SUNDEEP KANKANALA, BD

Sundeep Kankanala, PhD, is Vice-President of R&D for BD Medical – Pharmaceutical Systems (PS). His responsibilities include leading product and technology development across the PS project portfolio. Prior to this, he was the Director of Smart Device and Data Sciences focus area at BD Technologies and Innovation and a member of the Infusion Therapy business.

Prior to joining BD, Dr Kankanala was a Subject Matter Expert in Smart Materials and Advanced Safety Systems at Ford Motor Company. His fifteen years at Ford spanned a range of assignments, from leading research in biomechanics and smart materials to technology development and launch of advanced occupant safety systems in cars and trucks. He holds a PhD in Aerospace Engineering from the University of Michigan for his theoretical and experimental work in magneto-elasticity. He also earned an MBA from MIT's Sloan School of Management.

In this interview, Dr Kankanala discusses the challenges faced by today's biopharmaceutical industry, in particular those posed by the need for large volumes and the issues caused by the use of silicone in prefilled syringes. He goes on to detail BD's latest technology, BD XSi™, which builds upon BD Neopak™, and how it presents answers to these problems.

Q What would you say is the greatest challenge in the biopharmaceutical market today?

A The overriding challenge facing biopharmaceutical companies today is the increasing pressure around time to market. Factors influencing this include longer approval processes, more stringent guidelines, downward price pressure and high failure rates seen throughout development.

While this is true of all drug research, it is even more challenging for biosimilars and innovative biologics, due to problems encountered when developing suitable parenteral formulations and combination products. These biosimilar and innovative therapeutics are at the cutting edge of science; the fact that they are complex and potentially unstable molecules makes them very expensive to develop and manufacture, and therefore demands another paradigm shift.

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Q Given that, how has BD contributed to biopharma in the past, and how is it rising to the challenge now?

A Over the past three decades, BD has worked collaboratively with biopharmaceutical manufacturers to put solutions in place at the outset, to avoid disruption to manufacturing and to ensure regulatory readiness. This approach has been highly successful, and has earned BD a reputation for developing innovative technologies which help companies achieve ambitious time-to-market goals.

BD's long collaboration with biopharmaceutical companies has allowed us to anticipate emerging needs, improve components and find solutions to complex delivery requirements. One such requirement is to reduce dosing frequency to improve patient experience and compliance. Some companies try to achieve this by increasing drug concentrations. As this is often not possible or sufficient to the level required for optimum dose delivery, larger injection volumes of 2 mL or more are required.

The growing trend towards higher drug concentrations and larger injection volumes has presented new delivery challenges, including increased viscosity. Larger volumes of very valuable drugs also introduce a critical economic component as the cost of wastage increases. We responded by developing the BD Neopak™ glass PFS platform. This innovation was made possible by a near total redesign of our existing PFS, 80% of its features being either new or improved. Based on a quality-by-design approach, BD Neopak™ features single-digit ppm product performance attributes, aiming at Six Sigma level quality.

BD Neopak™ is available in both 1 mL and 2.25 mL formats, the latter of which has helped break the "1 mL barrier" for subcutaneous injections which had existed in the heads of many stakeholders; it has been actively adopted for the development of innovative therapies with larger volumes.

By reducing cosmetic defects and improving breakage resistance, we have also enabled our BD Neopak™ customers to significantly reduce their manufacturing costs by decreasing scrap and rates of rejection. Not insignificant numbers of PFS are scrapped by companies when they fail to meet the required standards. When filled with very expensive biological or biosimilar drugs, such scrappage costs can far exceed the purchase cost of the syringe. BD Neopak™ has been shown to significantly reduce scrap and rejection rates by up to 90%.

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The most recent development is the BD Neopak™ XSi™, an extension to the BD Neopak™ platform which allows companies to adopt a proactive, rather than reactive, approach to their combination product development. BD XSi™ features an innovative immobilised silicone coating that addresses potential silicone-related concerns while being fully compatible with existing practices and infrastructure. Our biopharmaceutical partners can now adopt a platform approach and transfer from BD Neopak™ to BD XSi™ if improved silicone functionality is required, enabling concerns to be addressed without major disruptions to, or investment in, the development and manufacturing process.

Q Could you elaborate on the concerns silicone poses to biopharmaceutical development, and what BD offers to mitigate them?

