
CLEAR end-of-dose and safety cues

INNOVATION WITHOUT CHANGE

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This product has not yet been evaluated by FDA

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