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PROCESSING *the Future*

From good buffer management to effective slurry preparation, experts from Asahi Kasei Bioprocess offer their tips – as well as thoughts on the importance of sustainability

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ARTICLE

Creating for Tomorrow

Asahi Kasei Bioprocess – based in Chicago and owned by a Japanese company – supplies bioprocess equipment, consumables, and scientific support, and has always considered itself to be a future-facing company. With the biopharma industry increasingly realizing the importance of sustainability, Asahi Kasei Bioprocess is putting its best foot forward. We interview Clayton Weber, Systems Engineering Lead/Sustainability Lead at Asahi Kasei Bioprocess, to learn more.

What is your role at the company?

I started my career with Asahi Kasei Bioprocess as a project engineer, but today I am the systems engineering lead, which means I get involved with almost every piece of equipment our company makes. I assist with kicking off discussions with the customer to understand their needs and timelines; we'll then go through full spec, procurement, assembly, and testing of the equipment until it is ready to be delivered to the customer. I'll then be involved onsite with training and set up.

I've built chromatography columns, chromatography systems, inline buffer formulation skids, virus filtration systems… a wide range of equipment. Right now, there is a strategic focus on oligo synthesis, and customers are also looking to update bioprocesses to be more efficient and cost-effective; for example, by moving to automated inline buffer formulation systems, which reduce cleaning and the amount of chemicals used – and get companies away from using "tank farms." Ultimately, adopting these kinds of processes can help companies reduce their environmental footprints.

What does sustainability mean to Asahi Kasei Bioprocess?

Sustainability is a growing trend in the pharmaceutical industry. We've always been focused on pioneering the biologics of the future by developing the equipment needed to manufacture them. Personally, I think the industry's future is brighter thanks to increased focus on efficiency and sustainability, but there is still much to do. Most biopharma companies are now establishing sustainability programs and targets – and asking their vendors to do the same. At Asahi Kasei Bioprocess, we regularly receive enquiries about what we are doing on the sustainability side. Sustainability is not proprietary and if

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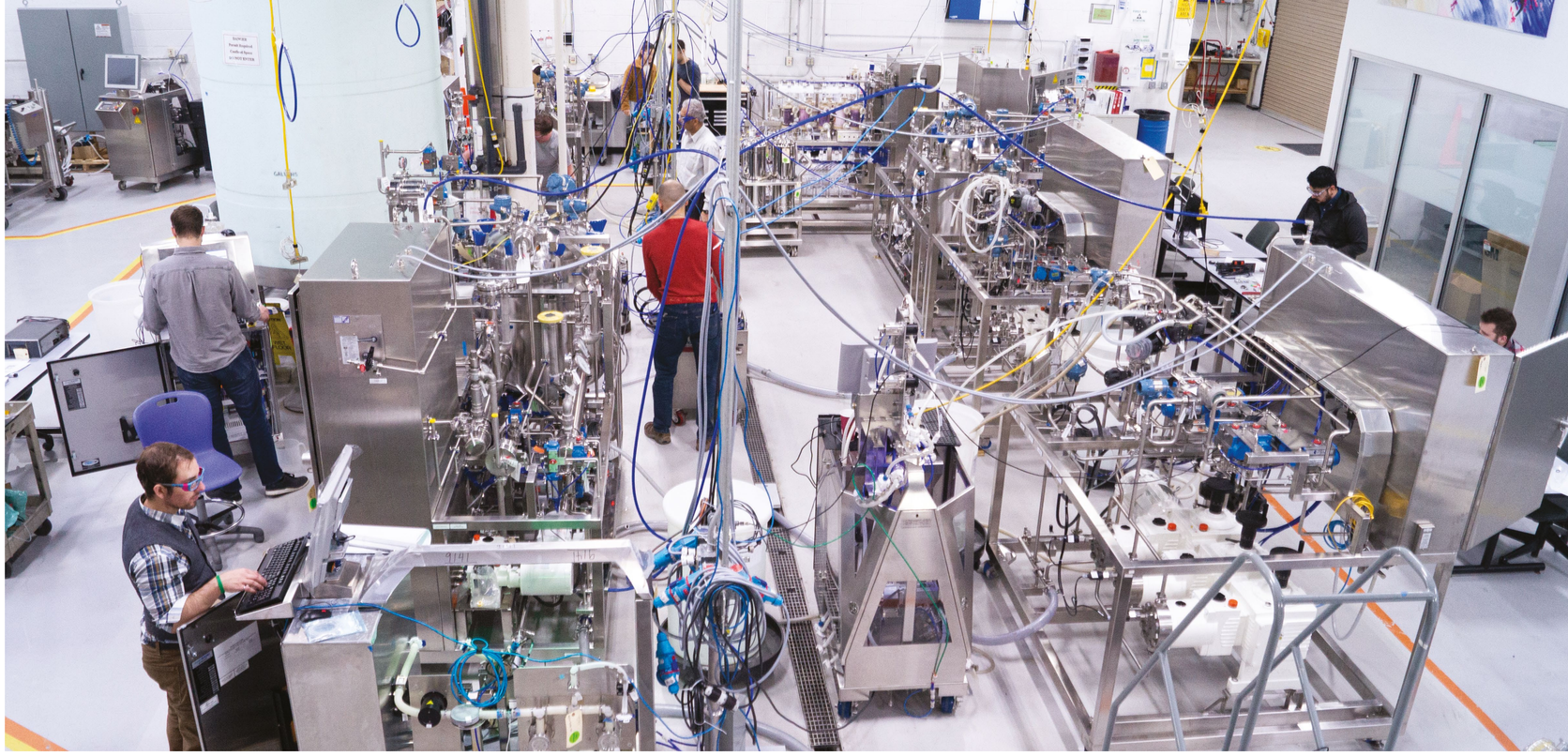


