pda.org/2018Taiwan

2018 PDA Taiwan Conference

November 6-7, 2018
Taipei, Taiwan

The Evolving Pharma Outlook on Primary Containers and Injection Devices

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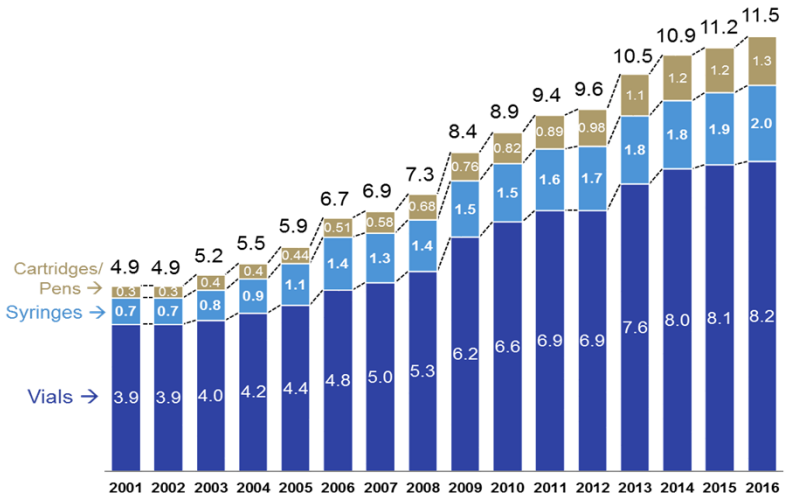
Seven of the Top 10 Drug in the World 2017 are Injectables

Drug Product	Company	Indication	Dosage form
Humira	Abbvie	Autoimmune Disease	Injection/Prefilled Syringe, Autoinjector
Harvoni	Gilead	Hep. C	Oral
Enbrel	Amgen /Pfizer	Autoimmune Disease	Injection/Prefilled syringe, Autoinjector
Rituxan	Roche/Biogen	Cancer	IV Injection/Vial
Remicade	J&J/Merck	Cancer	IV Injection/Vial
Revlimid	Celgene	Myeloma	Oral/Capsules
Avastin	Roche	Cancer	IV Injection/Vial
Herceptin	Roche	Cancer	IV and SC Injections/ Vial
Januvia	Merck	Diabetes	Oral/Film-coated Tablets
Lantus	Sanofi	Diabetes	Injection Pen

Source: Top 20 Drugs in the World 2017 Luca Dezzani, MD | 08.08.2017 https://www.linkedin.com/pulse/top-20-drugs-world-2017-luca-dezzani-md

The Small Volume Injectable Market in standard Units had a CAGR of 5.9% between 2001 and 2016 with Prefilled Systems growing faster

The Market of Small Volume Injectables in Volume by Systems (North America, Asia and EU without ROW**)



Total Sales Volume (SU bn)

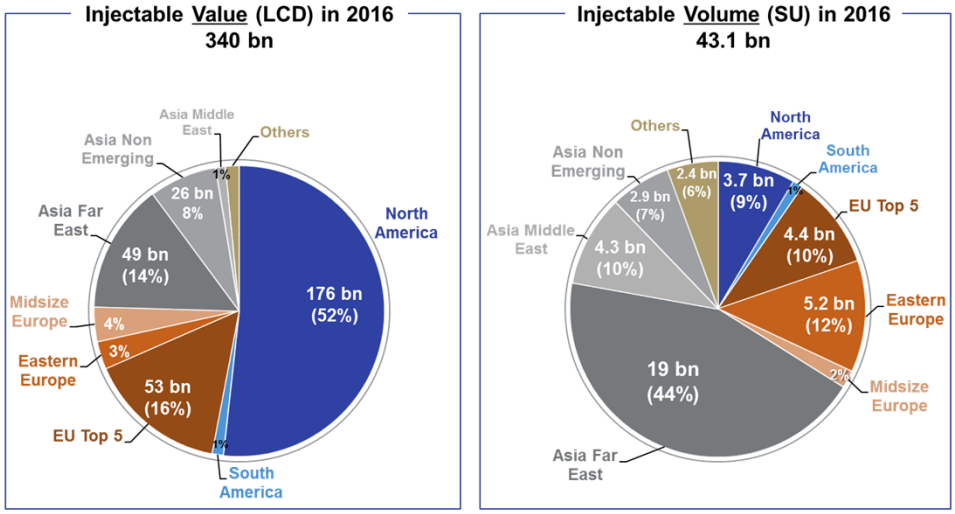
System	Share 2016	CAGR 2001-2016
Cartr./ Pens	11.4%	9.6%
Syringe	17.2%	7.6%
Vial	71.5%	5.1%
Total SVP*	100%	5.9%

