FROST & SULLIVAN

BEST PRACTICES AWARDS

BD

2020 GLOBAL AUTOINJECTOR DRUG DELIVERY TECHNOLOGY INNOVATION AWARD

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Background and Company Performance

Industry Challenges

Biological therapies for chronic diseases are on a steady rise owing to efficacy in treating chronic conditions. The present trend for self-managing chronic conditions, along with the increasing numbers of chronic illnesses like diabetes and cancer, evidences the need for delivering most top-selling biologics by injection. Unlike other conventional methods of drug delivery, an injectable allows maximum bioavailability of the drug as it bypasses the first-pass metabolism. Biologic injectables are often identified as unstable in a pre-filled solution, requiring reconstitution at times, necessitating manufacturers to develop solutions simultaneously to address patient adherence.

Need for Patient Centricity and Point-of-Care Drug Delivery

Injectable drug delivery innovations evolved traditional injections into a customized mode. Primary patient concerns associated with the use of injectable devices are needlestick injuries, needle phobia, pain perception, and anxiety, accidental intramuscular (IM) injection risk, and maintaining dose accuracy and consistency. Accordingly, the challenges increased the focus of injectable device industry players towards developing more user-friendly, efficient, and patient-compliant products. Additionally, minimizing injection frequency by increasing drug dose concentration or volume is a potential technique to bolster treatment adherence.

The resulting shift in device engineering seeks to identify safety risks and assist with patient compliance. Therefore, device designs became more patient-centric, and the market evidenced a shifting trend from administering injections in clinical settings to home care settings. Subcutaneous injections are evolving as a preferred choice of pharmaceutical (pharma) companies, device manufacturers, and patients owing to the benefit of self-administration through autoinjectors; the ideal injection volume is 1 milliliter (ml).[1] While the overall injectable drug delivery devices market is increasing at a compound annual growth rate of 8.1% from 2018 to 2023, the autoinjector market revenue will expand from $788.8 million to $3,237 million in the same period.[2]

High Viscous and High Volume Biologics Delivery Bottlenecks

Inherently biological drugs are complex, present as highly viscous formulations, and often require a robust design for effective delivery. The new generation biologics contain large molecules requiring administration in large volumes and concentration. Viscous or large volume administration is challenging for traditional delivery systems as they need more force and time to perform the injection, thwarting acceptability for patients, providers, and caregivers.

[1] "SPECIAL FEATURE - Injectable Drug Delivery: Key Trends Define Device Design Now & in the Future." Drug Development and Delivery, 13 June 2018, drug-dev.com/special-feature-injectable-drug-delivery-key-trends-define-device-design-now-in-the-future/.
[2] *Analysis of the Drug Delivery Devices Market, Forecast to 2023,* (Frost & Sullivan, September 2019)

Therefore, the biggest concern remains in identifying the best way forward to deliver high volumes and highly viscous drugs. Further, to treat chronic diseases requires repeated biologics dosing at regular intervals. This scenario creates a demand for self-administration autoinjectors providing safe and effective subcutaneous delivery of high-volume, high-viscosity drugs while offering convenience, ease of use, and patient comfort.[3]

Auto-Injector Challenges: Design Innovation, System Integration, and Project Management

Pharma companies are introducing self-administration therapies for ensuring dose compliance and administration ease. Self-injection devices comprise accurate dosage volumes and already reconstituted drugs. However, device and component availability from a variety of suppliers puts pharma companies at risk, which integrated systems, such as autoinjectors, reduce significantly. Thus, the autoinjector segment expects high growth due to advantages such as minimized chances of needle stick injuries, reduced needle phobia anxiety, and maintaining dose accuracy and consistency for better efficacy. However, auto-injectable drug manufacturers face the challenge of addressing issues such as product, market, and user dynamics for their devices. Risks include problems such as an increase in project management complexity and potential time delays. Moreover, challenges may only be identified late in the development cycle and, in some cases, post commercialization, after manufacturing the products in large quantities.

The manufacturers who are working closely with pharma partners to customize and develop robust, high-quality, designs surpassing system integration challenges, ensuring matchless compatibility between biologics and the primary container and secondary device for reproducible performance across millions of units,[4] and offering connected injectable drug delivery devices will emerge as market leaders.

Technology Attributes and Future Business Value of Becton Dickinson

Founded in 1897 and headquartered in Franklin Lakes, New Jersey, Becton Dickinson (BD) is a global medical technology company that develops and commercializes medical devices, instrument systems, and reagents. With a leadership position in injection systems, BD offers a differentiated self-injection systems portfolio leveraging a modular platform technology that allows rapid customization, optimizing time and cost, for pharma companies. Supported by its injection technique expertise, the company launched the two-step, handheld BD Intevia™ autoinjector, with unique ergonomics that enhance patient experience and usability for biologics drug delivery.

