INTERVIEW

In this exclusive interview, Lilli Zakarija talks with ONdrugDelivery's Guy Furness about how EdgeOne Medical provides a critical service to companies undertaking drug delivery device development programmes, from small biotech start-ups all the way up to major pharmaceutical players. As part of this discussion, Ms Zakarija delves into the evolution of the drug delivery device industry over the past decades, some common pitfalls companies fall into during device development and what makes this sector such an exciting one to work in.

LILLI ZAKARIJA, EDGEONE MEDICAL

Lilli Zakarija is Co-Founder and President of EdgeOne Medical and has over 20 years of experience in the medical device industry. Her expertise includes development and global launch of various single-use, disposable medical devices and combination products, strategic/technical development of device platforms and IP management. Throughout her career she has held management roles in engineering and project management and, prior to founding EdgeOne Medical, Ms Zakarija established and led the global engineering function supporting all device and combination product related needs for the bioscience division of Baxter Healthcare.

Ms Zakarija has a Bachelor of Science in Biomedical Engineering and a Master's in Engineering Management from Northwestern University, and an Executive MBA from Kellogg School of Management. In addition, Ms Zakarija currently serves on the National Board of Directors for Women in Bio (WIB), is Adjunct Faculty for NUvention Medical, Board of Advisors for BME department at Northwestern University and is a mentor in the FoundHer programme at Querrey InQbation Lab.

Q How has the world of delivery device development for prefilled syringes and injection devices changed since you started EdgeOne in 2012?

A Looking back at our industry, I view it from two perspectives. From the business side, when EdgeOne was founded in 2012, it serendipitously coincided with the US FDA's implementation of its combination product regulations – we were getting established just as the industry was learning to adapt to these new regulations. This kind of adaptation was common in medical device development but new to the pharmaceutical side, so there was resistance to overcome. Over time, the industry evolved to integrate various technologies into combination products, and what we have now became the norm.

On the other hand, as an engineer, I see this evolution as three-dimensional. Initially, it was about mechanical combination products, like prefilled syringes, autoinjectors, pen injectors and inhalers. Then further evolution introduced a second dimension in the form of digital and connected devices, which brought more complexity and required more resources, knowledge and partnerships. The third, most recent dimension is what I like to call "complex systems", driven mainly by gene and cell therapy companies. These systems incorporate integrated hardware, disposables and software, and often require multiple systems to deliver therapies to targeted organs – it's a new level of complexity.

This evolution has transformed our approach from just integrating devices into development processes to navigating a complex landscape of combination products. Despite the complexity, one constant remains – the process. It's what makes each development programme unique and exciting. As an organisation, we view ourselves as experts in that process, specialising in guiding different types of complex programmes through this process. It's fascinating to think about potential future dimensions that will emerge as technologies advance.

Q Given all the changes the industry has seen, what are some of the common issues and problems you see in combination product development?

A As I mentioned, the one real constant at EdgeOne is the process, as defined by the FDA and ISO standards. Despite the unique challenges presented by different product types, a common issue is what we call the "culmination point", which involves the design control process leading to critical testing before IND submission. During a development programme, there are numerous interdependent activities, such as requirements management, risk management, component selection, device design and test planning. However, everything converges at the testing phase prior to submission. This point is critical, as it's where you generate the objective evidence for regulatory agencies to show readiness for clinical trials or commercialisation.

At EdgeOne, we focus on helping development teams de-risk this stage. If you go in unprepared, things can start to unravel, such as not having the right requirements, realising your testing plans are flawed or lacking robust designs. Ideally, you should reach this point with high confidence. Our goal is to ensure that our partners don't experience delays or failures due to unresolved issues at this stage, which is often critical on the path to submission.

In a way, EdgeOne was born from this pain point. When I was leading the device development team for the Bioscience division at Baxter, I recognised the need for providers who could assist with device verification (DV) testing. I would talk to potential providers who said they could deliver what I was looking for but, when I pressed them on what they were going to do, the answer was often "what you tell us to do". Faced with that, I just thought that, if you were

Figure 1: EdgeOne Medical's headquarters in Wheeling (IL, US) – more than just a testing house.

really good at this, you'd already know what to do, already understand the process. I wanted a partner that would work with me rather than just for me, that would be experienced and knowledgeable enough to ask me all the right questions, and that simply didn't exist.

