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Finding Common Ground: Managing Medical Device Interoperability Expectations

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Agenda

- Connected device market overview
- Global regulatory expectations
- Integration considerations
- Integration challenges
- Conclusion

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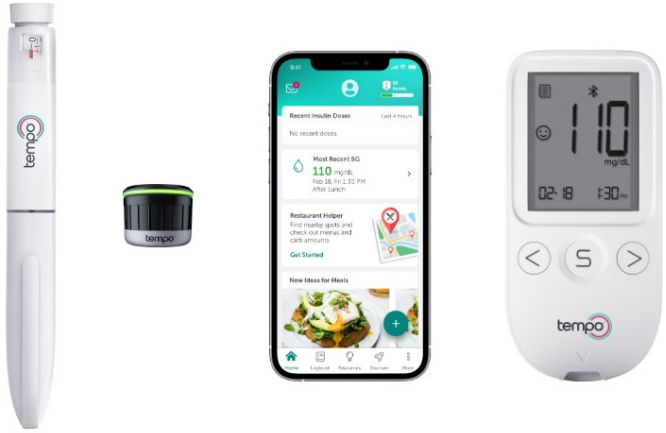
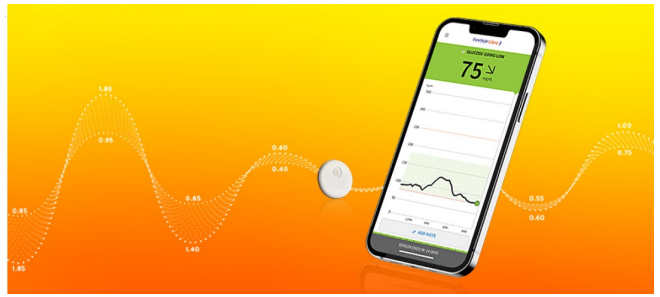
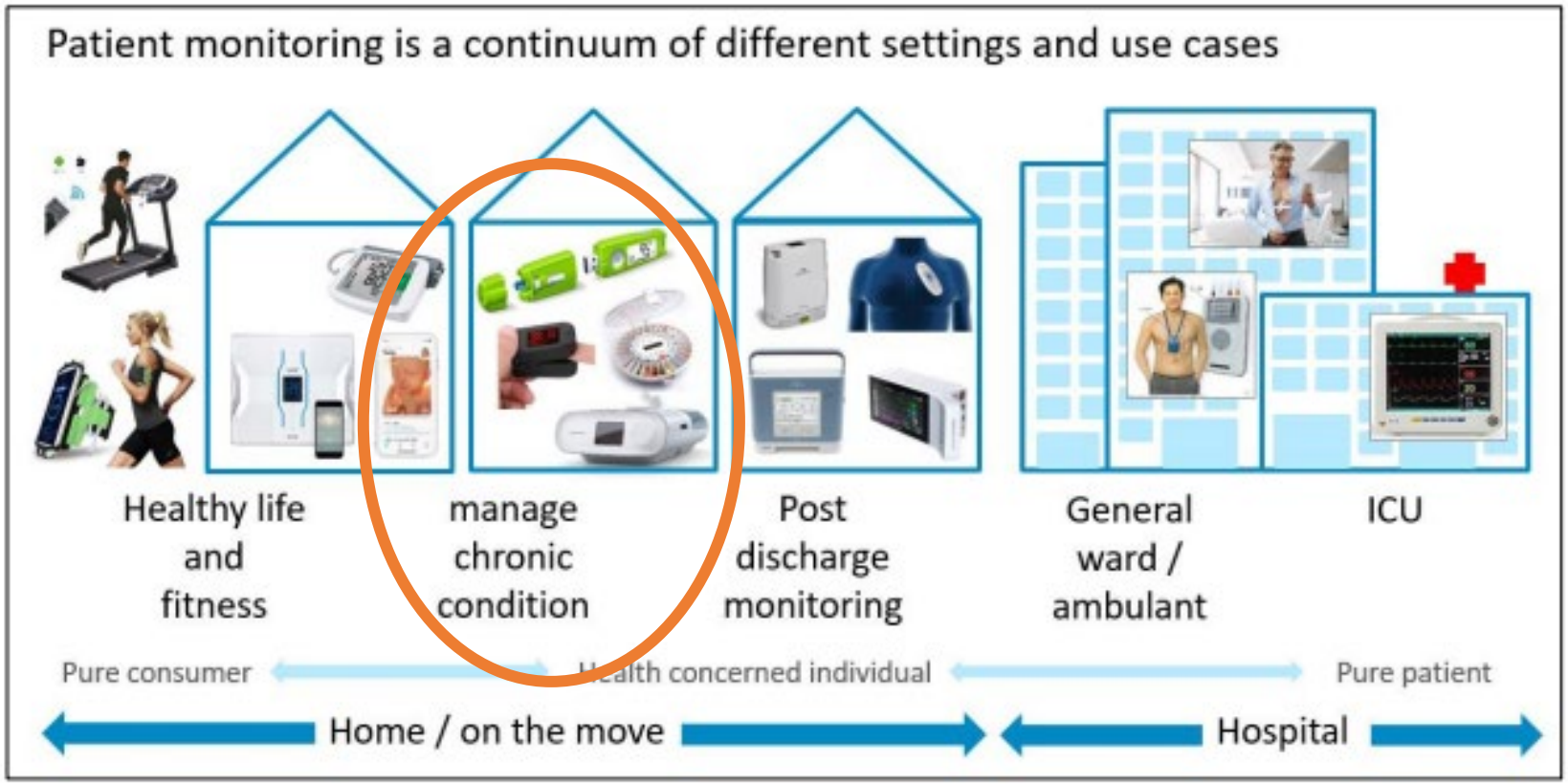
Interoperable Medical Devices



- Medical Devices linked to data collection and monitoring systems via computers, smartphones, and other devices
- Benefits include more immediate and consistent data about patients, adherence to regimens, earlier detection and prediction



Spectrum of Interoperable Devices



Credit: COCIR/MedTech Europe, “Interoperability standards in digital health: A White Paper from the medical technology industry” 06Oct2021

Connected Medical Devices Market

- ~$31.2 Billion USD in 2021 [1]
- Expected to grow at a rate of 22% through 2030 [1]
- Covid pandemic has accelerated uptake of connected medical devices to support telehealth
- Companies with expertise in medical devices do not always have expertise for SaMD and vice-versa

1 - Credit: Accumen Research and Consulting (https://www.acumenresearchandconsulting.com/request-sample/2930)

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Regulatory Considerations for Interoperable Medical Devices

Key Considerations when establishing regulatory compliance:

- Intended users
- Communication methods
- Interoperability boundaries
  - What are the interactions
  - Internally vs externally developed devices
  - System vs not a system
- Device classification

Key Regulatory Expectations in the EU:

- Regulation (EU) 2017/745 Annex I:
  - GSPR 3: Establish, implement, document and maintain a risk management system….which includes risks associated with device interactions (incorrect data transmission, missing data transmission etc.)
  - GSPR 4: Risk control measures adopted by manufacturers…eliminate or reduce risks from device interactions (flag transmission errors, push notifications, communication of residual risks)

Key Regulatory Expectations in the EU (contd.)