* SVP = Small Volume Parenterals: Vials, Syringes, Cartridges/Pens

Source: IMS-World Reports 2002-2015 and IMS Health 'Study M36279' for Y 2015/16 (*excluding infusion bottles/bags, ampoules and implants)
**ROW: Australia, Africa, Asia Middle East, South America

North America and Europe make up ¾ of the Value of Parenterals with only ~⅓ of Unit Volume. US has the highest drug prices

Regional Market Share of Injectables* by Value & Volume

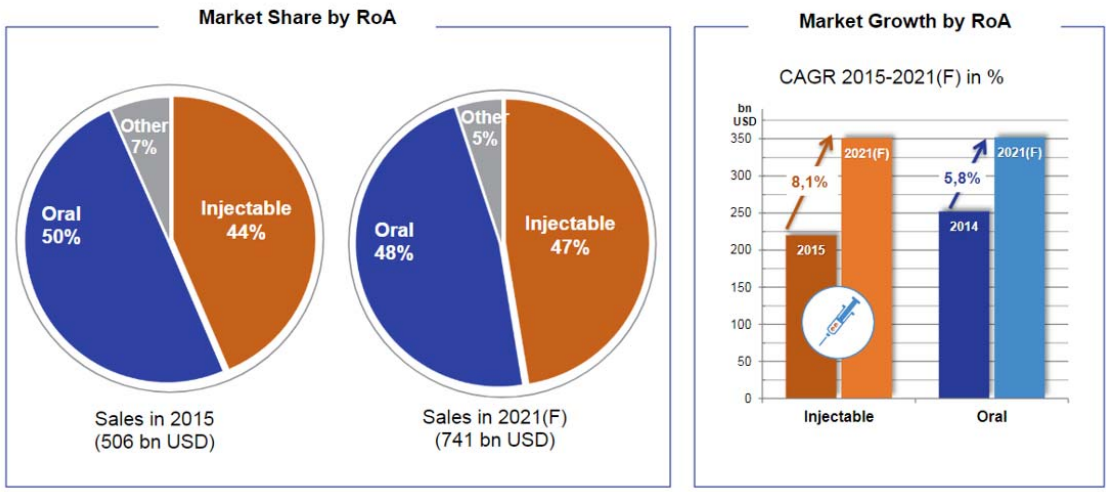


LCD=Local Currency Dollar / Local currency sales converted to US dollars at constant exchange rates

Source: IMS Health Data M36279, *excl. implants

The share of Sales Revenue for Injectables is expected to further Increase until 2021

Global Pharma Market Forecast by Route of Administration



Source: Global Data Sales Analytics, 26 January 2017
Other includes: topical, ophthalmic, suppository, nasal, sublingual, inhalation, transdermal

Drug Delivery matters

The pharmaceutical market is becoming more competitive	• Growth of biotechnology market • Patent expiry/Arrival of bio similars • Life cycle management/product differentiation • Many new Biotech products will be launched into markets with an existing standard of care
Regulatory compliance	• Accidental needle stick prevention
Market Evolution	• New technologies are becoming available • Existing device platforms relaunch with new innovative features • More self-injected drugs demand more patient friendly drug delivery solutions • Some pipeline drugs have new delivery needs, i.e. mabs have higher doses

