Regulatory landscape and key considerations for connected drug delivery devices

Juan M. Carriquiry, PhD
Partner, Beyond Conception GmbH

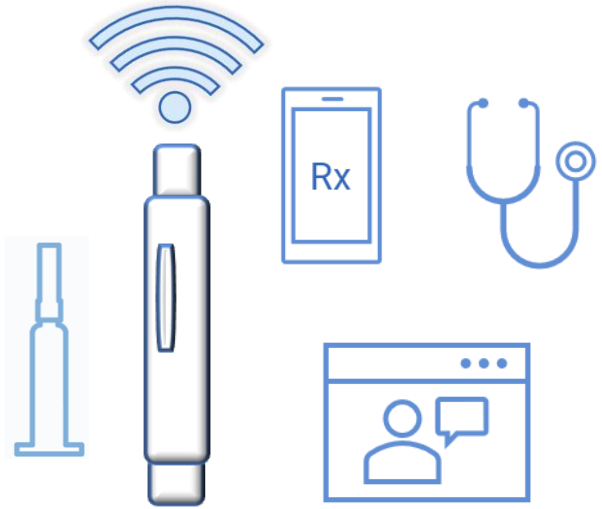
CONNECTING PEOPLE SCIENCE AND REGULATION®

PDA Parenteral Drug Association

PDA WORKSHOP

Connected drug delivery devices

1. Expected benefits
2. Regulatory identity
3. Complexity: stakeholders
4. QMS & Product Requirements
5. Key considerations to digital strategy



What are the expected benefits of connectivity?

- What is that we are trying to achieve?

To keep up – who isn't connected!

To be innovative and pave the way!

Collect massive amounts of useful data, which can be turned into product improvement!

To support the patient experience

To improve adherence to a treatment

To enhance the effect of the treatment/intervention through behavioral change

To maximize the value of complementary therapies (holistic patient/disease management)

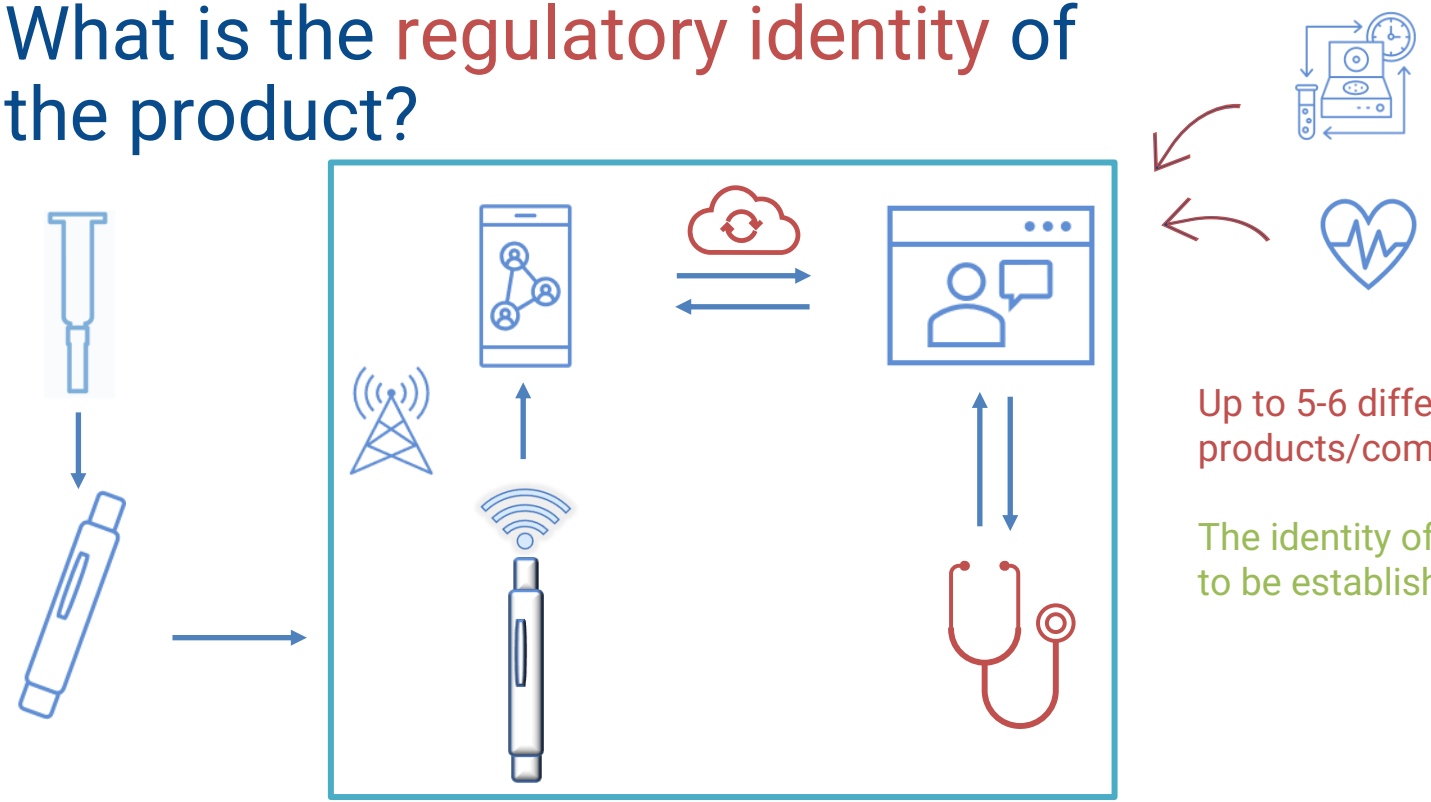
To trigger timely safety interventions by healthcare professionals