- Regulation EU (2017/745) Annex I:
  - 14.1 If the device is intended for use in combination with other devices or equipment the whole combination, including the connection system shall be safe and shall not impair the specified performance of the devices. Any restrictions on applying to such combinations shall be indicated on the label and/or in the instructions for use…
  - 14.5 Devices that are intended to be operated together with devices or products shall be designed and manufactured in such way that the interoperability and compatibility are reliable and safe

Key Regulatory Expectations in the EU (contd.)

- Regulation EU (2017/745) Annex I:

  Labeling (IFU)

  - 23.4(q) for devices intended for use together with other devices and/or general purpose equipment:
    - Information to identify such devices or equipment, in order to obtain a safe combination and/or
    - Information on any restrictions to combinations of devices and equipment

Key Regulatory Expectations in the EU (contd.)

- Regulation EU (2017/745) Annex II (Technical Documentation):
  - 6.2(g) If the device is to be connected to other device(s) in order to operate as intended, a description of this combination/configuration including proof that it conforms to the general safety and performance requirements when connected to any such device(s) having regard to the characteristics specified by the manufacturer

EU System Requirements (Article 22)

- Article 22: System Declaration of Conformity
  - Verification of mutual compatibility
  - supplied relevant information to users
  - Appropriate methods of internal monitoring, verification and validation were applied for the system
- Article 22 and Annex I: Labelling must identify system producer, reference to manufacturers of CE marked devices, include instructions for use as a system
- Registration in EUDAMED as System Producer economic operator
- Conformity assessment needed if system is sterilized

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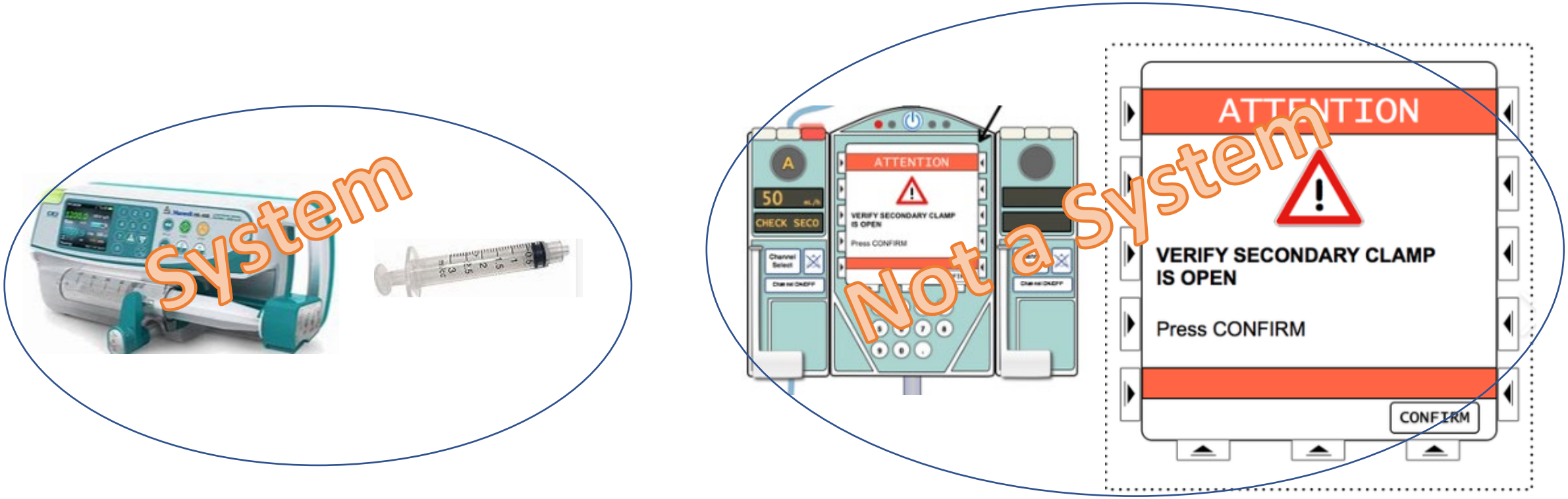
EU: System or not a System?

- EU MDR defines a system as a combination of products either packaged together, or not, which are intended to be interconnected or combined to achieve a specific medical purpose



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FDA Guidance: Design Considerations and Pre-Market Submission Recommendations for Interoperable Medical Devices

Key considerations for Manufacturers

- Purpose of the electronic interface
- Anticipated Users
- Risk Management
- Verification and Validation
- Labeling considerations
- Use of consensus standards

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FDA Guidance: Design Considerations and Pre-Market Submission Recommendations for Interoperable Medical Devices – **Purpose of Electronic Interface**

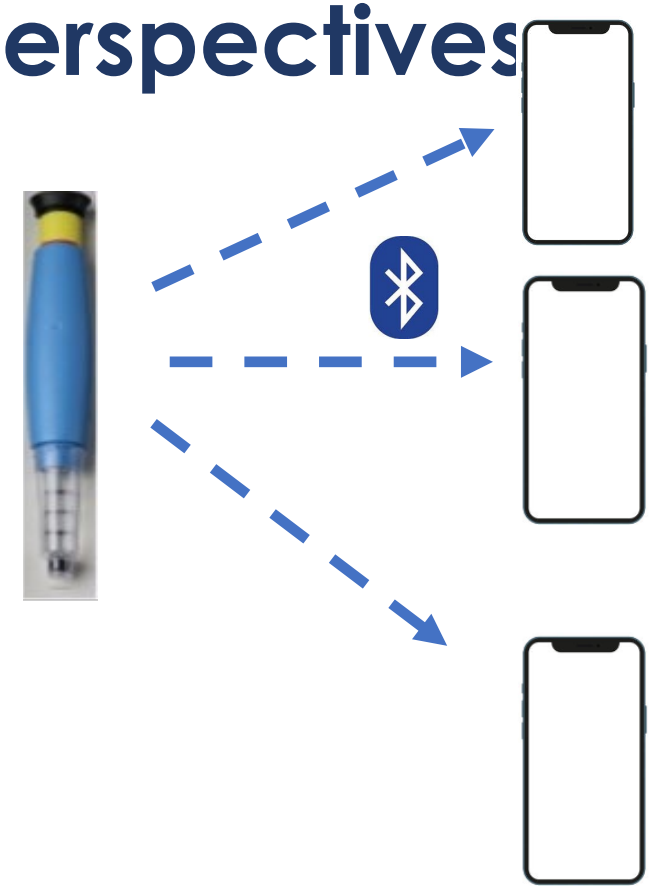
- Manufacturer should consider level of interoperability needed to achieve the purpose of the interface:
  - Types of devices meant to be connected
  - Defining data sent, received, command and control methods
  - Need for time synchronization
  - Functional and performance requirements of the device as result of information exchanged
  - Labeling should have sufficient detail to allow users to connect and use the medical device and interface as intended