Benefits of Pre-Fills and Devices

Patient convenience	• Minimizes time for preparation • Easy administration • Address needle phobia • Improve compliance, patient outcomes • Reduce risk of dosage errors, contamination
Physician/health care worker benefits	• Reduce/eliminate needle stick injuries • Reduce cost of therapy • Substantial time savings
Pharmaceutical company benefits	• Product differentiation in the marketplace • Enabling technology • Compliance with legislation/directives
Payers	• Potentially lower cost to administer drugs • Patient outcomes

Prefill Need is often driven by Competition and varies according to Therapeutic Areas

Stand alone Pre-filled syringes (w/ or w/o safety)	▪ Vaccines ▪ Ophthalmic drugs ▪ Contrast media ▪ Heparin
Diluent pre-filled syringes	▪ Some vaccines ▪ Factor VIII Drugs ▪ GnRh Analogues
Injection pens	▪ Diabetes treatments ▪ Human growth hormones ▪ Fertility treatments ▪ Osteoporosis
Auto-injectors	▪ Multiple sclerosis ▪ Rheumatoid arthritis ▪ Anti-migraine ▪ Psoriasis ▪ IBD ▪ Anemia ▪ Anaphylactic shock

Examples of Parameters to define suitable Device Platforms

Formulation	• Formulation for clinical trials • Formulation for commercial • Viscosity, injection volume • Single or multi dose • Liquid or lyophilized
Dosing	• Acute or chronic • Fixed or variable dose • Route of administration • Volume (ml) • Concentration • Viscosity • Frequency of administration
Usage	• Primary drug container/device • Self-injection vs. HCP administration • Human factors/usability studies • User requirements for device performance • Any digital requirements • Other like needle size etc.

Since 2006 a lot of PFS based disposable AIs have launched

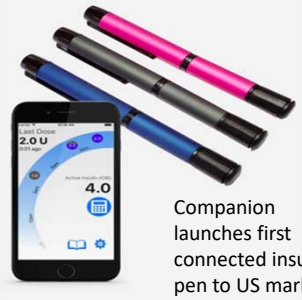
Device / Drug	Device Manufacturer	Pharma	Year
Humira Pen	Owen Mumford	AbbVie	2006
SureClick/Enbrel	SHL	Amgen	2006
SureClick/Aranesp	SHL	Amgen	2006
Simponi Pen	Owen Mumford	J&J	2009
MyCLIK/Enbrel	SHL	Pfizer	2009
Sumatriptan	SHL	Sun Pharma	2011
Pegasys Pen	SHL	Roche	2011
Avonex Pen	SHL	Biogen	2012
Rebidose / Rebif	BD	EMD Serono	2013
Actemra Pen	SHL	Chugai	2013
Otrexup	Antares Pharma	Antares Pharma / Leo	2014
Rasuvo	BD	Medac	2014
Sumatriptan	Bespak	Dr. Reddy	2014

More so in the middle of the Decade

Device / Drug	Device Manufacturer	Pharma	Year
Trulicity Pen	Lilly OEM	Lilly	2014
Plegridy Pen	SHL	Biogen	2014
Praluent Pen	SHL	Sanofi/Regeneron	2015
SureClick Repatha	SHL	Amgen	2015
Cosentyx Pen	SHL	Novartis	2015
Sumatriptan	Antares Pharma	Antares Pharma/Teva	2016
Click-Ject Pen (Orencia)	BD	BMS	2016
Cimzia	Bespak	UCB	2016
Taltz Pen	Lilly OEM	Lilly	2016
Benepali/Enbrel bios.	SHL	Biogen/Samsung	2016
Zembrace	SHL	Promius	2016
Erelzi	SHL	Sandoz	2016