(…)

Why is the reason for connectivity so essential?

1. The ultimate purpose of developing the product: its intended use/purpose
2. Understanding the product regulatory identity
3. The claims that may or not be made
   The clinical data that will be required to support those
4. Requirements for the development
   Timelines and resources

What is the regulatory identity of the product?



Up to 5-6 different products/components

The identity of **each** needs to be established upfront

What does the *device* part of the product do?

Intended use/purpose:

- Administer the drug product (e.g. subcutaneously) as intended when actuated

- Does it deliver data to an app, such as
  - Injection time/date? Location?
  - Injection completion/success/injection duration?

- Does it include QR/Data Matrix codes in the labeling to e.g.,
  - Direct users/patients to a website with additional info for use of the device?
  - Does it include data on the drug identification or expiry date?

What does the app do?

It receives/captures data!

- From the device (part)?
- From the user (e.g., manually inputted)?
- From other apps or devices (e.g., activity tracker, pressure monitoring device)?
- From other sources (i.e., physician, emergency services, MAA, support program, etc.)?
- Time/location/access
- Barcode read for drug identification

- **Does it process data?**

- Archive/log received data (e.g., from the app, user, physician/HCP)?
- Does it transform the data for better visualization i.e., in a chart/diagram?
- Calendar/reminder function?
- Alarms/notifications meant to modify patient/user behavior e.g., regarding disease progression/management?
- Does it diagnose, measure or monitor any disease or condition?
- Advice to the patient to improve treatment outcome?

MEDICAL DEVICE

- **Does it send/transfer data?**

- E.g., to a portal, patient management system, patient support program system, MAA databases etc.

What does the portal do?

It receives data!

- From the app?
- From the user (e.g., manually inputted)?
- From other apps or devices (e.g., activity tracker, pressure monitoring device)?
- From other sources (i.e., physician, emergency services, MAA, support program, etc.)?

- **Does it process data?**

- Archive/log received data (e.g., from the app, user, physician/HCP)?
- Does it transform the data for better visualization i.e., in a chart/diagram?
- Calendar/reminder function?
- Alarms/notifications meant to modify patient/user behavior e.g., regarding disease progression/management?
- Does it diagnose, measure or monitor any disease or condition?
- Advice to the patient to improve treatment outcome?

MEDICAL DEVICE

- **Does it send/transfer data?**

- E.g., to a portal, patient management system, patient support program system, MAA databases etc.