FDA Guidance: Design Considerations and Pre-Market Submission Recommendations for Interoperable Medical Devices – **Anticipated Users**

- Determining anticipated users will aid application of risk management some of these user categories include
  - IT professionals
  - System integrators, system designers, medical device designers
  - Patients
  - Clinicians

Design Verification US vs EU Perspectives

- FDA Guidance Interoperable Devices, Section V(D) – For devices meant to work with many devices it may be appropriate to test the device against the interface specification and with representative devices for verification.
- EU MDR requires DV testing on the actual combination of devices (i.e. equivalency route is not available)



FDA Guidance: Content of Premarket Submissions for Management of Cybersecurity in Medical Devices

- Interoperable devices utilize communication methods, such as Bluetooth, to connect to other devices need to consider the following in design:
  - Identification of assets, threats and vulnerabilities
  - Impact of threats and vulnerabilities on device functionality and end users/patients
  - Likelihood of threat or vulnerability being exploited
  - Determine risk levels and mitigation strategy
  - Assess residual risk and risk acceptance criteria

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FDA Guidance: Content of Premarket Submissions for Management of Cybersecurity in Medical Devices – **Security Considerations**

Methods utilized to Detect, Respond and Recover

- Features that allow security compromises to be detected and logged
- Information to be supplied to user concerning appropriate actions
- Device features that protect critical functionality when cybersecurity has been compromised
- Methods for retention and recovery of device configuration

MDCG 2019-16 Guidance on Cybersecurity for Medical Devices

Integration of Cybersecurity criteria into Technical Documentation:

EU MDR Annex I:

- Identification of threats, vulnerabilities, hazards, risks – GSPR 3b
- Protection against risk during use and foreseeable misuse – GSPR 3c, 8
- IT security – GSPR 17.4, 23.4(am)
- Operation Security- GSPR 14.1, 14.2, 17.1

Recognized Standards

- ANSI/AAMI/UL 2800-1:2022 – Standard for Medical Device Interoperability
- ANSI/AAMI/UL 2800-1-1:2022 – Risk Concerns for Interoperable Medical Products
- ANSI/AAMI/UL 2800-1-2:2022 – Standard for Interoperable Item Development Life Cycle
- ANSI/AAMI/UL 2800-1-3:2022 – Standard for Interoperable Item Integration Life Cycle

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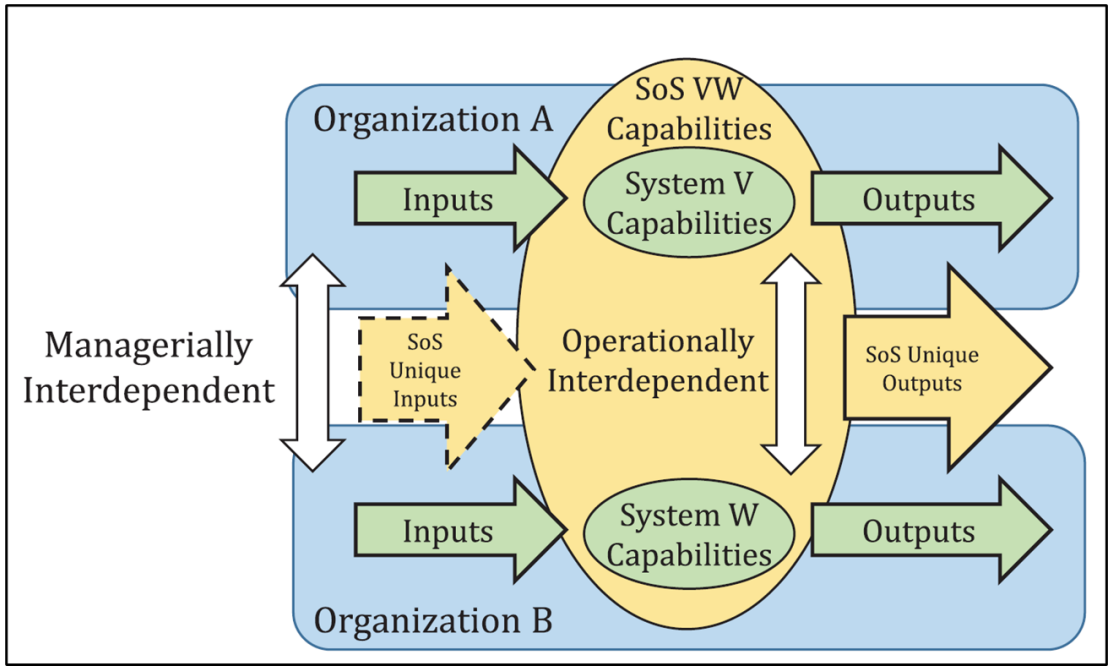
ISO/IEC/IEEE Systems Engineering Standards

System of Systems (SoS):

Set of Systems or System Elements that interact to provide a unique capability that none of the Constituent Systems can accomplish on its own.

Constituent System:
Independent system that forms part of an SoS.



System Element:
Member of a set of elements that constitute a system.

Managerially Independent Systems
Systems that are managed, at least in part, for their own purposes rather than the purposes of the whole.

Operationally Independent Systems
Systems that fulfill valid purposes in their own right & continue to operate to fulfill those purposes if disassembled from the overall system.

References:
- ISO/IEC/IEEE 15288:2015 Annex G
- ISO/IEC/IEEE 21839 through 21841:2019