Mega Trends - Connectivity

Novo Nordisk launches first connected insulin pen in Sweden



Companion launches first connected insulin pen to US market

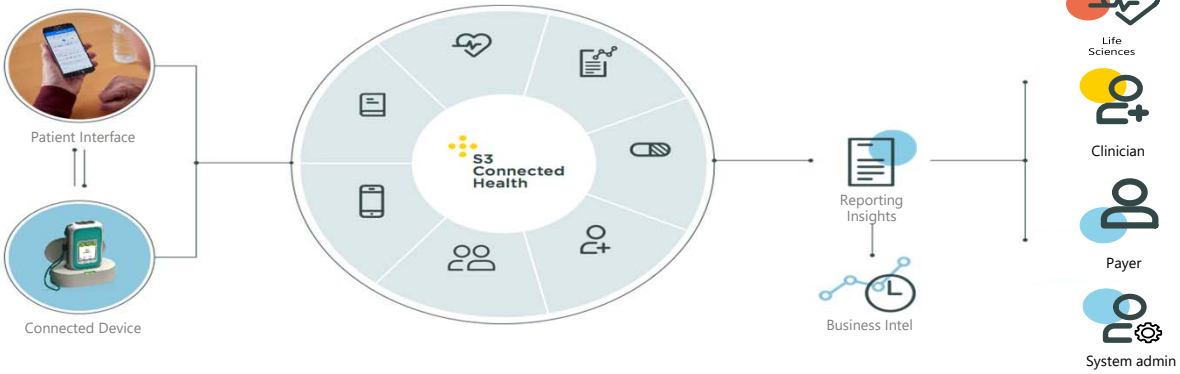
Otsuka Pharmaceuticals and Proteus launch MyCite patch to confirm oral delivery of Abilify

SHL partners with QuiO to develop reusable auto-injectors and pens with connectivity

Bayer electromechanical reusable auto-injector BetaConnect receives US approval for connectivity capabilities

Patient Ecosystem

Companies developing connected ecosystem for users
Eg Rebismart



Mega Trends – Electromechanical Devices

Merck Serono reusable electromechanical injectors for MS and growth hormone

Panasonic – developing reusable electromechanical devices for syringe and cartridge. Growjector marketed in Japan

Biocorp OneJet – disposable connected autoinjector

Amgen launches auto-injector 'Auto Touch' for Enbrel in the US

UCB submits reusable auto-injector 'AVA' for RA drug Cimzia

Elcam reusable electromechanical device for syringes and cartridges

Other Mega Trends – Examples

- Amgen on-body device OnPro for Neulasta grows to 63% market share in 2Q2018
- AZ announce launch of 3rd generation device for weekly GLP-1 Bydureon leveraging SHL cartridge based auto-injector 'Maggie'
- Needle free technology gets a boost thru Takeda/Portal Instruments deal
- Roche launch IV drug Ocrevus for MS treatment. Drug only requires 2 injections per year vs. Biogen IV drug Tysabri that needs to be infused every 28 days
- Next gen of powerful biological anti-migraine drugs from Amgen, Teva and Lilly entering market with self-injection devices. Hence moving a new TA to patient self-administration
- Sanofi atopic dermatitis drug Dupixent is offered in 2.25 ml prefilled syringe with 2 ml fill (300 mg dose in 150 mg/ml concentration). This is one of the highest SC doses in the self-administration space

Trend: On-Body Injectors (OBI) started launching

SMARTDOSE®
Electronic Wearable Injector

West's SmartDose® Drug Delivery Technology Platform - Launched by Amgen for Pushtronex™ System

On-body Infusor with Prefilled Cartridge to Deliver Monthly Doses of Repatha® (evolocumab)

