Post-Market Safety Reporting

Examples for implementation

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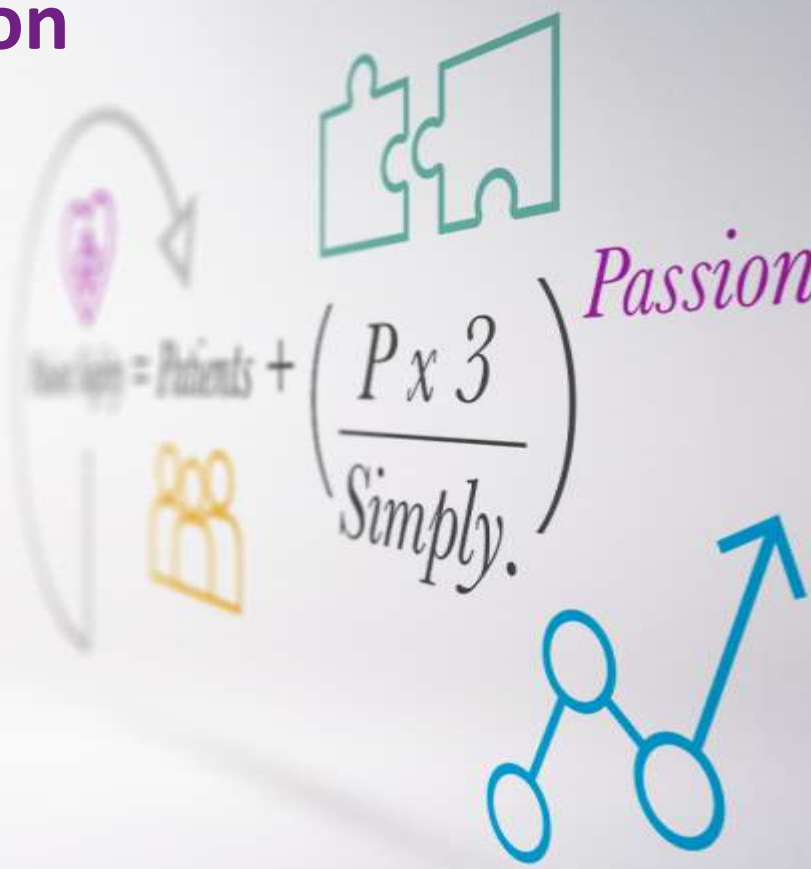


Working Session – Part F - "Post-Market Safety Reporting"

Following the launch of the BlockUVInjector-1 the following scenario has been observed:

PM1 - An increase in number of adverse events from IMalilbaby patients of bacterial sore throats and ear infections

1. Discuss the approach to post-market safety reporting in light of the proposed guidance? Describe the reportability decision and the supporting discussion.
2. Number of mandatory reports to be submitted? Responsible party?
3. Challenges.

Working Session – Part F - "Post-Market Safety Reporting"

Following the launch of the BlockUVInjector-1 the following scenario has been observed:

PM2 - An increase in injection site reactions

1. Discuss the approach to post-market safety reporting in light of the proposed guidance? Describe the reportability decision and the supporting discussion.
2. Number of mandatory reports to be submitted? Responsible party?
3. Challenges.

Working Session – Part F - "Post-Market Safety Reporting"

Following the launch of the BlockUVInjector-1 the following scenario has been observed:

PM3 - An increase number of LabeledSAE1 and LabeledSAE2 in IMadult patients

1. Discuss the approach to post-market safety reporting in light of the proposed guidance? Describe the reportability decision and the supporting discussion.
2. Number of mandatory reports to be submitted? Responsible party?
3. Challenges.

Working Session – Part F - "Post-Market Safety Reporting"

Following the launch of the BlockUVInjector-1 the following scenario has been observed:

PM4 - An increase number of UnLabeledSAE3 in IMadult patients

1. Discuss the approach to post-market safety reporting in light of the proposed guidance? Describe the reportability decision and the supporting discussion.
2. Number of mandatory reports to be submitted? Responsible party?
3. Challenges.