That's why we founded EdgeOne to be more than a testing house – we engage in the entire design control process, providing design history file documents and taking development programmes from start to finish (Figure 1). It's crucial not to underestimate the significance of the culmination point, where everything comes together, and to ensure that everything possible has been done to de-risk it for the success of the entire programme.

Q Has EdgeOne's evolution over time been driven by avoiding that culmination point – expanding your scope to include services prior to and around testing, so as to avoid testing becoming a crunch point?

A Yes, a major reason for that being that we've been in our customers' shoes. Before EdgeOne, I was responsible for device development of combination products at Baxter, so we understand what our customers are trying to achieve, the requirements and how things should be interconnected. Educating our customers, especially those who are less informed, is a key part of our approach. We educate through the sales process, ensuring that they understand how to do things correctly, even if they don't choose us as their provider.

It's a natural evolution for us. Success in testing relies on ensuring that it's part of the process and planning for it, not just treating it as a transaction – here's the list of tests, give us the data and let's move on. EdgeOne is about understanding how these components integrate into the entire system. It's like a 3D chess game where all pieces have to move together in concert. Our clients are often surprised by the depth of our questions, but that's because we've experienced the pitfalls of development and aim to help our customers avoid them. We ensure a high chance of success by understanding the nuances of each programme.

Q Regarding EdgeOne's client base, do you mainly work with companies new to device development, or do you collaborate with large pharma and device companies with gaps in their experience?

A We work with all types of companies. From small start-ups where a scientist working on the molecule side is tasked with incorporating the device, to large pharma companies with established device teams. For example, just before the holidays, we were in the second part of the proposal process with a client who came to us and said "We don't know what we don't know, we need you to educate us". So, as part of our sales call, that's what we did, hopefully ensuring that, whether they use us or not, they will have gained valuable insights.

We range from being the entire device team for some clients to supporting large pharma companies that might have new device personnel, new projects or lack the resources to cover all their programmes. Our flexibility allows us to provide support as needed, depending on the client's resource bench and their organisational structure for R&D.

Q How can organisations ensure that they don't fall prey to the issues we've discussed?

A One key aspect is beginning with the end in mind. It's crucial to define key requirements not only in terms of what they are but also their limits. Sometimes, we find that some requirements provided by clients aren't even testable or don't make sense for the intended use. So, we work with our customers to revisit these requirements. In our industry, having to renegotiate the requirements due to failures during testing is the wrong way to do it. The right way is to ask, well in advance of starting testing, "What's my right requirement?", "What makes sense?" and "What makes sense for this product?"

A particular example of this is requirements around delivered volume. Sometimes, the set values are unachievable given the system's design, leading to unnecessary complexities and delays. Understanding and setting realistic requirements are vital for testing, and the product's end use.

The other key area is developing an appropriate testing strategy. This includes characterisation or, as we call it, feasibility testing with and without a simulant in order to de-risk the programme. For example, we've encountered scenarios where the drug was only introduced during the DV stage, leading to unforeseen issues, such as clogged needles in prefilled syringes. These incidents cause delays and require rapid problem-solving. A solid testing strategy, including decisions on sample sizes, test method validations and when to introduce the actual product is essential to catch potential issues early in the development process.

Q At this stage of development, are these programmes disclosed to the market? If there's a major issue with a public company's programme, could it impact them significantly?

A Sometimes, yes. It can be very detrimental. If a company had made public commitments in, say, its quarterly financial reports about its goals and, suddenly, it found that those goals were unattainable due to problems encountered in device testing then, yes, such setbacks have significant consequences within organisations. The culmination point often comes late in the game, and you can't afford delays when you're on a critical path with everyone's eyes on you. The data from testing is usually the last piece to be slotted into the submission package, followed by a quick 30-day review by the FDA before starting clinical trials.

When you're only months away from the excitement of starting clinical trials, the last thing you want is to find out that they won't start on time. The good news is that situations like that are entirely avoidable – it's about planning ahead. While you might still encounter unforeseen issues, many can be averted with proper planning, correct requirements and the right dialogue with all stakeholders. It's about avoiding unnecessary setbacks and ensuring a smooth journey towards clinical trials.