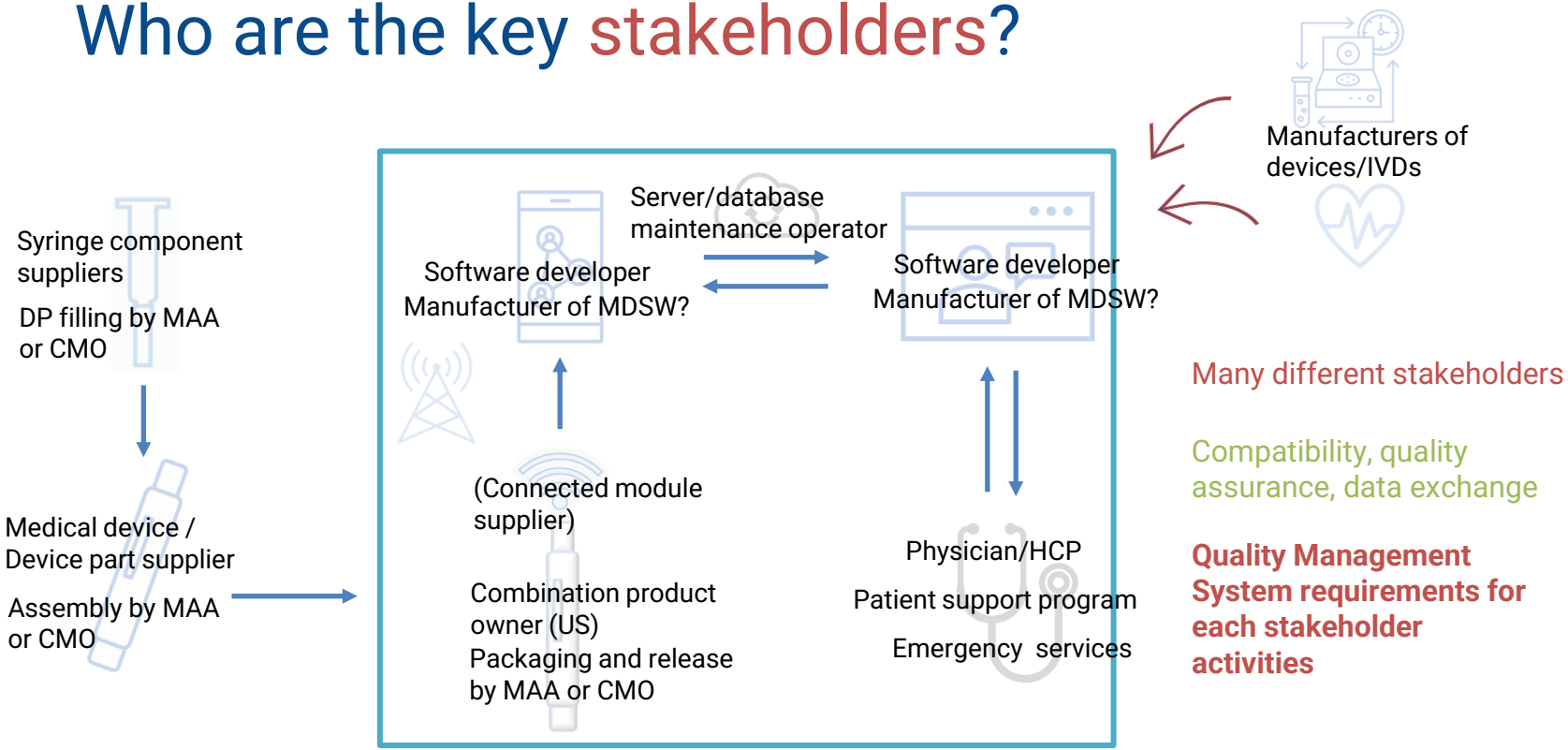
Product identity/classification

	EU	US
Drug	Medicinal Product	Drug
Device 	Injector and the proposed medicinal product form a single integral product	One of the common procodes: KZH Introducer, Syringe Needle
	Intended for the **treatment and monitoring of a disease / injury / disability and the prognosis of a disease, by measuring and transmitting injection data and influencing the user behaviour in relation to the underlying therapy**	
	Consult National CA	513(g) request to FDA
Final	Medicinal product. MAA	Combination product. BLA, NDA, ANDA

Classification and pathway defined by the INTENDED USE

Complexity

Who are the key stakeholders?



Many different stakeholders

Compatibility, quality assurance, data exchange

Quality Management System requirements for each stakeholder activities

QMS & Product Requirements

Overview of regulatory requirements for Quality Management System & Product Development

QMS Requirements

	EU	US
Drug 	Regulation (EU) No 1252/2014 GMP for active substances Directive 2003/94/EC GMP for medicinal products	Current Good Manufacturing Practice (CGMP) 21 CFR 210, 211, 600
Device 	Medical Device Harmonised standard EN ISO 13485 QMS related requirements as stated in MDR (e.g. Article 10)	21 CFR 820 Quality System Regulation, QSR
Final 	Separate applicable regulatory requirements based on the drug and the device(s) development and manufacturing	21 CFR 4 Regulation of Combination Products Streamlined approach