we're going to make a difference as an industry then we need to keep communication open and share success stories.

We are a small part of the overall Asahi Kasei Group, but we want to lead by example. In doing so, we can influence other business units, as well as our customers and suppliers.

As part of your role, what sustainability actions are you taking?

Sustainability is very important to me personally (I've always had a love of the outdoors in particular), which is why I am delighted to have stepped up as "sustainability lead" within the company. Sustainability can be broken down into different areas including environmental, social, and economic. However, my role focuses primarily on the environmental side. For now, we are focusing on three core areas: the emissions and waste that we produce as a company and that is directly under our control; emissions and waste caused by our products; and external emissions, such as those produced by vendors (remember – if your vendors are not sustainable then it can affect your own company and the carbon footprint of your products and services).

The first two areas are easier to address because it is about looking at your own company and what you can do – and they are within your control. To help reduce our emissions, we have signed a contract for a solar initiative. We have a lot of roof space and we have calculated that we will be able to offset 100 percent of our energy consumption – a phenomenal first step, which will also save substantial energy costs.

We have also looked at our waste management. We receive a lot of boxes and packaging materials, which can be recycled. Recycling is commonplace, but do not assume that this is already happening at your company, even if you already have recycling bins around your offices. It is important to find out what your waste team is actually doing. In fact, I recommend this as a good starting point for any sustainability strategy. At our company, I discovered that our waste team was disposing of everything as general waste. We took swift action to resolve this, and we now have a specific company that manages the waste and recycling. Due diligence and conversations can make a big difference!

When it comes to manufacturing, we are also increasing the implementation of single use to be more sustainable. There is a perception that single use components have a negative impact on sustainability, due to the disposal of consumables; but they can actually help reduce cleaning needs (less water, less energy, and less chemicals). We are now looking into how single use can be recycled and disposed of appropriately – and some single use tubing manufacturers are also taking a stand to discuss solutions.

What are your top tips for other companies looking to implement sustainability initiatives?

You can choose how far to take your recycling scheme, but it should be tailored to the type of waste that your company produces. Recycling cardboard, plastic, and bottles are easy wins; but there are also companies that handle other materials, such as polystyrene and foam. Just keep in mind, you may not be able to identify a single stream for your recycling, which can complicate matters. I advise seeking recommendations

from companies that have similar waste outputs, or even your current waste management company. In our case, we looked online, through sustainability forums and articles for perspectives, and we also talked to our sister companies, which ultimately secured us a good deal with a company that could handle six different categories of waste. The important thing is to ensure proper disposal.

How can companies support their vendors?

As noted previously, some pharmaceutical companies are now requiring their vendors to have sustainable programs in place. This trend will likely continue, pushing more companies to introduce sustainability strategies with more concrete measures and to think bigger about their efforts.

