



A portfolio-based approach to meeting market needs in combination products

Leveraging insights to enable enhanced system integration

Beth DiLauri, BD
6 November 2017

Recognizing the needs of healthcare are changing...

FDA
APPROVED  **TIGHTENED**
REGULATION

ALZHEIMER
DIABETE HEART ATTACK
HYPERTENSION OBESITY
CANCER HIV
CHRONIC
DISEASES

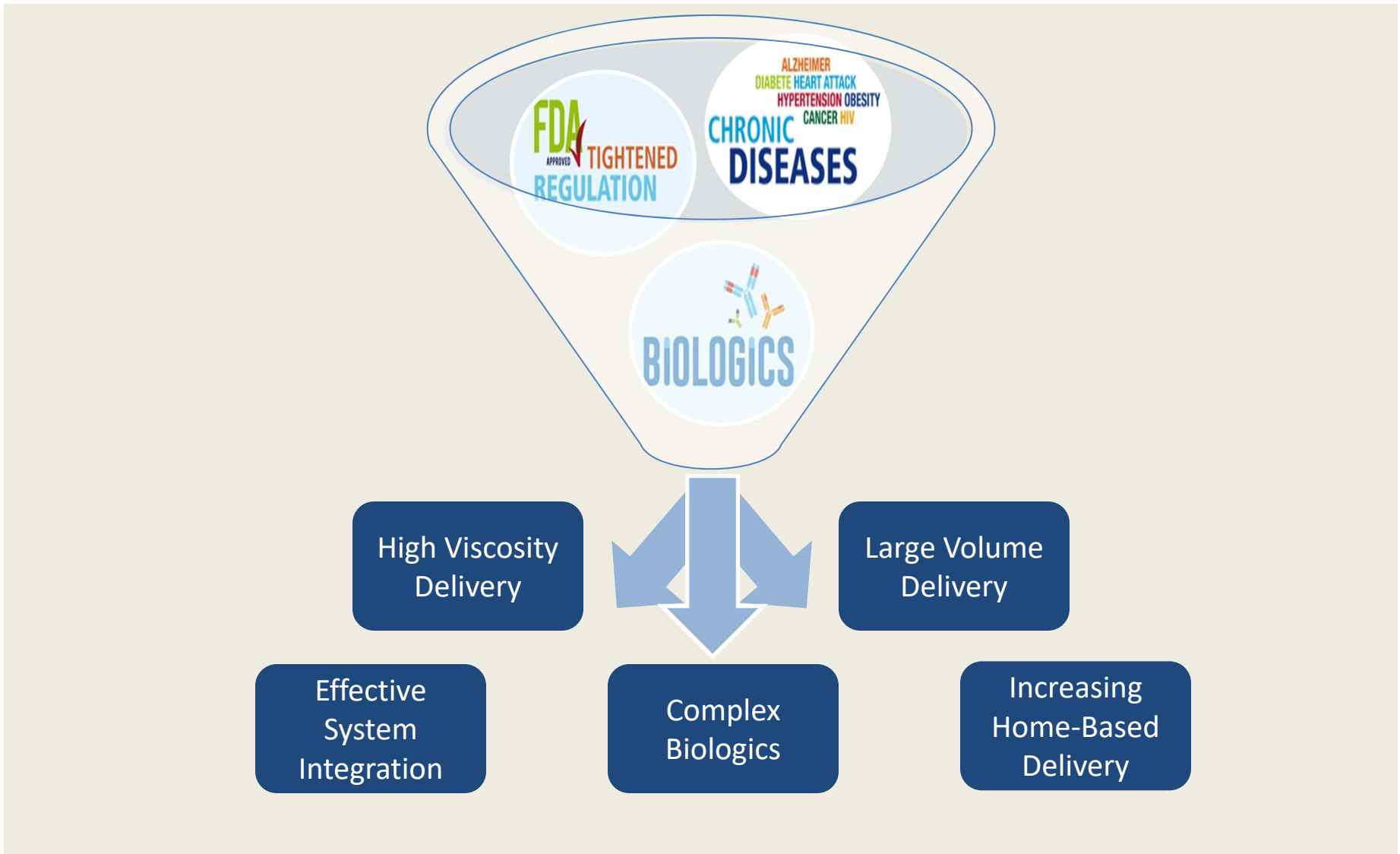
DIGITAL
HEALTH 
& **CONNECTED**
DEVICES


HEALTHCARE
COST

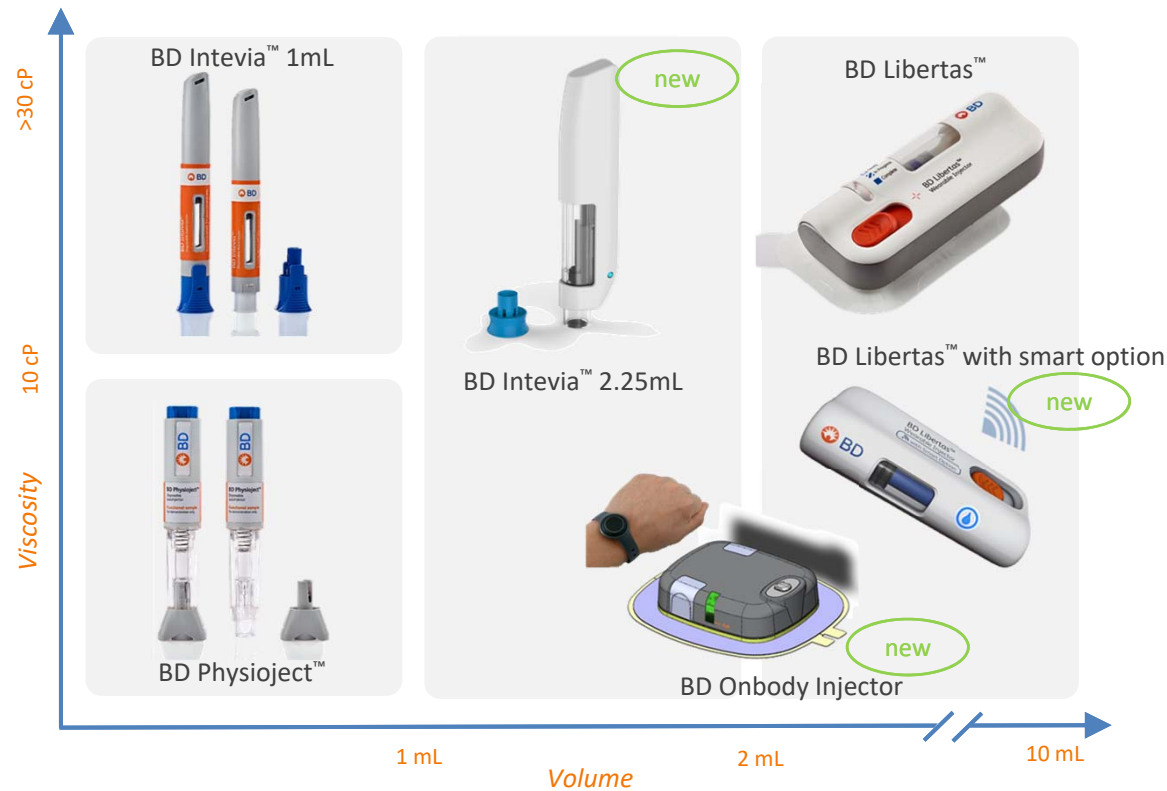

BIOLOGICS

EMERGING
MARKET 

At BD, we are aligning our capabilities to meet those needs



BD is intensively focused on developing a portfolio of solutions to meet these needs



Addressing challenges in delivering large volume, high viscosity biologics

BD Libertas™ wearable injector



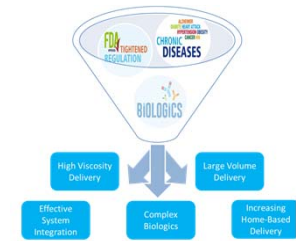
- **No patient assembly required**
- **Delivers 2-5mL, 5-10mL & $\geq 50\text{cP}$ biologics**
- **No minimum injection time**
- **Hands-free drug delivery**
- **Single-use, disposable, prefilled container delivery system**

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*BD Libertas™ is a product in development; some statements made are forward-looking that are subject to a variety of risks and uncertainties.