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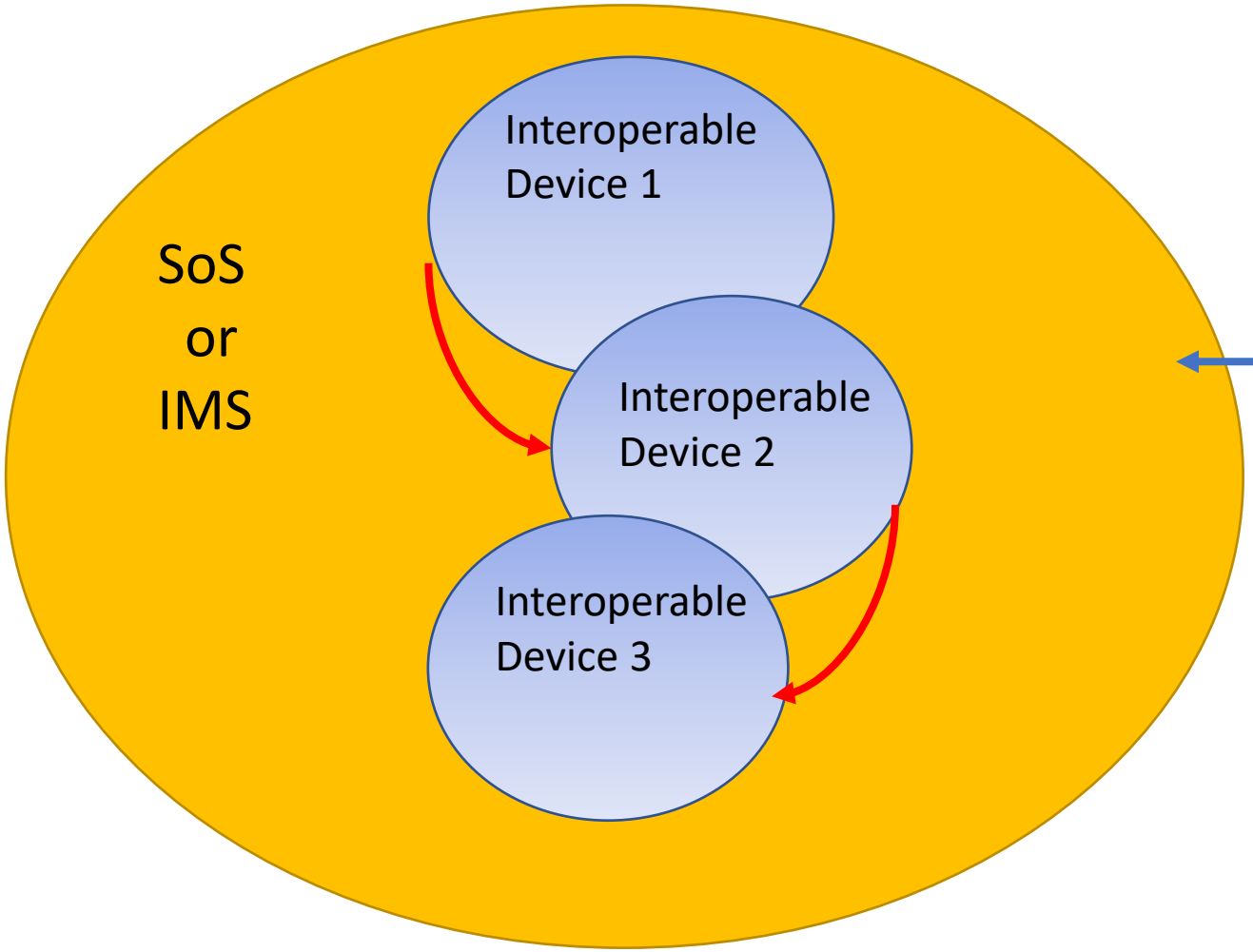
System of Systems (SoS) vs Interoperable Medical System



System of Systems:

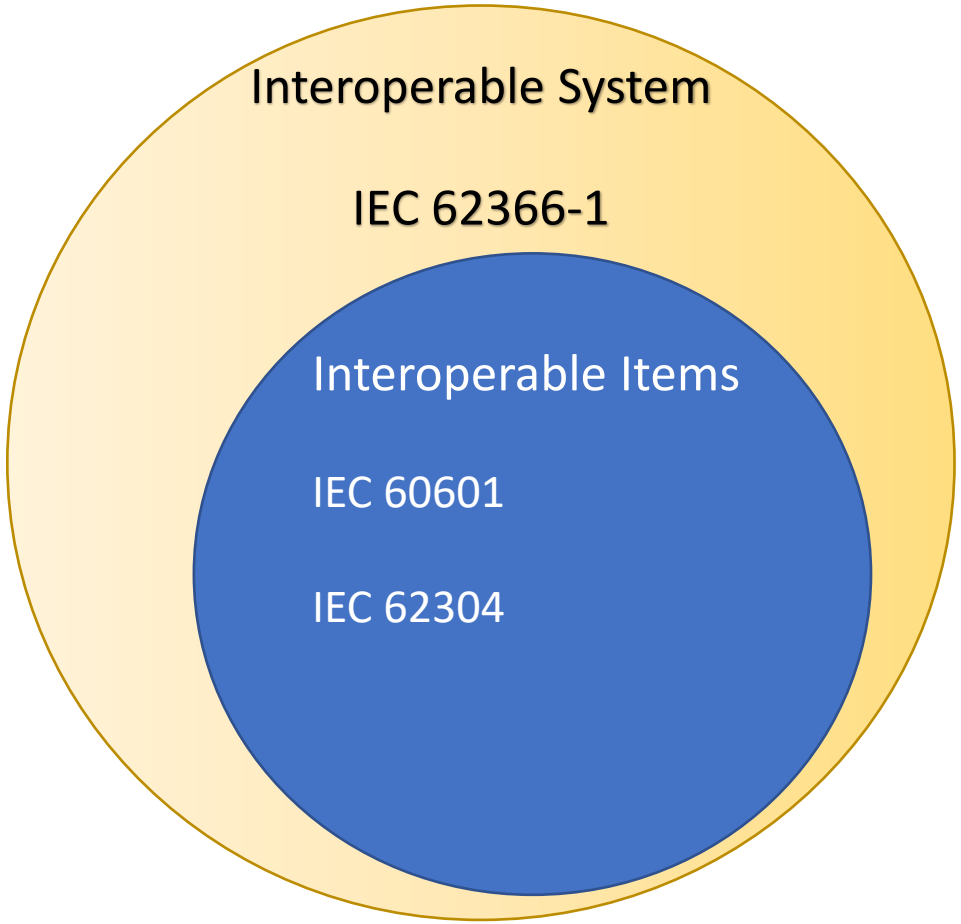
- ISO/IEC/IEEE 21839 and ISO/IEC/IEEE 21840 – set of systems or system elements that interact to provide a unique capability that none of the constituent systems can accomplish on its own

Also

Interoperable Medical System:

- AAMI 2800-1 – one or more integrated sub-items with a clinical intended use

Recognized Standards



Interoperability Requirements in Other Markets

- Brazil ANVISA RDC 546 Article 26: When a medical device is intended to be used with other products or equipment, the combination, including the connection system, must be safe and not alter intended performance
- Upcoming UK Medical Device Regulations is expected to largely align with EU MDR with respect to interoperability GSPRs
- Australia TGA: Medical Device Cyber Security Guidance for Industry- includes recognition of AAMI/UL 2800 to fulfill multiple essential principles