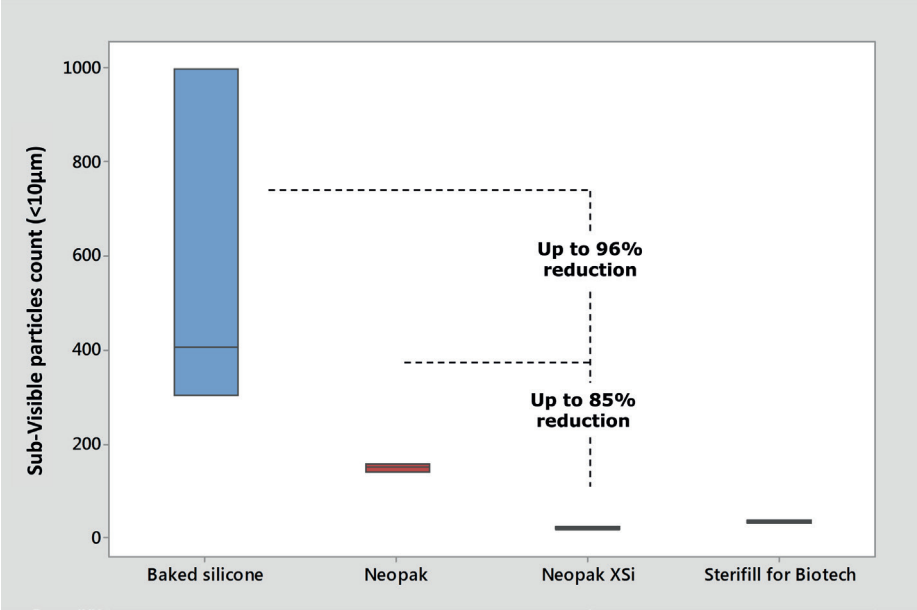

Figure 1: BD Neopak™ XSi™ displays significantly reduced particles >10 µm compared with alternatives.

A A critical factor in syringe gliding performance is the integrity of the silicone coating that lines the glass barrel. This requires a robust lubrication layer, especially in high-dose formulations where the surfactants used can "wash away" the silicone coating. Degradation of the silicone layer can become a significant barrier to development if it reduces gliding efficiency and the capacity to deliver a full dose, risking complaints and product recall.

On the other hand, migrating silicone can generate sub-visible particles (SbVPs) which, in the worst-case scenario, leads to non-compliance with USP 788 standards and registration failure. US and EU licensing regulations specify permissible numbers of SbVPs with a diameter over 10 µm and over 25 µm, although the US FDA has begun asking for data on smaller particles in the 2-10 µm range. This may become even stricter, as it is now possible to look for particles smaller than 0.5 µm in diameter.

It should be noted that the same regulatory standards apply to all containers below 100 mL, as they are defined per syringe rather than per mL, making it even more challenging to comply with those standards for larger volumes. Companies who foresee these potential challenges early in drug development, and adopt a successful risk mitigation strategy, avoid the risk of delays and registration failure.

Overcoming the problems associated with silicone requires a more stable silicone layer which can protect against drug interactions, minimise SbVP levels, retain gliding performance, improve patient experience, and reduce complaints and recall risks.

BD XSi™ incorporates a more inert, immobilised crosslinked silicone and this significantly reduces the number of SbVPs.