Compelling solution for in-home delivery of large volume biologics

BD Libertas™ wearable injector



Maximizing Success for Pharma

- Reduces need to concentrate biologics
- Enables formulation flexibility
- Leverages BD Neopak™ technology to ensure primary container performance
- Integrated systems designed for end-to-end compatibility

Driving Confidence for Patients

- Enables ease of use through no patient assembly
- Allows for convenience of in-home administration
- Delivers dose with the push of a button
- Patient needle based on BD PentaPoint™ technology

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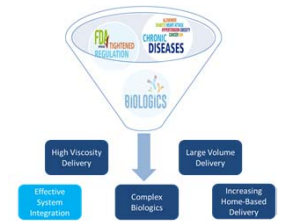
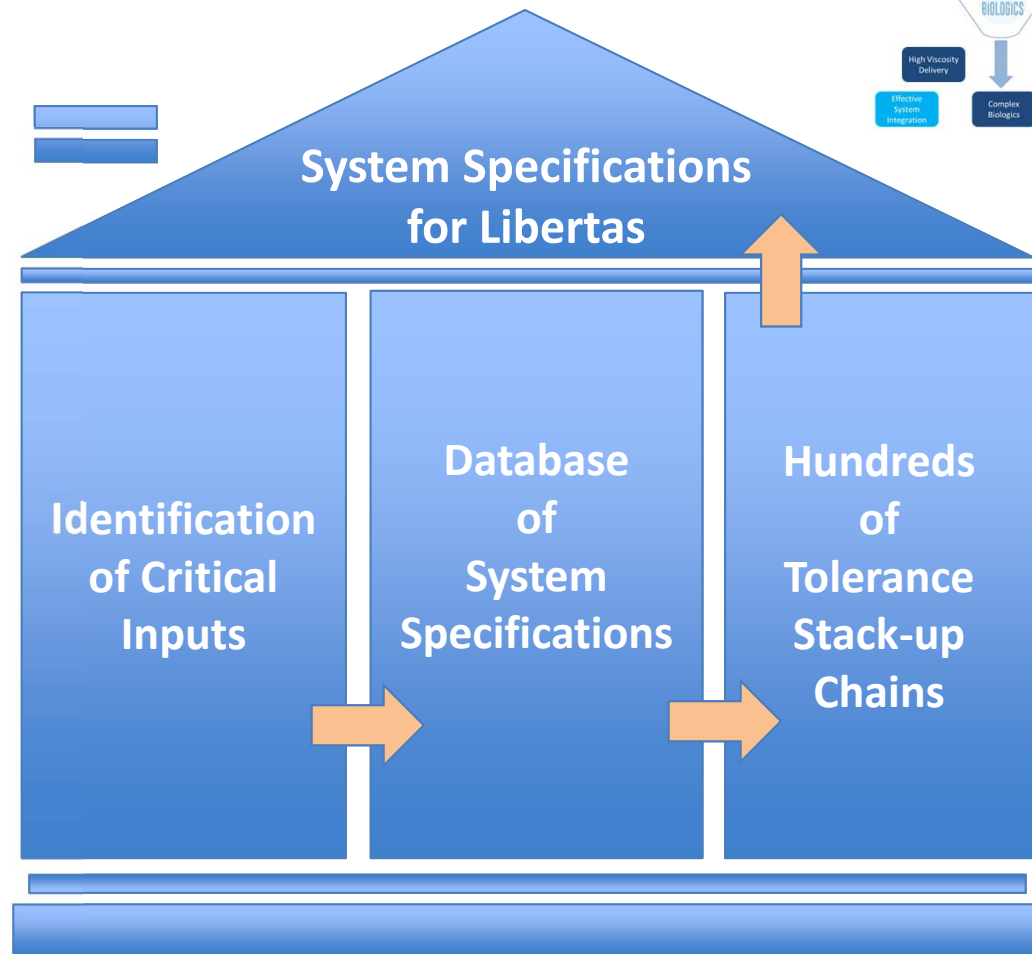
Seamless systems integration is critical to success of Combination Products



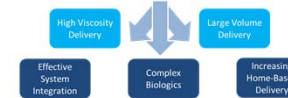
BD Libertas™ wearable injector



BD Libertas™ wearable injector with Smart option



De-risking development: characterizing large volume subcutaneous injections



Clinical Evaluation of Large Volume Subcutaneous Injection Tissue Effects, Pain and Acceptability