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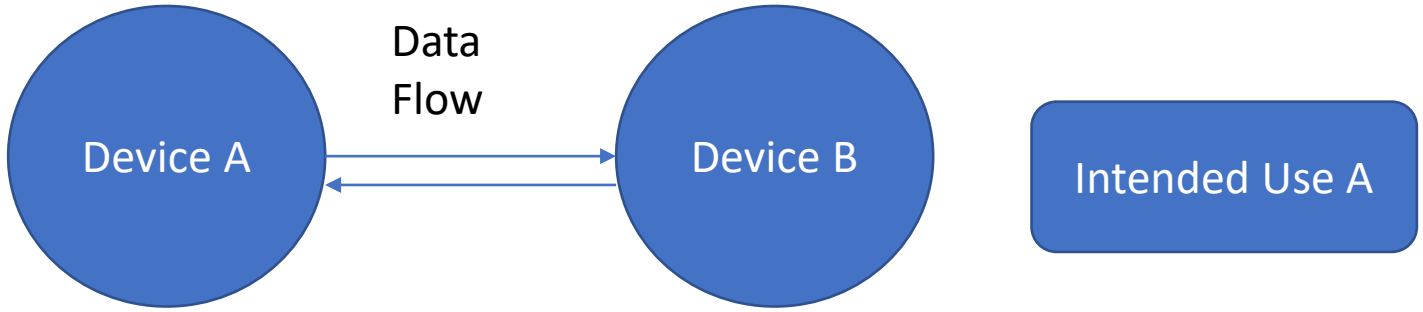
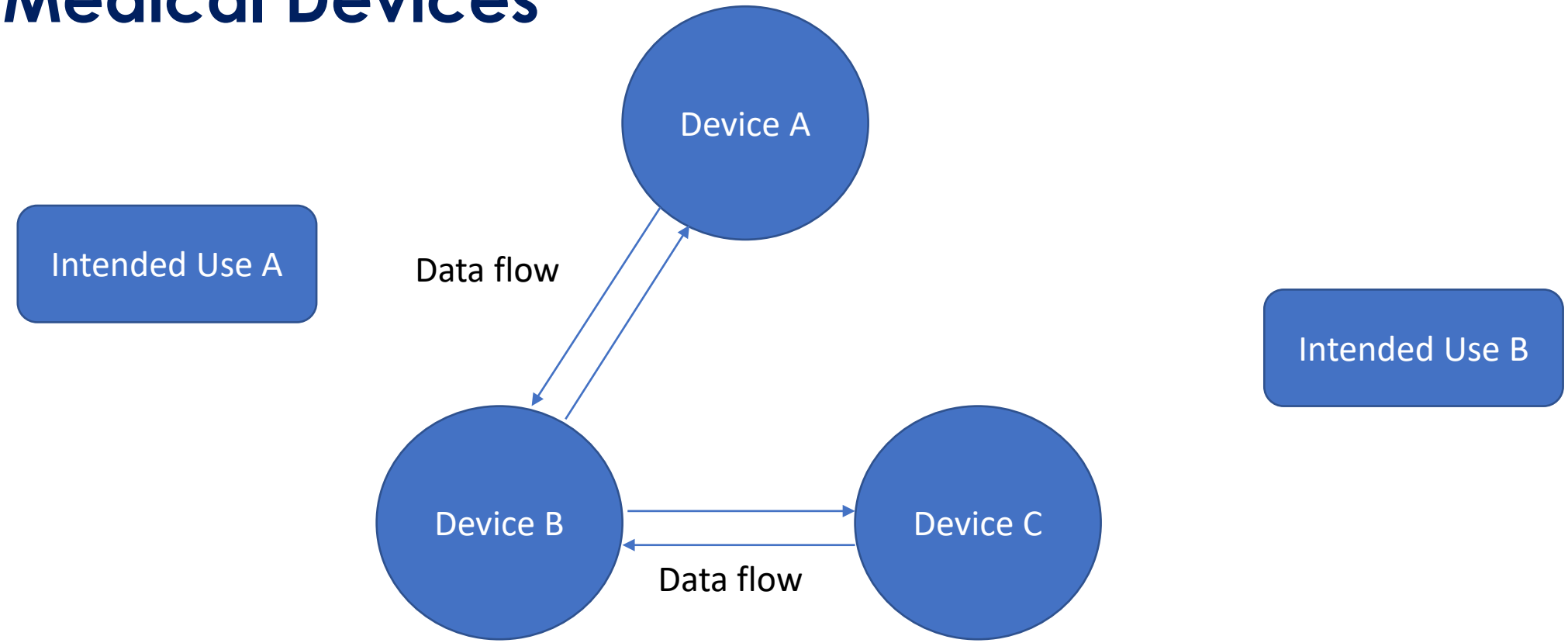
Case Study: Integration Considerations

Complexity of Design Controls for Interoperable Medical Devices



Complexity of Design Controls for Interoperable Medical Devices

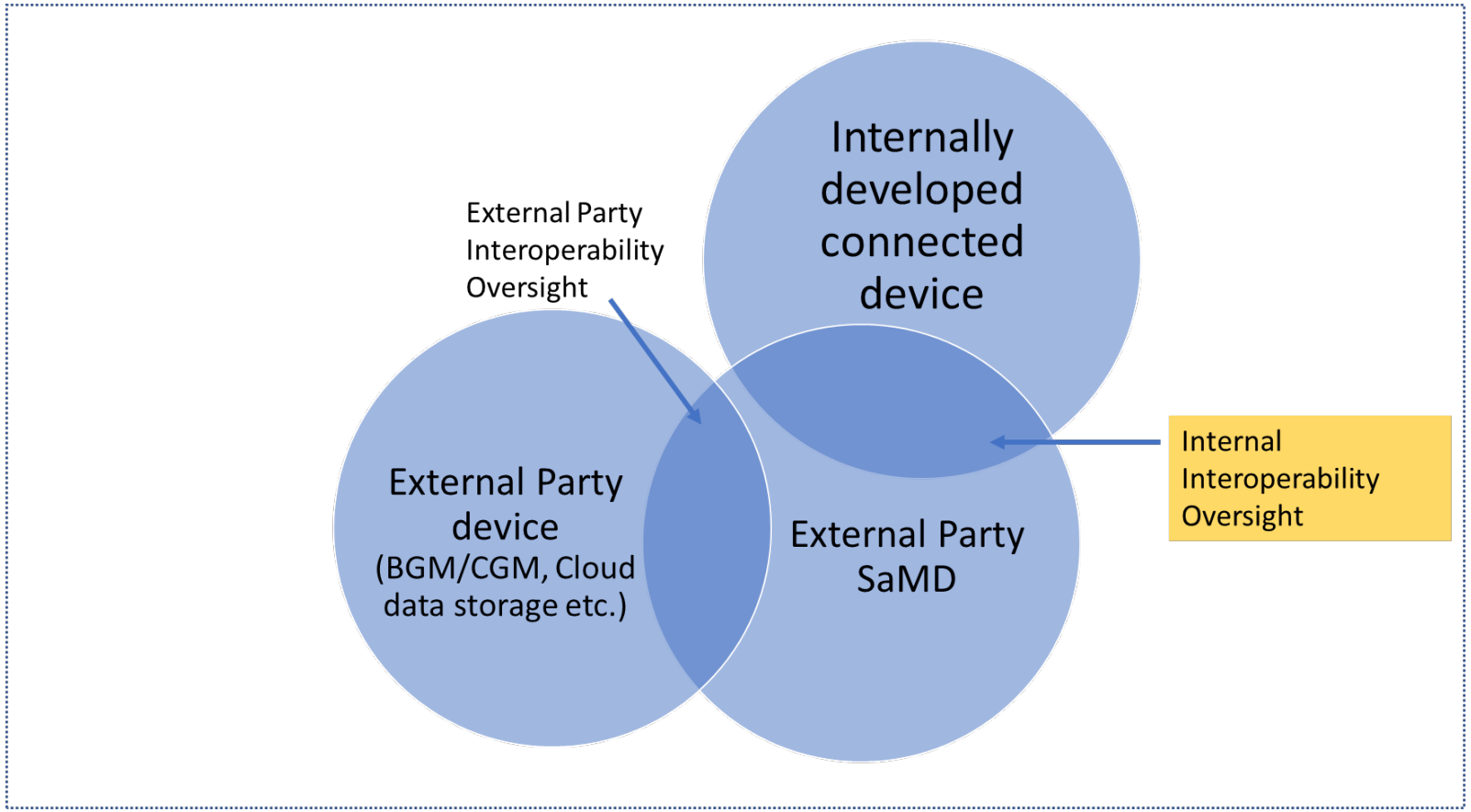


Example Device

- Pen injector with integrated electronics to capture dose, date, time (Internally developed)
- Communicates drug brand, dose, date time to SaMD (cellphone app)