We believe we have a responsibility to help our vendors with their sustainability goals – particularly the smaller companies that do not have the same resources as larger businesses. We've sent surveys to our vendors to understand who is ready to ally with us on sustainability. Not everyone is going to get on board straight away – and right now we certainly don't have all the solutions – but by starting conversations with vendors we can push the issue to the forefront to find a path forward. For example, tube set manufacturers may not yet be looking at sustainable sources for their raw materials, but if they are willing to explore this option, it is a good first step. Any partnerships in this area may also inspire additional partnerships further down the line.

What are the challenges that the industry faces in being more sustainable?

One of the biggest challenges in sustainability for the biopharma industry will be embedding it throughout whole supply chain – from procurement of raw materials all the way to recycling. We don't yet have all the answers, but people are trying different approaches. Collaboration will be required to get initiatives across the board. There are a lot of vendors out there, and if a vendor refuses to engage in finding sustainable solutions, then ultimately, they run the risk of being replaced.

At Asahi Kasei, we like to say, "As the world constantly changes, we will continue to contribute to life and living for people around the world by Creating for Tomorrow." The pharma, bioprocess, and biotech industries all contribute to life and living, but we must go beyond therapeutics. You can't say that you are contributing to life and living in one aspect, but then refuse to contribute to sustainability efforts and reducing the waste and harm produced on an industrial scale. We've already made big progress at Asahi Kasei Bioprocess – with our work on solar panels and the partnerships with vendors being some of our biggest sustainability success stories to date. But there is more to come. Sustainability is not going to stop; in fact, the emphasis on sustainability will only increase – and, in time, it will move beyond emissions and the environment to other aspects, such as community. Whenever we finish one goal at the company, we'll have another one right behind it. I have a great team to support me and what we can achieve is an open book. We will continue to support the biopharma industry

Next:
Getting More from Your Buffer Management Strategy

ARTICLE

Getting More from Your Buffer Management Strategy

By implementing MOTIV™ buffer management technology, Lonza has seen many gains, including saving space, greater efficiencies, and being more sustainable. We delve into the story behind the company's collaboration with Asahi Kasei Bioprocess America.

Featuring Matt Macknight, MSAT Manager at Lonza Biologics, Portsmouth, NH, and Chris Rombach, Senior Vice President of Sales and Marketing at Asahi Kasei Bioprocess America, Glenview, IL

When embarking on a facility expansion focusing on a state-of-the-art 4 X 6,000 L bioreactor multi-product manufacturing suite for complex products, Lonza had limited space for the overall manufacturing area. Buffer preparation and storage can take up a large footprint in a biopharma facility, so the company was keen to look at alternative options, which led them to Asahi Kasei Bioprocess America's (AKBA) MOTIV inline buffer formulation technology.

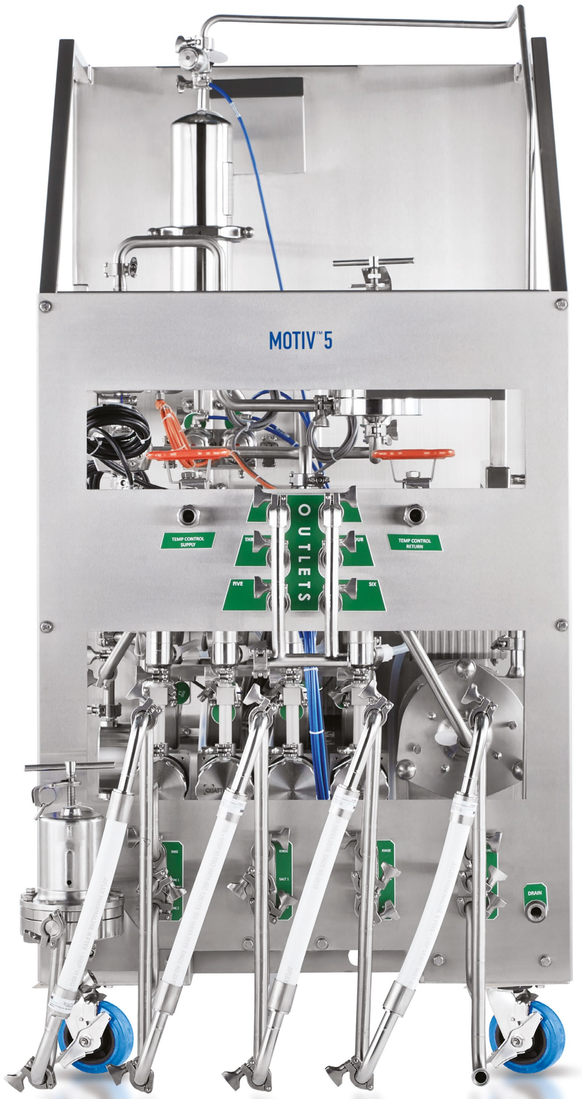
At Lonza, Matt Macknight developed the method of modelling and applying the MOTIV system across a wide variety of platforms – with help from his engineering partner Joe Conley. Together, they have collaborated with experts at AKBA to further refine how the technology is used. In this interview, Matt Macknight and Chris Rombach from AKBA discuss the benefits of updating buffer management strategies.