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Background

Subcutaneous (SC) large volume injectable therapies for the biological treatment of chronic diseases enable transition from intravenous (IV) administration to subcutaneous (SC) self-injection in otherwise healthy, increasing patient convenience/ compliance and potentially decreasing health care costs and injection frequency when performed with effective, innovative delivery systems. Current literature has investigated patient tolerance and acceptability of large volume injections (3-10mL) with and without permeation enhancers¹. The present study investigated subject pain, tissue effects and acceptability over 72 hours for 2 (low) concentrations, constant rate (250µL/hr) injections in the abdomen or thigh (2ml only) at volumes up to 20mL without permeation enhancers.

Methods

Harvard PhD Ultra syringe pumps delivered constant rate (250µL/hr) SC injections in the abdomen and thigh (2ml only) of 1, 5, and 10mL aliquots to 50 healthy human volunteers (Table 1) via a COMET™ Dual-Needle, 23Gx4, venous cannula (Bioscience Resource Project, Boston, MA) inserted at a 90° angle to the skin surface.

Results

Wheal Volume: 0.5h, 1h, 2h, 3h, 4h, 5h, 6h, 7h, 8h, 9h, 10h, 11h, 12h. 1h, 2h, 3h, 4h, 5h, 6h, 7h, 8h, 9h, 10h, 11h, 12h.

Figure 3. Wheal volume (mm³) at 0-2 hours post-injection. Resection is more rapid for lower volumes and volumes.

Figure 4. Wheal volume (mm³) at 0-2 hours post-injection. Resection is more rapid for lower volumes and volumes.

Figure 5. Subject pain scores (0-10) at 0-2 hours post-injection. Pain is higher during injection at 0 hours post-injection. Resection is more rapid for lower volumes and volumes.

Figure 6. Subject pain scores (0-10) at 0-2 hours post-injection. Pain is higher during injection at 0 hours post-injection. Resection is more rapid for lower volumes and volumes.

Figure 7. Subject pain scores (0-10) at 0-2 hours post-injection. Pain is higher during injection at 0 hours post-injection. Resection is more rapid for lower volumes and volumes.

Conclusions

Subcutaneous injection of viscous solutions up to 20mL or 12ml in the abdomen or thigh is feasible. Rapid resolution of injection pain and tissue effects with favorable subject questionnaire response indicate broad acceptability across the breadth of injection conditions.

Resolution of the anticipated tissue effects observed immediately post-injection (wheals 85.7%, erythema 89.0%) was complete for the majority by 2 hours post-injection (wheals 54.3%, erythema 88.6%). Resolution of wheals was more rapid for lower volumes and viscosity injections.

There was no correlation between in-line injection pressure and subject pain scores or tissue effects (wheal, erythema).

Wheal reversion additional clinical studies exploring ambient injection conditions over broader demographics (BMI, age, ethnicity) and additional formulation characteristics.

References

1. Shi, C. et al. 2013. Tolerability of injection pain across a spectrum of access device buffer conditions across study in healthy human adult volunteers. J Clin Pharmacol. 2013; 53(6): 757-768.

2. Kimura, K. et al. 2014. Subcutaneous injection of large volume of aqueous solutions. J Pharm Sci. 2014; 103(12): 3935-3942.

3. Shi, C. et al. 2015. Tolerability of injection pain across a spectrum of access device buffer conditions across study in healthy human adult volunteers. J Clin Pharmacol. 2015; 55(12): 1235-1243.

4. Shi, C. et al. 2015. Tolerability of injection pain across a spectrum of access device buffer conditions across study in healthy human adult volunteers. J Clin Pharmacol. 2015; 55(12): 1235-1243.

5. Shi, C. et al. 2015. Tolerability of injection pain across a spectrum of access device buffer conditions across study in healthy human adult volunteers. J Clin Pharmacol. 2015; 55(12): 1235-1243.