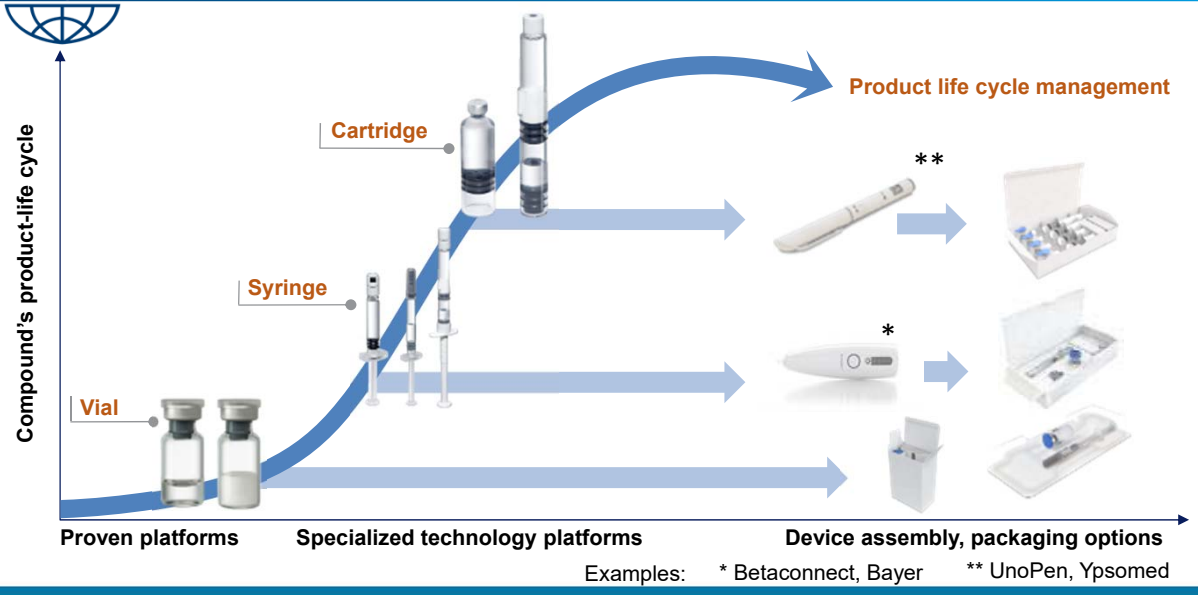
First FDA-Approved Commercial Use

Offers monthly vs. bi-weekly dosing

Integrated Containment and Delivery

On-body Self Administration

There is a clear Trend for User Convenience and hence for prefilled Systems



Self-Injection Is Moving Center Court and better Tools Are Needed

Vial / Syringe and Pre-Filled Syringe Suited to Trained HCPs

One-size fits all form factor

- Can be difficult to manipulate

Manual plunger

- Can be difficult to control

Exposed needle

- Safety
- Injection anxiety

Self-Administration Requires Patient-Centric Devices

Products should focus on overall patient experience

- Patients "**can** use" the product
  - Safe and effective administration
- Patients "**want** to use" the product
  - Motivated to use as frequently and as long as clinically beneficial

A Few User Needs May Be Applicable across the Board

Ease of Use	• Patient is comfortable with injection process and consequently treatment compliant / adherent • Provide solutions for patients with limited dexterity, eyesight
Convenience	• Device is 'portable' • Discrete and compact • Few steps as possible; easy and fast to administer • Easy device disposal post use • Fast and tolerable dose delivery
Reliability	• Pre-filled / preloaded is preferred • Complete prescribed dose is delivered each and every time • Status of injection is available throughout the process • No device failure
Minimize Pain	• Injection minimizes injection pain and site bruising

A Lot of Commonalities but Changes Are on the Way

Commonalities

- Mostly subcutaneous injections
- Injection volume 1 ml or lower
- Established primary container technology
- Fixed single doses use pre-filled syringes
- Multi dose presentations are cartridge based
- So far limited in-roads for dual chamber presentations and needle free technology

Drivers of Change

- Higher injectable volumes device platforms
- Higher viscosity drugs
- Longer intervals between injections
- Digital health opportunity
- Device innovations driven by e.g., user preferences and human factors studies
- Competitive activities

Concluding Remarks

- Drug and market competition was/will remain the big driver for many of the innovations and product launches we witnessed lately and for years to come
- Prefilled systems come with many advantages/benefits and have hence grown disproportionally
- The industry still has to demonstrate the value of enhanced patient adherence and engagement for better outcomes
- Moving forward disposal and ‘green markets’ could become a bigger consideration
- Connectivity may offer an opportunity to innovate but the value proposition is still work in progress

PDA
Parenteral Drug Association
Acknowledgments
• Brigitte Reutter –Haerle, Vetter
• Simon Wilson, Pfizer
• Claire Everitt, Pfizer