What benefits can new technologies bring to buffer management?

CR: Process buffers are ubiquitous in biopharma manufacturing. Often viewed as a background function, they are not always seen as a key focus area for improvement. However, as companies scale and diversify, material management and storage space become more pressing challenges. At the same time, sustainability is a focus for virtually all drug manufacturers today. All these trends make it a good time to review buffer management strategies.

MM: At Lonza, we've found that technologies like MOTIV allow us to do more with less. Biopharma processes use the same basic chemicals to purify API, but they are used in differing concentrations and different pH targets throughout each process. A traditional manufacturing suite making buffers the old-fashioned way requires a suitable facility footprint to house buffer preparation vessels and store formulated buffers. It also requires the staff to continuously replenish the formulated buffers according to the production schedule, in order to keep purification processes running.

We found that MOTIV removes a lot of these requirements. Instead of making formulated buffers, we can make either highly concentrated individual chemical concentrates that can be mixed with MOTIV to formulate on demand, or we can create a highly concentrated formulated buffer and dilute inline with water for injection. The system also reduces our use of plastic by eliminating the need for single-use bioprocess containers. In a traditional suite, we would be cycling through 50kL–100kL in single use containers for formulated buffer storage per batch. With MOTIV, we are now sending formulated solution directly to the chromatography and TFF systems, with no need for a break tank or containers.



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What was the inspiration behind AKBA's MOTIV technology?

CR: AKBA has had buffer systems in the field since 2005 and we were awarded Bioprocess International's Technology of the Decade in 2012 for our inline buffer formulation (IBF™) systems. In recent years, there has been greater focus from industry on streamlining buffer prep, which inspired us to launch the MOTIV line in 2021, as a rebranding and product expansion of our IBF technology. We offer standard three and five pump designs, coupled with our patented "Pro Yield" mixing technology, and sensing and monitoring instruments to enable PAT.

We also respect that space can be a premium in today's facilities. We develop our systems to have the smallest feasible footprint possible. The fact that the system can also handle concentrated materials also saves space since companies don't need large storage tanks anymore.

MM: The space consideration was a huge focus for Lonza because we only had 10,000 L of storage space for chromatography and TFF concentrates. I reviewed formulated buffer consumption in my asset and found that a typical process would require approximately 50,000 L to 100,000 L of formulated buffer per batch. With the MOTIV system, 10,000 L of storage space is enough, and the concentration is so high that we need only to use small amounts at a time. We have concentrates wherein a single make-up will get us eight production batches. Since we are not using bioprocess containers or a break tank, we only need a very limited number of buffer preparation vessels to supply the concentrates. Zero footprint is required to store chromatography and TFF formulated buffers, as well as reduced resources to maintain buffer supply. The production schedule also only needs ~1-2 buffer make-ups per 24-hour period when in campaign versus 10-12 in an equivalent asset without MOTIV.

Did Lonza face challenges when implementing the technology?

MM: We have manufactured eight different products in a GMP setting and over 50 unique formulations using the technology. The sheer volume of formulated buffer we have produced using the reduced footprint, equipment, and resource has been a huge advance in the manufacturing process. However, whenever you implement a new technology in a novel way, some challenges will arise. For all our customers, we perform at-scale formulation testing. As a part of this process, we compare inline MOTIV pH and conductivity to offline using traditional instruments (considered the gold standard). The conductivity discrepancy between inline and offline instruments has been consistent at about 5-8 percent difference in every buffer formulation scenario. This difference is not an issue because conductivity ranges are typically at least +/-10 percent from target. When formulating to a specific conductivity, the system can very reliably maintain midpoint with very little fluctuation. We also incorporate the inline/offline discrepancy into our alarming strategy.