QMS & Product Requirements

Horizontal (QMS)	Vertical (Product)
Risk Management ISO/EN ISO 14971 + ISO/TR 24971:2020 ISO/IEC, EN IEC 80001-1 IEC 62304:2006/Amd 1:2015 AAMI TIR57:2016 (R2019) IEC TR 80001 series	Performance (device): ISO 11608 series – needle-based injection systems FDA guidance (various) - SaMD IEC 60601:2010 series - Medical electrical equipment
Human Factors Engineering/Usability IEC 62366-1:2015 ANSI/AAMI HE75:2009 (R2018) IEC 60601-1-6:2010 +AMD1:2013+AMD2:2020 CSV Consolidated version FDA HFE guidance (various)	Safety: ISO 10993 – Biocompatibility ISO 23908:2011, FDA guidance - Sharp injury protection FDA guidance - Devices Intended for Home FDA guidance - IEC 60601:2010, IEC 61010-1:2010, IEC 62479:2010 - Electric safety and EMC, Electrostatic discharge, Battery, Radio frequency identification, Software, Cybersecurity

What to consider in your digital strategy

What to consider in your digital strategy

1. What are the **expected benefits** of each system element?
2. Are the elements approved/mandated to be used as **part of the treatment** for the medicinal product?
3. Is your organization ready to meet the **QMS requirements** (combination product owner, MDSW manufacturer)?

What to consider in your digital strategy

4

Were products developed following **Design Controls** and meets all the regulatory requirements (e.g., usability, risk management, design verification and validation, cybersecurity, data protection, etc.)?

5

Are your systems ready for the **inter-dependencies** among stakeholders/system functionalities?

- Do you have the technical, legal and QA agreements with the relevant service providers for data exchange, storage and processing?
- Is it clearly established who has reporting obligations to HA and how this is carried out?

6

Geography: Is the regulatory status of the product(s) defined for **each country**?

- Are the products regulated differently across geographies? Should certain functions be available only in some countries and not other?
- You may want to consider an earlier release in those countries which as less highly regulated in an initial phase

CONNECTING PEOPLE SCIENCE AND REGULATION®

Thanks!

Amelia Yang – Beyond Conception
Stephanie Goebel – Beyond Conception

QMS Requirements with various suppliers

	Supplier/third party service provider	Combination Product Owner
Drug 	Drug substance Drug product	Operating quality system to ensure all GxP requirements are met throughout the product lifecycle Challenges are often seen in • R&R (responsibility to comply) • Information flow and collaboration • Cybersecurity 
Device 	Design and manufacturing of device parts Software developer	
Final 	Fill-finish Assemble the drug product and the drug delivery device	

QMS Requirements with various suppliers

	Supplier/third party service provider	Combination Product Owner
Drug 	Drug substance Drug product	Operating quality system to ensure all GxP requirements are met throughout the product lifecycle Challenges are often seen in • R&R (responsibility to comply) • Information flow and collaboration • Cybersecurity 
Device 	Design and manufacturing of device parts Software developer	
Final 	Fill-finish Assemble the drug product and the drug delivery device	

QMS Requirements (horizontal)

	Guidance/Standard/Guideline
Drug 	ICH (International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use) guidelines: ICH Q7 & Q10 PIC/S (Pharmaceutical Inspection Co-operation Scheme) GMP Guide
Device 	Region specific (FDA/MDCG guidance), ISO, IEC, ASTM, ANSI AAMI, IEEE standards • IEC: International Electrotechnical Commission • ASTM: American Society for Testing and Materials • ANSI: American National Standards Institute • AAMI: Association for the Advancement of Medical Instrumentation • IEEE: Institute of Electrical and Electronics Engineers
Final 	AAMI TIR105:2020 Risk Management Guidance For Combination Products ISO 20069:2019 Guidance for assessment and evaluation of changes to drug delivery systems

QMS Requirements (horizontal)

Device 	Quality Management System Personal Data: EU General Data Protection Regulation/US California Consumer Privacy Act ESD: Requirement necessary to design, establish, implement and maintain an electrostatic discharge control program Label: Symbols to be used with medical device labels, and information to be supplied, safety signs, Graphical symbols for electrical equipment in medical practice, cybersecurity labeling Identification (UDI)

CDS v. device

1.Your software function does NOT acquire, process, or analyze medical images, signals, or patterns.
2.Your software function displays, analyzes, or prints medical information normally communicated between health care professionals (HCPs).
3.Your software function provides recommendations (information/options) to a HCP rather than provide a specific output or directive.
4.Your software function provides the basis of the recommendations so that the HCP does not rely primarily on any recommendations to make a decision.
If all four criteria are met, your software function may be non-device CDS.