[3] PhD, Adeline Siew. "Wearable Injection Devices Address Delivery Challenges." BioPharm Home, 10 May 2018, www.biopharminternational.com/wearable-injection-devices-address-delivery-challenges.
[4] Pager A, "8 mm Needle – Improving Subcutaneous Chronic Drug Delivery". ONdrugDelivery Magazine, Issue 101 (Oct 2019), pp 28-32

Design Innovation Enhancing Ease of Drug Delivery, Patient Comfort, and Adherence

BD is developing a family of autoinjector products with BD Intevia—1-ml and 2.25-ml dose configurations—to meet the needs of the pharma companies for viscous and high volume biologics and with a commitment to enable delivery for a range of viscous biologics. The drug-device combination product improves the self-injection experience in home settings, thereby assisting pharma companies in delivering solutions to chronic disease patients for disease management, patient adherence, and improved life quality.

Firstly, within the 1 ml design, the company's innovative control point feature is designed to improve patient acceptance significantly. Historical data reveal stronger patient acceptance for three-step autoinjectors as these allow patients to control the final device activation. The newer systems with the two-step autoinjection are easier to use but sacrifice the patient's device control. To that end, BD Intevia's 1 ml design configuration (launched in October 2019) supports the control point feature that allows probing the target site without activating—empowering patients to control and explore the target location before pressing down and activating the device.

BD's device differentiates in the market by enabling balancing the control aspect of three-step autoinjectors while offering the ergonomic simplicity of a two-step autoinjector for the patient. With ongoing work on smart solutions, BD completed its feasibility study and will consider an open architecture approach to communicating dose injection events, based on customer requirements.

Secondly, the company's design innovations include the BD Neopak XtraFlow™ pre-filled syringe used with Intevia (2.25 ml), designed around application with a shorter 8 millimeters (mm) needle length and thin wall diameter. A smaller needle size versus the standard 12.7 mm needle suffices an unmet market need to enable limiting the injection-related anxiety, pain perception, and IM injection risks within the constraint of traditional injection times. Moreover, administering at a 90-degree angle can reduce the IM injection risk by 72% in adults and 32% in children (aged 7 to13 years).[5] Further, the shorter needle enables smooth drug administration without raising the injection force.

BD's human factors validation study corroborates end-users' positive perception in lowering the injection force through an 8 mm needle compared to the standard 12.7 mm needle. The study showed that 40% of end-users found the injection force acceptable when using an 8 mm needle versus 15% when using a 12.7 mm needle. Furthermore, the company conducted simulation studies with variable fluid viscosity delivery at a 15 second injection time to ascertain the short 8 mm needle reduced the injection force by nearly 14%. BD commercialized the short 8 mm needle solution, based on the BD Neopak™ glass pre-fillable syringe. [6]

[5] Pager, Aurelie. "8 MM NEEDLE – IMPROVING SUBCUTANEOUS CHRONIC DRUG DELIVERY." Drug Development and Delivery, Becton Dickinson & Company, 2019, drug-dev.com/trends-in-pharmaceutical-primary-packaging-for-injectables-solutions-for-new-challenges/.
[6] Ibid

The company's additional needle technology innovations include the BD Physiolis™ 29G Thin Wall needle to limit needle insertion pain, and the BD Hyflow™ 27G special Thin Wall needle to lower increase injection flow rate. Increasing inner needle diameter further improves viscous drug delivery. To that end, BD developed its prefilled syringe solution with an 8 mm (small) needle and an ultra-thin wall (UTW) needle.

The UTW technology widened the needle's inner diameter without altering external diameter (that impacts needle insertion pain perception and related anxiety), reduced injection force by 46% for highly viscous solutions without affecting needle insertion pain and pain-perception.

Integrated Offering Ensuring Seamless Performance and Scalability for Pharma Clients

BD positions itself as an advanced drug delivery solutions partner to pharma companies and ensures the successful launch of their combination products (autoinjectors) having robust subsystem integration. To that end, the company assures a robust combination device (prefilled syringe and device subsystem) performance throughout the device's technical management.

BD measures its performance against BD Physioject™, its standard configuration commercial offering, having a 3 ppm performance level. Offering a standard configuration with broad capabilities allows the company to leverage that design across a larger volume and scale so that robustness and performance reliability has the potential to be validated across a range of unit volumes and multiple drug molecules.