  (Externally developed)

Identify scope of Interoperability



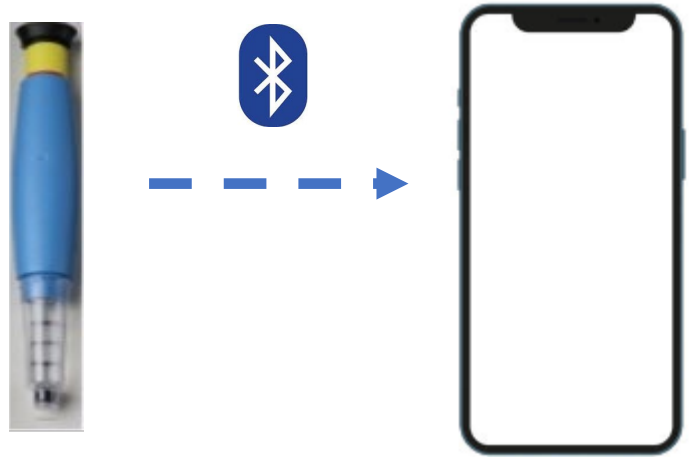
Defining Requirements for the Interoperable System

- Must include the functional and performance requirements of the device as a result of the exchanged information
  - Use of standards (data format, transmission, interface standards, standard terminologies)
  - The necessary timeliness and reliability of information (e.g. sample rate, transmission rate)
  - Identification of warnings and precautions on the use of exchanged information
  - Interactions between the interoperable device and the user (i.e. user is asked to perform an operation on the hardware device after the App gives a signal)
  - Interactions between the environment and the interoperable device(e.g. use of the interoperable device on an airplane)

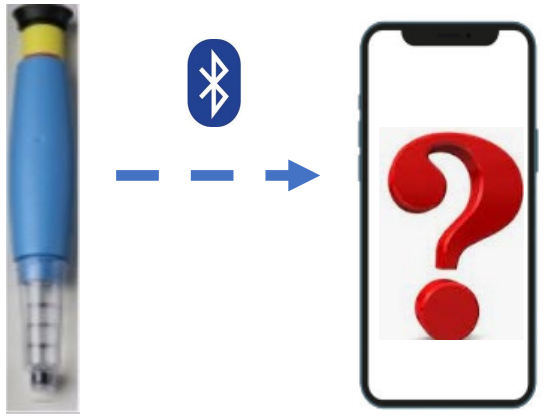
Interoperability Specifications

- Interoperability specifications are used to provide the known or contractually provided requirements for interoperability performance and interface characteristics for integration
- Interoperability specifications address requirements and address the boundaries, functions, and performance of the interoperable device and situations in which the interoperable device is intended to be integrated

Risk Management



- Risk Scenarios include
  - Missing, incorrect, or incomplete data transfer
  - Risks arising from security vulnerabilities that may be involved with the presence of an electronic interface
  - Data is lost or corrupted after data transfer
  - Time and date of data transfer is incorrect or misinterpreted
  - Failure to detect and notify interoperability failures
  - Degradation in performance which leads to inability to maintain secure and accurate data exchange



Cybersecurity Risk Considerations

- Examples include:
  - Risks associated with unauthorized access, modification, misuse or denial of use of interoperable devices must be identified and mitigated if necessary
- Security controls needed depend on device's intended use, intent of electronic data interfaces, intended use environment, cybersecurity vulnerabilities present
- Mitigations
  - Includes methods implemented to ensure user/data authentication
  - Includes methods to ensure data integrity

Risk Controls

- Risk Control measures
  - Integrate fault tolerant behavior, boundary conditions, and fail-safe behaviors
  - Cybersecurity controls
- Measures need to demonstrate
  - Inherently safe design and manufacture
  - Protective measures for the forms of data management and communication to preserve data integrity
  - Information for safety (e.g. product labels, labeling or instructions for use), and where appropriate, training to users

Design Verification

- Perform boundary testing to assure the device continues to operate safely with data is received outside parameter boundaries
  - Can this be detected
  - What is the impact to the rest of the system
- Verify only authorized users are allowed to use the interoperable system and exchange information
- Ensure reasonably foreseeable interactions do not cause incorrect operation of other networked systems
- Simulate real-world use of the device

Design Validation

- Human Factors testing on the interoperable device combination/intended use
- Clinical evaluation
- Interoperability testing

Labeling

- Include the functional and performance requirements of the electronic interfaces that may be used to connect the device with other electronic equipment
- Communicate unresolved anomalies to end user

RF Emission Test	Compliance	Electromagnetic environment guidance
RF emission CISPR 11, IEC 60601-1-2	Group 1, Class B	The device RF emissions are not likely to cause interference in nearby electronic equipment.

5 Compliance

European Union and United Kingdom, compliance with Radio Equipment Directive

What if there are unresolved anomalies (software bugs)

- Rank unresolved anomalies by risk to patient/ end user
- If resolution of unresolved anomalies is deferred, need a risk-based rationale for why it will not impact device safety or effectiveness

ID	Classification	Description	Safety Impact	Performance Impact	Mitigation	Correction Timing

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Integration Challenges with External Partners