The Universe of Pre-filled Syringes & Injection Devices

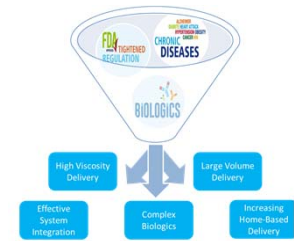
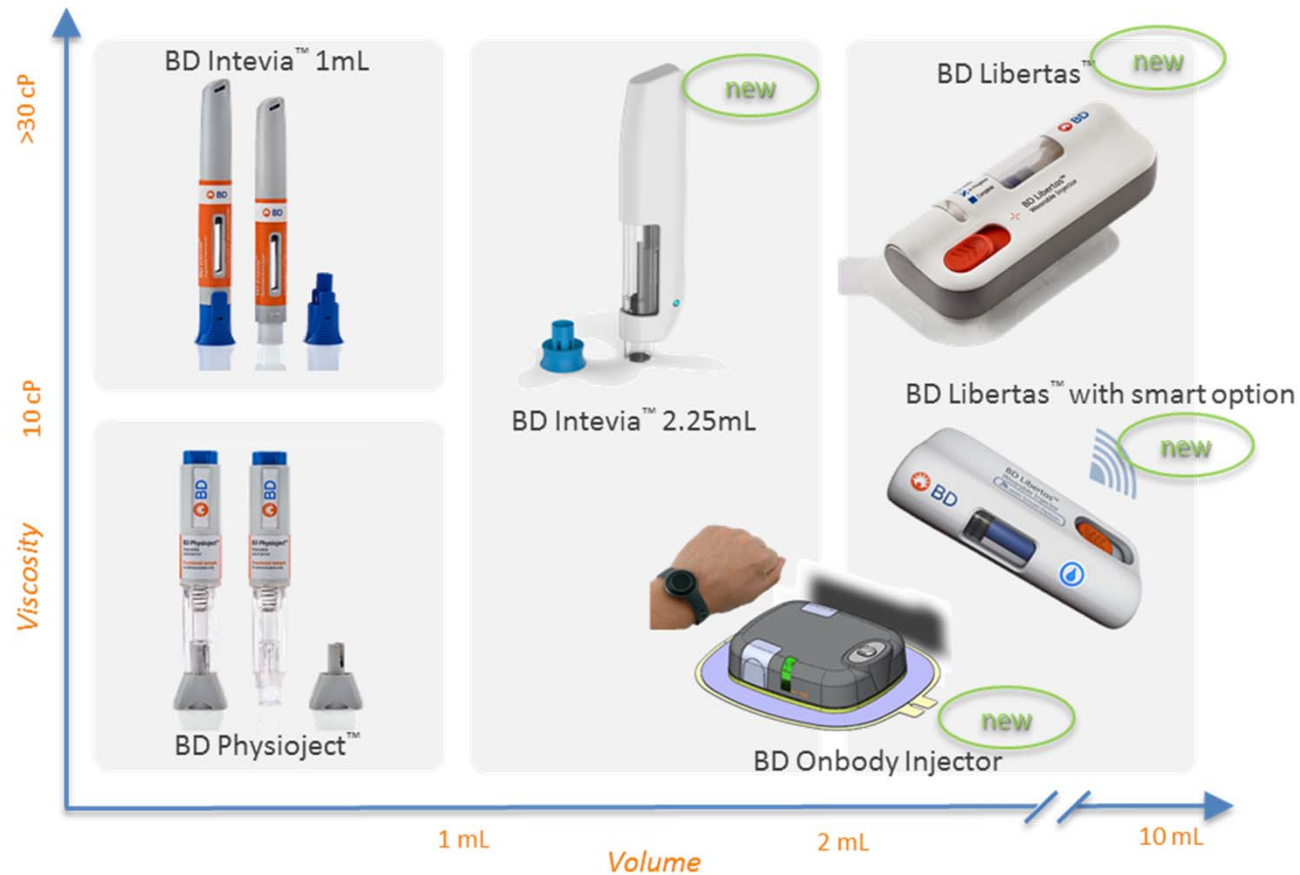
7- 8 November 2017
 Vienna | Austria

De-risking Clinical Trial Outcomes through Preclinical In Vivo Models for Large Volume Subcutaneous Injections

Natasha Bolick, MS, Manager, Parenteral Sciences, BD Technologies
 W. Woodley, D. Morel, D. Sutter, S. Gerth, D. Sherman, L. Chandler, R. Pettis

Wednesday, 8 November 2017
Track A: Patient-Device Interface
9:30 am, Hall D

Committed to driving innovation across the volume and viscosity continuum



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Acknowledgements