Q Considering the significant changes that we've seen in the drug delivery industry over the last 10 to 20 years, how well do you think regulators are keeping pace with the industry's ongoing evolution?

A Given that regulatory agencies are government bodies and tend to move slowly, I think they've done a commendable job. They've released substantial guidance on software as a medical device and digital innovations, for example. I teach a class at Northwestern University (IL, US) called "NUvention Medical", which includes graduate students from Northwestern's medical, engineering and business schools. They develop medical devices for unmet clinical needs, which can be physical devices or digital apps. I was impressed with the quantity and variety of guidances available on the FDA's website that are available to anyone considering development of a digital app.

The key approach by agencies that enables them to keep up as industry evolves, is allowing companies to present their plans and then providing them with clear feedback and input. This dialogue is crucial, especially in areas where the guidelines aren't completely clear. It's about getting feedback and adjusting accordingly. The agencies need practical experience from the industry to formulate their guidelines.

Looking ahead, the challenge for regulators will be adapting to advancements in the use of AI in the medical field. There are numerous questions around AI, like trustworthiness, data sourcing and validation. The industry is already contemplating how AI can transform our processes to become more efficient. AI's potential to create predictive correlations is immense, but regulatory agencies will require evidence over time to ensure that using it doesn't compromise patient safety and effective outcomes. The evolution in AI will be significant, and it should be a key focus for everyone in the industry.

Q Looking back at past trends and anticipating future changes, what excites you most about what's happening in the industry?

A There are two main points that excite me. Firstly, the industry is continually evolving. The changes we've seen over the last decade will persist and take new shapes, particularly with the addition of AI as a future disruptor. It's exciting to embrace change and, for those comfortable with it – as entrepreneurs such as myself tend to be – it feels like the next chapter is always going to be an exciting one. These changes won't all happen in 2024, but they're part of almost every conversation we're having.

Reflecting on 2023, a highlight for us was seeing several smaller biotech companies we work with get acquired, such as Chinook (WA, US, acquired by Novartis) and MiroMatrix (MN, US, acquired by United Therapeutics). Being part of the teams that helped these companies reach their acquisition goals was incredibly rewarding. Our aim with smaller biotech companies isn't customer retention over very long periods, as they often get bought out, but rather to ensure their success and programme effectiveness so that, when potential acquirers start to look at the details, their testing processes, and indeed the processes leading up to and around testing, are in great shape.

Looking ahead, embracing change is crucial. It's about enjoying the journey and seeing where it takes us. The constant evolution in our industry keeps it interesting and rewarding.

Q Is there anything else you'd like to add or any points you'd like to make that we haven't covered?

A One thing that comes to mind, tying into the theme of change and excitement, is the importance of having fun with what we do. It's one of our values at EdgeOne – this industry is dynamic and being able to enjoy the work and the challenges it brings is crucial. For me, it's always been about enjoying the journey and the work itself.

It can be about achieving milestones and successes, the excitement of new challenges and innovations coming our way and more. Fun encompasses the daily enjoyment of work, the positive attitude we bring and the camaraderie we have with our teammates and clients. At EdgeOne, we value what we call being "humorously serious", which means enjoying our work while being deeply committed to it. It's about loving the process, solving problems and working with people. We screen for this passion and attitude in our team.

For example, when I hear about innovative technologies and the problems they're solving, I'm often amazed. A recent example is MiroMatrix's work on growing porcine livers, decellularising and then recellularising them with the patient's blood for transplantation. How can you hear about that and not just think "Wow, I want to be a part of that"? Being a part of the process to bring such groundbreaking technologies to market is where the real fun lies. It's about the daily joys as much as the long-term rewards of seeing technologies succeed and make an impact.

ABOUT THE COMPANY

EdgeOne Medical is a global contract device development organisation that supports the compliant device development and testing of combination products. Since 2012, EdgeOne Medical has been elevating medical device and combination product development teams including in over half of the global top 20 biopharma companies. EdgeOne Medical has a unique combination of multi-disciplinary product development experts combined with in house ISO 13485 certified Testing Labs. These capabilities, known as *Edgineering*, and EdgeOne Labs provide clients with the peace of mind that they have complemented their teams with a partner with a successful track-record of de-risking, navigating, and accelerating device development programmes.

EdgeOne medical

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