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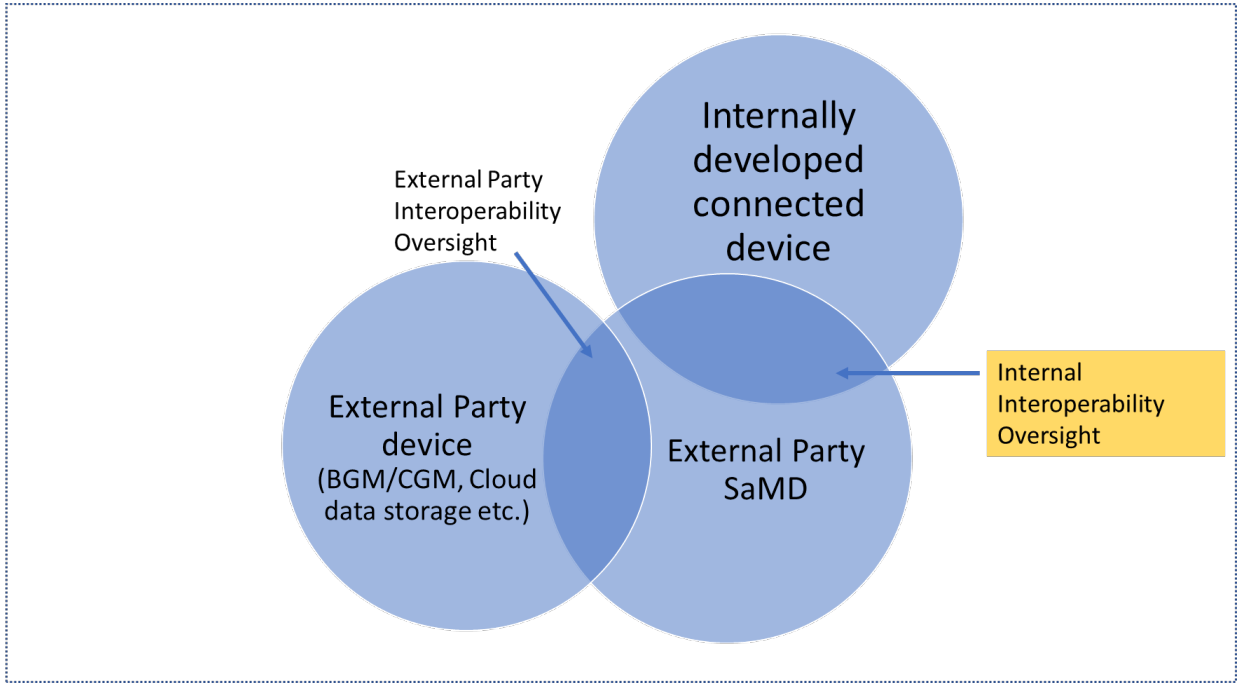
Considerations for Working with External Parties



Determine scope of collaboration:

- Focus only on direct interoperable interactions
- System of systems approach with collaboration
- System of systems approach without collaboration

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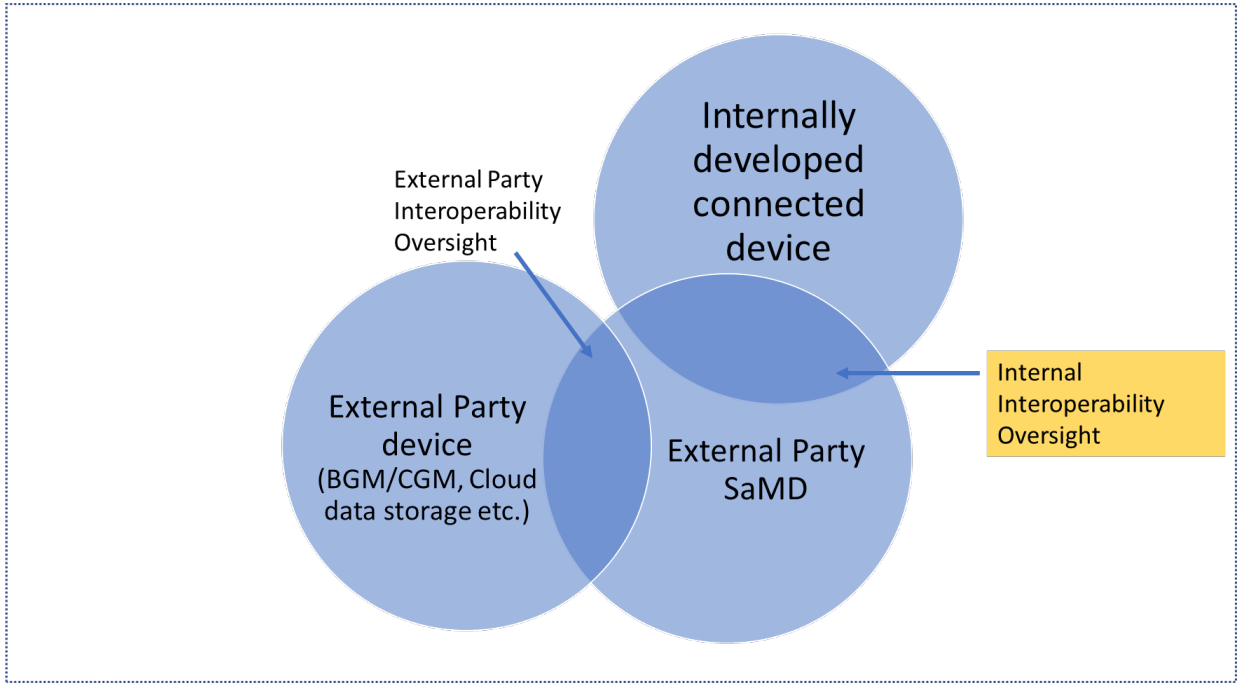
Considerations for Working with External Parties



Who will perform interoperability testing between internally developed device and external SaMD:

- Access to external party SaMD
- Sufficient knowledge and capacity to create/execute testing