The pH inline/offline comparability has proven to be a little trickier. We have observed that above concentrations of about 50 mM of any chemical and with pH in the 5.5 to 7.5 range, the discrepancy between inline and offline is quite good at <0.05 units. However, at pH of ≤3.5 and/or a combined concentration of <50 mM of any chemical, the discrepancy is significantly higher and unacceptable for process control.

With pH discrepancies that are considered not comparable or acceptable, the solution can still be formulated by flow rate alone, not relying on inline pH measurement. As we are unable to trust inline pH measurements in these scenarios and unable to alarm for pH, we do more extensive at-scale testing with multiple source concentrates to prove that offline pH measurements are reliable and repeatable using flow rate alone. This has proven to be a

Matt Macknight

Chris Rombach

"Ultimately, all scenarios are solvable using a mix of pH and conductivity control, flow control on its own, inline dilution, and inline formulation."

very effective alternative control with this system. Ultimately, all scenarios are solvable using a mix of pH and conductivity control, flow control on its own, inline dilution, and inline formulation. As a CDMO that sees a wide variety of different process designs, having a system capable of all these control mechanisms is incredibly useful for us.

How are you collaborating to further enhance the technology?

MM: AKBA listened to our concerns. We provided them with a list of challenging formulations and AKBA has since built a development system. Our two teams are now collaborating to write a test protocol to recreate Lonza's observations, and to identify where on the molarity and pH spectrum the accuracy starts to decrease. Once confirmed, we will work together on system modifications or a new instrument that measures accurately in these scenarios.

CR: At AKBA, we build these systems and test them, and we know that they work well – but ultimately, we are not using them every day. Getting to know Matt, one of the key people using the equipment every day, gave us tremendous insight into the power of this technology and how it can be further refined. We're now recreating the issues that Matt has experienced in certain conditions. We believe that it all comes down to physics and chemistry in action. At low concentrations, we have observed that low levels of solute in the liquid may have an impact on the mixing and measurement by inline sensors. We continue to explore how the technology can be finetuned.

In this collaboration, we all recognize the importance of confidentiality, but it's great to see that Lonza had the open mind to share insights with us. In this industry, equipment providers and users need one another; we are all working towards the end goal of making medicines for patients, and to make manufacturing as easy and as repeatable as possible. It is a pleasure to collaborate with Lonza to improve upon what is already a very advanced technology.

Next:
Say No to Subpar Slurry Preparation

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ARTICLE

Say No to Subpar Slurry Preparation

Discover how Asahi Kasei Bioprocess is engineering a streamlined approach to chromatography media preparation.

Should we, as an industry, settle for bureaucratic inertia when better options exist? This is the very question Asahi Kasei Bioprocess (AKB) is asking downstream process operators. To date, bioprocessing has relied on manual, time-consuming strategies in chromatography media preparation. However, alternatives do exist. Meet SLURIPREP™, a media preparation and column charging system that can upgrade purification processes.

To learn more, we spoke with Steve Foy, Manager of Products and Brand Strategy at AKB, which not only provides bioprocess equipment and consumables, but also scientific support.

What is your role at the company?

My primary goal is to understand both our products and customers – and then to ensure we pair strategic goals and customer needs with concrete measures. Day-to-day, I work alongside our interdisciplinary team of scientists and engineers to communicate what our customers and the market need at large. I do this by working closely with customers, answering their questions and discussing their interest areas. Once a project starts, our engineers and project managers interface often with our customers to make sure they get exactly what they need, on time and as promised.

How do companies typically approach chromatography media preparation?

Chromatography media receives a lot of attention, but not always for the right reasons – it's expensive and companies must mitigate wastage. Most importantly, the preparation and mixing processes are still largely performed manually which, again, is not terribly efficient and can lead to extended equipment downtime. And despite there being alternatives to manual preparation, the demanding regulations of the manufacturing environment can make pharma companies reluctant to implement new technologies. In biomanufacturing, much focus goes on the final product, but there is a lot to be gained by looking at chromatography media.

Take buffers, for example. These are essential throughout biomanufacturing, particularly downstream. For years the standard industry approach has been to prepare buffers manually (a highly labor-intensive and inefficient approach) and store them in large tanks, which takes up a huge footprint within the facility. Because buffers are ubiquitous in the industry, the process can sometimes be overlooked in terms of seeking further optimization.