Unlike other market participants, BD's role as a delivery system integrator enables the company to manage end-to-end iterative developmental events and requirements—delivery system, subsystem, components, and manufacturing process requirements—and design controls (human factors usability testing, engineering, preclinical and clinical evaluation).

Besides, the company demonstrates this process with supporting documentation adhering to regulatory authorities' guidance. For example, BD regulates design control as per FDA's 21 CFR 820 in the United States (US). Marshaling a cross-functional team comprising technical, quality, and clinical experts enables the company to create comprehensive developmental data and implement necessary routine checks for the pre-fillable syringe and the device subsystem.

Enabling Pharma to Optimize Time, Cost, and Risk During Product Development

By offering Physioject's standard configuration, BD eliminates the potential for additional time and spending by pharma companies in the development phase. A well-proven commercially available solution that passed the entire development process to get a commercial release with a standard configuration can offer a shorter and cost-effective means to incorporate the learning into a combination product project.

The company's single modular platform approach allows pharma companies to handle only one platform for the entire pipeline without requiring customization, thus minimizing risks during development. For example, for a Physioject customer having eight different volumes of single molecules, BD provides one catalog number set for the eight different variants—convenient for supply chain management; such an offering integrates one configuration for different volumes and presentations, providing cost and time advantage. Additionally, customers working on dedicated projects have access to the company's preclinical research insights and data and can incorporate that information into their risk management plans. The collaborative approach to risk management allows customers to improve the risk management planning process.

BD also offers an integrated system integration documentation package (PFS and autoinjector) and provides services for feasibility and combination product testing in its laboratories—a convenience for both small and large pharma companies. A partner in customer assembly and filling process, the company assists pharma customers in installing facilities for filing and assembly equipment at their production site or at their contract manufacturing organization (CMO). BD is partnering with CMOs (in the US and Europe) to provide the full-scale capability to customers requiring scale-up. With a tiered volume approach to unit pricing, the company partners with customers on technology access fees to deliver value.

BD focuses on scientific aspects of delivering high-volume and viscosity biologics, bringing awareness, engaging with customers on issue-basis, and sharing its expertise in solving customer challenges to increase market adoption. Maintaining a global footprint with manufacturing, commercial, and technical organizations across multiple geographies, the company's breadth of capabilities allows it to support pharma companies in meeting their domestic and export needs while emerging as a global leader in self-injection systems.

Conclusion

Large molecule biologics require administration in high concentration. The resulting high-viscous, high-volume formulations create bottlenecks for traditional drug delivery systems. Therefore, pharmaceutical companies face the challenge of transforming a simple drug delivery system into a technology-fueled device for administering biologics effectively. In addition, self-administration and home care trends demand a painless delivery mechanism aligned to clinical outcomes, patient-centricity, comfort, and adherence.

Becton Dickinson (BD) designed the BD Intevia two-step, push-on-skin, handheld autoinjector for high-volume, high-viscosity biologics delivery for chronic disease therapies. The product design incorporates simple ergonomics, needle technology innovation around a shorter 8-millimeter needle length, and an ultra-thin wall diameter, offered in the 2.25 ml design configuration and control points offered in the 1mL configuration to minimize the injection-related anxiety, pain perception, and intramuscular injection risks.

Designed for home care settings, the autoinjector can reduce user-related risks with the goal of improving patient adherence. BD Intevia enables smooth drug administration without raising the injection force within the traditional injection time constraint. BD's technology manages the variance and variability of all component interfaces for robust subsystem integration and compatibility, enabling high performance and scalability.

With its strong overall performance, Becton Dickinson earns Frost & Sullivan's Global 2020 Technology Innovation Award in the autoinjectable drug delivery device market.

Significance of Technology Innovation

Ultimately, growth in any organization depends on finding new ways to excite the market and maintaining a long-term commitment to innovation. At its core, technology innovation, or any other type of innovation, can only be sustained with leadership in 3 key areas: understanding demand, nurturing the brand, and differentiating from the competition.

Understanding Technology Innovation

Technology innovation begins with a spark of creativity that is systematically pursued, developed, and commercialized. That spark can result from a successful partnership, a productive in-house innovation group, or a bright-minded individual. Regardless of the source, the success of any new technology is ultimately determined by its innovativeness and its impact on the business as a whole.

Key Benchmarking Criteria

For the Technology Innovation Award, Frost & Sullivan analysts independently evaluated 2 key factors—Technology Attributes and Future Business Value—according to the criteria identified below.

Technology Attributes

Criterion 1: Industry Impact
Requirement: Technology enables the pursuit of groundbreaking ideas, contributing to the betterment of the entire industry.