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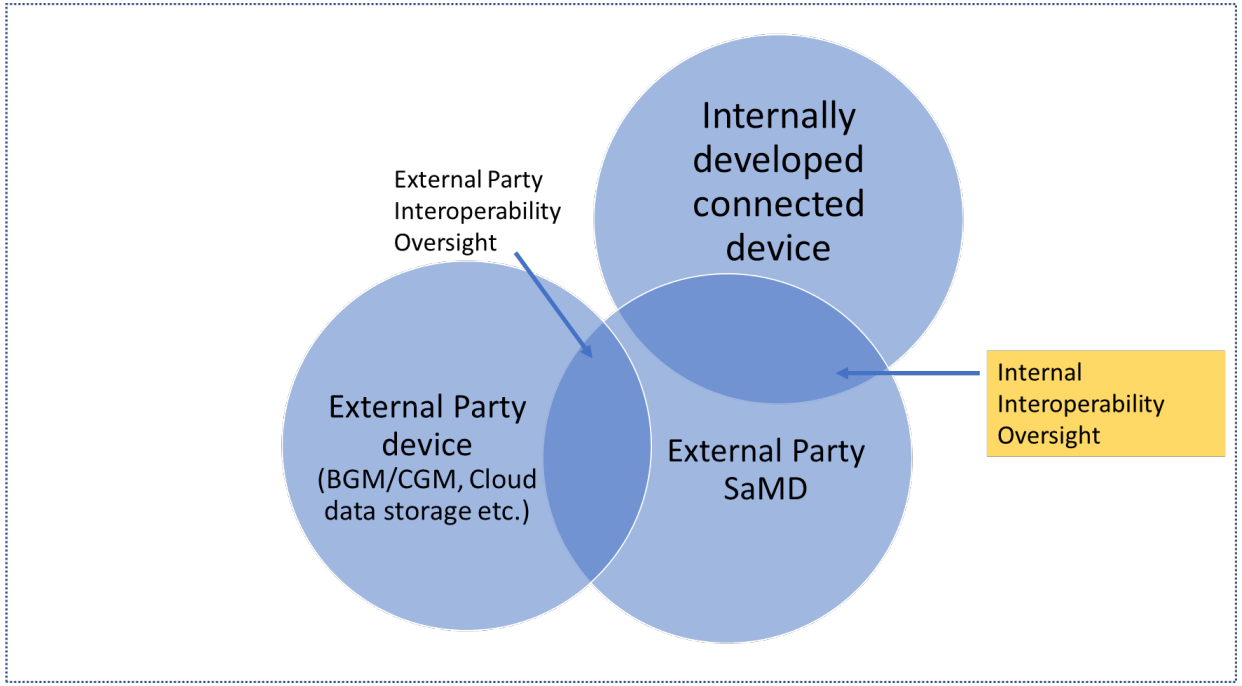
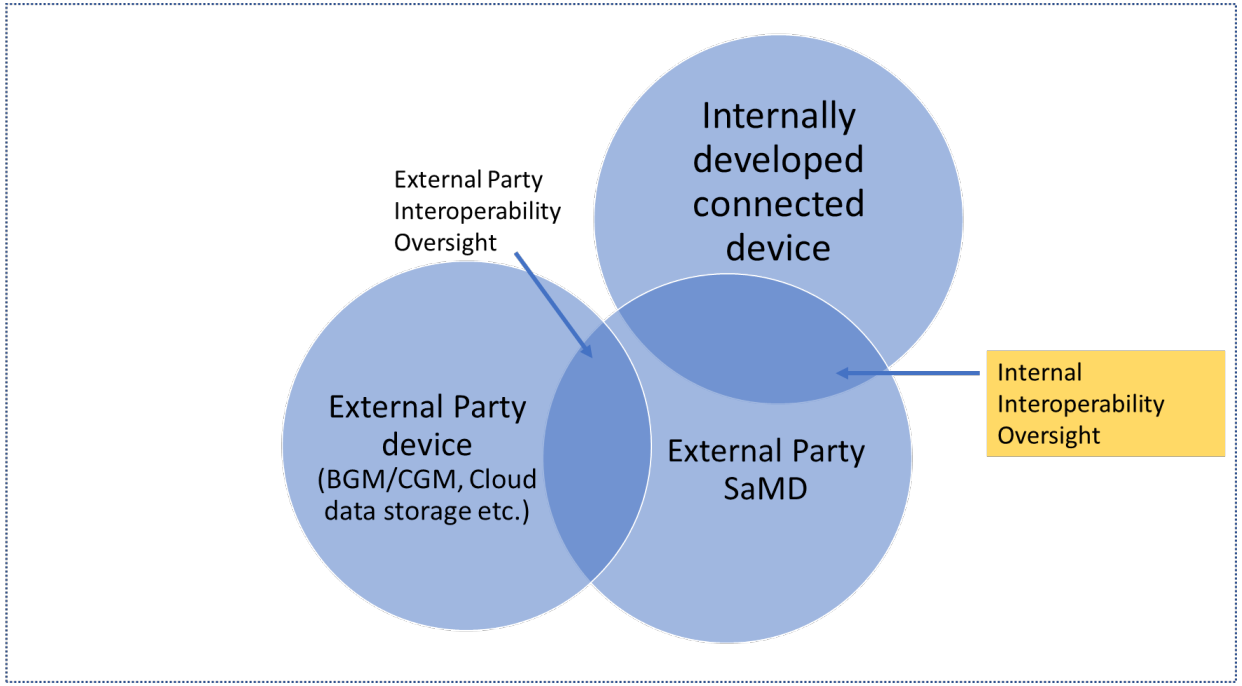
Considerations for Working with External Parties



Risk Management between internally developed device and external SaMD:

- Shared risk management file (RMF)
  - Align on definitions and scoring for hazardous situation (P1), hazardous situation leading to harm (P2), probability of harm
- Separate RMF

Considerations for Working with External Parties



How will Clinical Investigation and Clinical Evaluation be managed between internally developed device and external SaMD:

- Who will perform clinical investigation for system
- How will data be shared

Considerations for Working with External Parties

Who owns Human Factors between internally developed device and external SaMD:

- Joint Human Factors study
- HF equivalency for multiple equivalent SaMDs

Baseline App Activity	Comparator App Activity	Evaluation of HF Equivalency
App/device pairing App #1	App/device pairing App#2	

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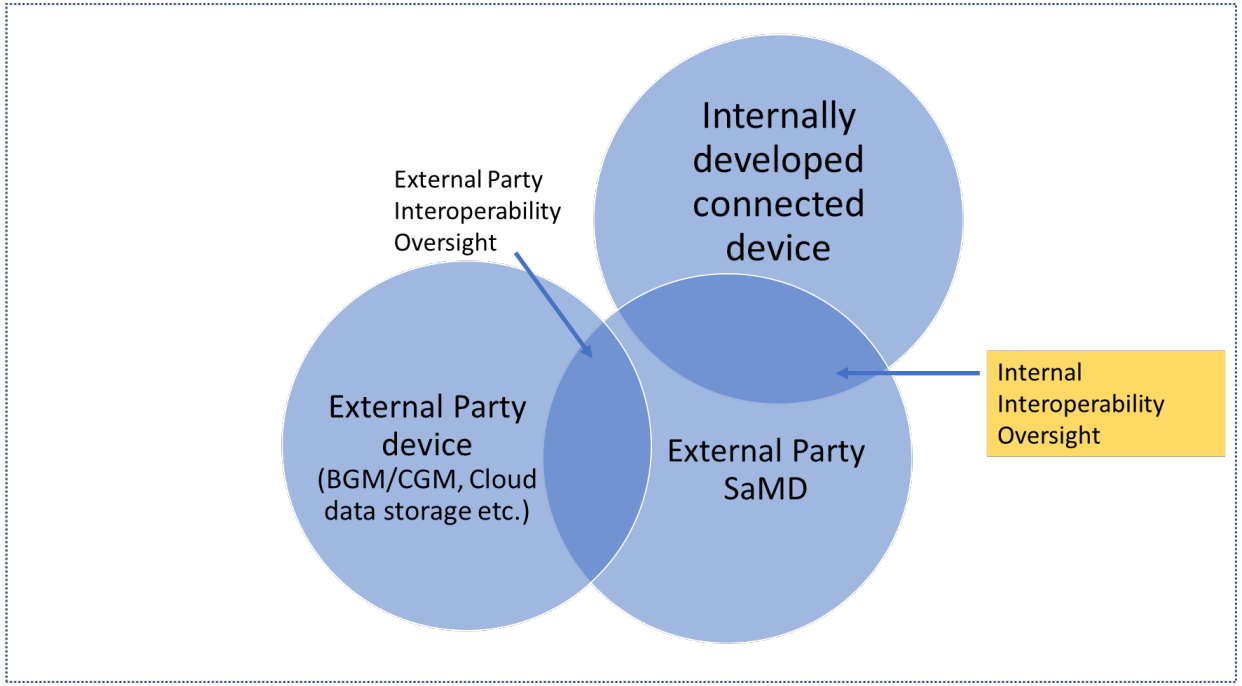
Considerations for Working with External Parties



Post-Market Considerations:

- Complaint Management
- Change Management

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Conclusion

In our ever-connected world, interoperable medical devices are bringing a wealth of data to patients, caregivers, and HCPs

- Standards and regulations are evolving with available technology
- Considerations over non-connected medical devices need to include
  - Communication methods
  - Human Factors
  - Risk management
  - Interoperability verification