Sacrifice for future gain is something we should become more comfortable with as an industry. By investing time in a new strategy for slurry preparation specifically, you can streamline processes and be more productive.

What are the consequences of incorrect media preparation?

There are several kinds of chromatography media, with silica gel being one of the most popular. The media arrives at the facility in containers that are usually premixed with buffers, and then operators will often prepare the slurry manually before dumping it into a receptacle or column to get them packed. This is not a quick process; it involves a lot of labor and is tedious – and resettlement can occur within the column before you begin packing. In chromatography media, the beads themselves can settle to the bottom while the liquid rises to the top. This is not dissimilar to when you buy orange juice at the grocery store – the pulp may have settled to the bottom so that you have to mix it up before pouring it into your glass. Also, if mixed incorrectly, the optimization and efficiency of the bed pack can be affected.

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When handling media, particularly silica, it's also important to be gentle. The material can withstand pressures within the column (if applied evenly), but the beads can break if shaken improperly, or prepared incorrectly. This can lead to fines – essentially very small shards of glass – which will settle at the bottom of a container or column. And though the fines won't necessarily make their way into the final product, they can clog column frits more quickly and decrease batch productivity.

Some purification media can arrive at a bioprocessing facility in the form of powder, the preparation of which requires additional steps – such as hydration – and the use of personal protective equipment since the powder can become airborne. Once again, manual methods for preparation can be tedious and lengthy.

What are the benefits of SLURIPREP?

So the saying goes, "An ounce of prevention is worth a pound of cure." And it holds true in the face of media preparation. The industry lacks awareness of viable alternatives to the manual-centric methods of media preparation, but the technologies do exist. It may take training to use a new approach, but in the long run, you will operate with enhanced capacity.

AKB's SLURIPREP Systems (SPS) can be provided as ancillaries to our liquid chromatography systems and columns. These systems have large tanks and are driven by air pressure. They do not require electricity, which means they are usable in hazardous areas. Once you have your container of media, all you need to do is mix it, then pour it into the SPS. The agitator homogenizes the media gently and circulates it. You can also decant fines.

Because the system is connected to the column, packing and pressurization can occur very quickly, leaving less time for anything to resettle. This helps maintain a balanced mixture and allows for a more homogenized packed bed – and thus, a more efficient purification process.

We have been offering our SPS equipment to customers for years, but we are now expanding the technology by launching the SLURIPREP Mixer, which can combine the media gently within the container received from the manufacturer. This device can also pull the slurry into the SPS itself, allowing for further preparation. Fundamentally, it helps ensure that the media is as optimized as possible before moving onto packing.

SLURIPREP allows for an entirely closed process – hazards such as spills and airborne powder are reduced, improving operator safety, and increasing productivity.

What feedback have you had from customers?

At AKB, we focus on mitigating the logistical challenges that surround drug development. And the demands of customers are clear: increase productivity using safe and reliable systems that are (relatively) easy to operate. These demands have largely informed our practice. Our customers have been aware of the benefits of SLURIPREP for years, but in the wider market, there is less awareness of alternatives to manual methods. It's important for the market to know that not everything has to be done manually.

We have received overwhelmingly positive feedback regarding SLURIPREP's functional use. Being mechanical and driven by pressure, there are no requirements to learn new software. Other positives relate to the system's capacity to minimize labor hours. In fact, we've found a single operator can use SLURIPREP, as opposed to several preparing media manually.

Customers are also pleased with the customizable nature of our products. For example, the typical SLURIPREP system is up to 600L, but this can be customized to 1000L if required. In addition, our preparation systems

are attached to (or correspond with) columns from anything between 30 to 120 cm in size, which includes compatibility with low, medium, and high pressure liquid chromatography requirements.

Ultimately, we want to develop strong partnerships with customers and, to do this, we require a clear understanding of what companies want. This is dependent on knowledge sharing; we must communicate to create high-quality products for the benefit of patients. In terms of SLURIPREP and preparing chromatography media, we are directly focused on incremental gains to optimize production and internal efficiency.

What lies ahead for AKB?

Asahi Kasei Bioprocess has a clear mission: "to build strong partnerships and innovative equipment in pursuit of helping deliver medicines that patients can trust." We are immensely proud of our products, but in alignment with our purpose, we are always looking for ways to improve the processes that underpin successful drug development.