Criterion 2: Product Impact
Requirement: Specific technology helps enhance features and functionalities of the entire product line for the company.

Criterion 3: Scalability
Requirement: Technology is scalable, enabling new generations of products over time, with increasing levels of quality and functionality.

Criterion 4: Visionary Innovation
Requirement: Specific new technology represents true innovation based on a deep understanding of future needs and applications.

Criterion 5: Application Diversity
Requirement: New technology serves multiple products, multiple applications, and multiple user environments.

Future Business Value

Criterion 1: Financial Performance
Requirement: Potential is high for strong financial performance in terms of revenues, operating margins, and other relevant financial metrics.

Criterion 2: Customer Acquisition
Requirement: Specific technology enables acquisition of new customers, even as it enhances value to current customers.

Criterion 3: Technology Licensing
Requirement: New technology displays great potential to be licensed across many sectors and applications, thereby driving incremental revenue streams.

Criterion 4: Brand Loyalty
Requirement: New technology enhances the company's brand, creating and/or nurturing brand loyalty.

Criterion 5: Human Capital
Requirement: Customer impact is enhanced through the leverage of specific technology, translating into positive impact on employee morale and retention.

Best Practices Recognition: 10 Steps to Researching, Identifying, and Recognizing Best Practices

Frost & Sullivan analyst follow a 10-step process to evaluate Award candidates and assess their fit with select best practice criteria. The reputation and integrity of the Awards are based on close adherence to this process.

	STEP	OBJECTIVE	KEY ACTIVITIES	OUTPUT
1	**Monitor, target, and screen**	Identify Award recipient candidates from around the globe	• Conduct in-depth industry research • Identify emerging sectors • Scan multiple geographies	Pipeline of candidates who potentially meet all best-practice criteria
2	**Perform 360-degree research**	Perform comprehensive, 360-degree research on all candidates in the pipeline	• Interview thought leaders and industry practitioners • Assess candidates' fit with best-practice criteria • Rank all candidates	Matrix positioning of all candidates' performance relative to one another
3	**Invite thought leadership in best practices**	Perform in-depth examination of all candidates	• Confirm best-practice criteria • Examine eligibility of all candidates • Identify any information gaps	Detailed profiles of all ranked candidates
4	**Initiate research director review**	Conduct an unbiased evaluation of all candidate profiles	• Brainstorm ranking options • Invite multiple perspectives on candidates' performance • Update candidate profiles	Final prioritization of all eligible candidates and companion best-practice positioning paper
5	**Assemble panel of industry experts**	Present findings to an expert panel of industry thought leaders	• Share findings • Strengthen cases for candidate eligibility • Prioritize candidates	Refined list of prioritized Award candidates
6	**Conduct global industry review**	Build consensus on Award candidates' eligibility	• Hold global team meeting to review all candidates • Pressure-test fit with criteria • Confirm inclusion of all eligible candidates	Final list of eligible Award candidates, representing success stories worldwide
7	**Perform quality check**	Develop official Award consideration materials	• Perform final performance benchmarking activities • Write nominations • Perform quality review	High-quality, accurate, and creative presentation of nominees' successes
8	**Reconnect with panel of industry experts**	Finalize the selection of the best-practice Award recipient	• Review analysis with panel • Build consensus • Select recipient	Decision on which company performs best against all best-practice criteria
9	**Communicate recognition**	Inform Award recipient of Award recognition	• Present Award to the CEO • Inspire the organization for continued success • Celebrate the recipient's performance	Announcement of Award and plan for how recipient can use the Award to enhance the brand
10	**Take strategic action**	Upon licensing, company is able to share Award news with stakeholders and customers	• Coordinate media outreach • Design a marketing plan • Assess Award's role in future strategic planning	Widespread awareness of recipient's Award status among investors, media personnel, and employees

The Intersection between 360-Degree Research and Best Practices Awards

Research Methodology

Frost & Sullivan's 360-degree research methodology represents the analytical rigor of our research process. It offers a 360-degree-view of industry challenges, trends, and issues by integrating all 7 of Frost & Sullivan's research methodologies. Too often companies make important growth decisions based on a narrow understanding of their environment, leading to errors of both omission and commission. Successful growth strategies are founded on a thorough understanding of market, technical, economic, financial, customer, best practices, and demographic analyses. The integration of these research disciplines into the 360-degree research methodology provides an evaluation platform for benchmarking industry participants and for identifying those performing at best-in-class levels.

360-DEGREE RESEARCH: SEEING ORDER IN THE CHAOS

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