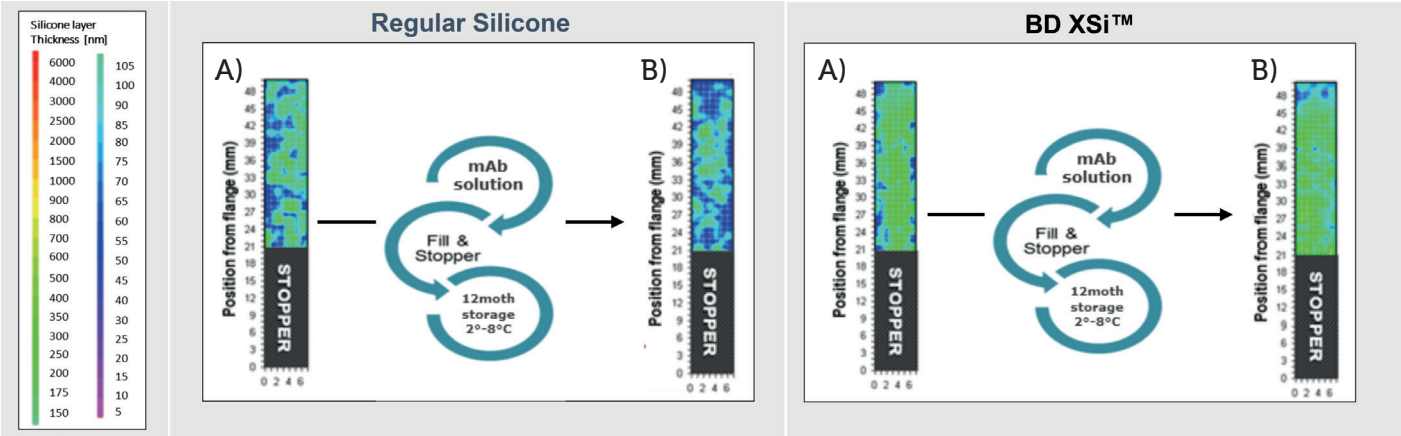

Figure 2: BD Neopak™ XSi™ maintains coating integrity and gliding performance compared with regular silicone, both at baseline (A) and at 12 months (B), measured by reflectometry.

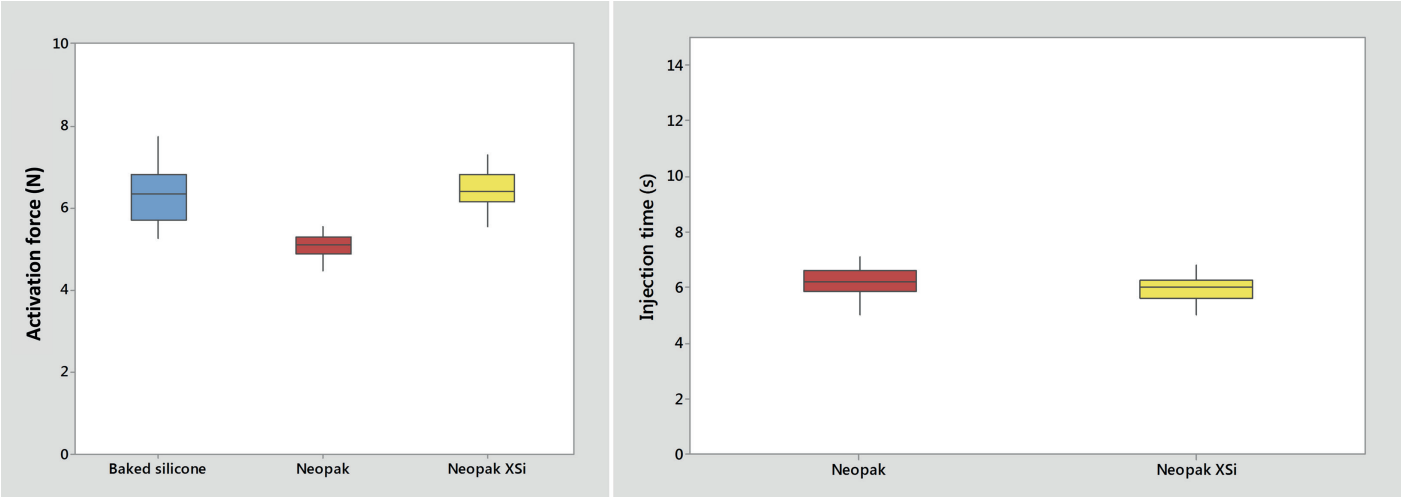

Figure 3: BD Neopak™ XSi™ maintains state-of-the-art gliding performance.

This notably outperforms other coatings, such as baked and sprayed silicone, and achieves true particle reduction across the 2-25 µm diameter range, not just shifting counts from one size to another.

This breakthrough technology uses the gold-standard DC360 silicone, and so does not introduce any new chemistry.† It builds on the best in class BD Neopak™ syringe and is fully compatible with existing development and manufacturing practices and secondary device standards.

BD XSi™ is a revolutionary offering to biopharmaceutical companies, as it allows them to initiate development with BD Neopak™ and then later opt for BD XSi™ if a particular molecule in their pipeline requires its additional features. As both products belong to the same manufacturing platform, this poses minimal risk to development timelines.

In a 2017 study, BD XSi™ was shown to significantly reduce particles of less than 10 µm compared with BD Neopak™ and BD's baked silicone solutions by up to 85% and 96%, respectively (Figure 1). The particle production with BD XSi™ was comparable to that of a non-siliconised polymer syringe, for example BD Sterifill™ for Biotech.

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Furthermore, the BD XSi™ layer has been shown to generate a very low percentage of SbVPs compared with other silicone coatings even after 48 hours of agitation, which may predict long-term stability. This is supported by previous study from Depaz *et al*, which showed that the required thickness and homogeneity of the lubricant coating was maintained over 12 months with BD XSi™. In comparison, the conventional silicone layer became thinner and disintegrated, making full dose delivery from an autoinjector less likely (Figure 2).

The stability of the BD XSi™ layer is key to maintaining coating integrity and gliding performance. BD XSi™ achieves a similar level of filled gliding force to conventional siliconised syringes, including BD Neopak™, which is particularly important for autoinjectors (Figure 3).

Q **Finally, can you succinctly explain the benefits of the BD XSi™ technology?**

A BD XSi™ is a significant step forward for the development of innovative, PFS-based biologicals, bringing multiple benefits to biotechnology manufacturers and patients with chronic diseases. Manufacturers now have a stable, robust product for advanced biological formulations, with reduced risk of development delays, registration failures, field complaints or product recalls. All these factors contribute to reduced total ownership costs and time to market, helping to maximise the number of patients who can benefit from innovative therapies.

This determination to deliver new technologies led to a paradigm shift, aimed at minimising delays in approval and decreasing time to market, and earning BD the trust of the pharmaceutical industry in the process. A benchmark study conducted by a leading pharmaceutical company evaluated four manufacturers against set criteria, and led to BD being selected as the partner of choice because of superior process capability, innovation potential and strategic fit.

†BD XSi™ does not introduce new chemical substances and only modifies the distribution of chemical functions which already exist in PDMS silicone.

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ON drugDELIVERY

2018/19 EDITORIAL CALENDAR

Publication Month	Issue Topic	Materials Deadline
March 2018	Skin Drug Delivery: Dermal, Transdermal Microneedles	Feb 8th 2018
April 2018	Pulmonary & Nasal Drug Delivery	Mar 8th 2018
May 2018	Injectable Drug Delivery: Devices Focus	Apr 5th 2018
June 2018	Connecting Drug Delivery	May 3rd 2018
July 2018	Novel Oral Delivery Systems	Jun 7th 2018
August 2018	Industrialising Drug Delivery Systems	Jul 5th 2018
September 2018	Wearable Injectors	Aug 2nd 2018
October 2018	Prefilled Syringes & Injection Devices	Sep 6th 2018
November 2018	Pulmonary & Nasal Drug Delivery	Oct 4th 2018
December 2018	Connecting Drug Delivery	Nov 1st 2018
January 2019	Ophthalmic Drug Delivery	Dec 6th 2018
February 2019	Prefilled Syringes & Injection Devices	Jan 3rd 2019

THE DIFFERENCE OF ONE DRUG DELIVERED

BY TACKLING SILICONE-RELATED CONCERNS.

At BD, we're committed to improving delivery of injectable drugs—for every patient, every time. It's why we partner closely with leading pharmaceutical companies to support their successful development and commercialization of combination products. Our partners have made clear that in some cases silicone, used as standard lubricant in syringes, has been a source of concerns in relation to drug quality and flawless delivery–concerns that could delay drug development timelines, impact drug availability and even lead to recalls of combination products. With BD Neopak™ XSi™, BD has developed an innovative lubricant technology to help alleviate silicone-related concerns while building on gold standards to be most compatible with processes and infrastructures. Discover the difference of better technology. **Discover the new BD.**

Minimizes sub-visible particle generation with BD Neopak™ XSi™[1]

Learn more about our prefilled syringes at **bd.com/NeopakXSi**

BD

[1]BD Neopak™ XSi™ competitive benchmark [internal study]. Le Pont-de-Claix, France: Becton, Dickinson and Company; 2017.