Working Session – Part F - "Post-Market Safety Reporting"

Following the launch of the BlockUVInjector-1 the following scenario has been observed:

PM5 - An increase in reports of broken needles upon investigation determined to be associated with GoEurope123 lot of the InjectBest subassembly

1. Discuss the approach to post-market safety reporting in light of the proposed guidance? Describe the reportability decision and the supporting discussion.
2. Number of mandatory reports to be submitted? Responsible party?
3. Challenges.

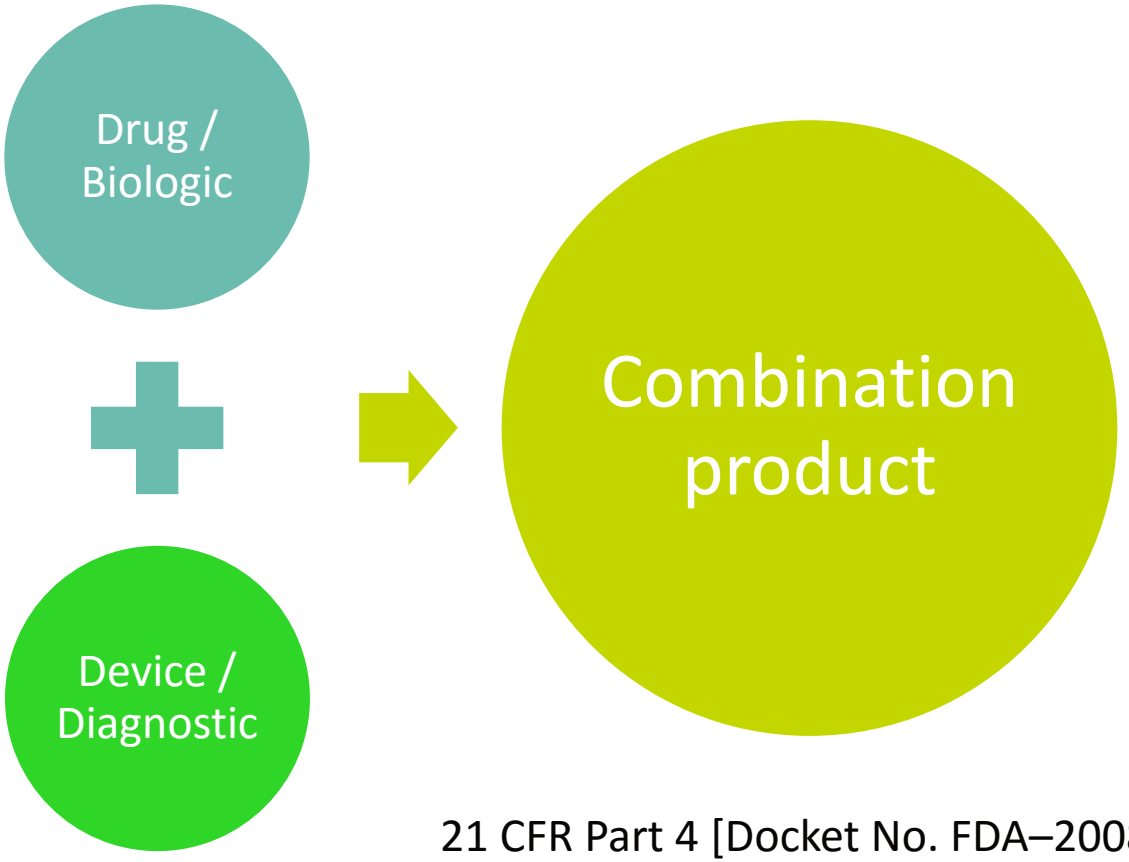
Working Session – Part F - "Post-Market Safety Reporting"

Following the launch of the BlockUVInjector-1 the following scenario has been observed:

PM6 - Spontaneous activation of the injector during uncapping with potential to cause poke-in-the-eye adverse event, should it recur

1. Discuss the approach to post-market safety reporting in light of the proposed guidance? Describe the reportability decision and the supporting discussion.
2. Number of mandatory reports to be submitted? Responsible party?
3. Challenges.

Combination Product Post-Market Safety Reporting



21 CFR Part 4 [Docket No. FDA–2008–N–0424]

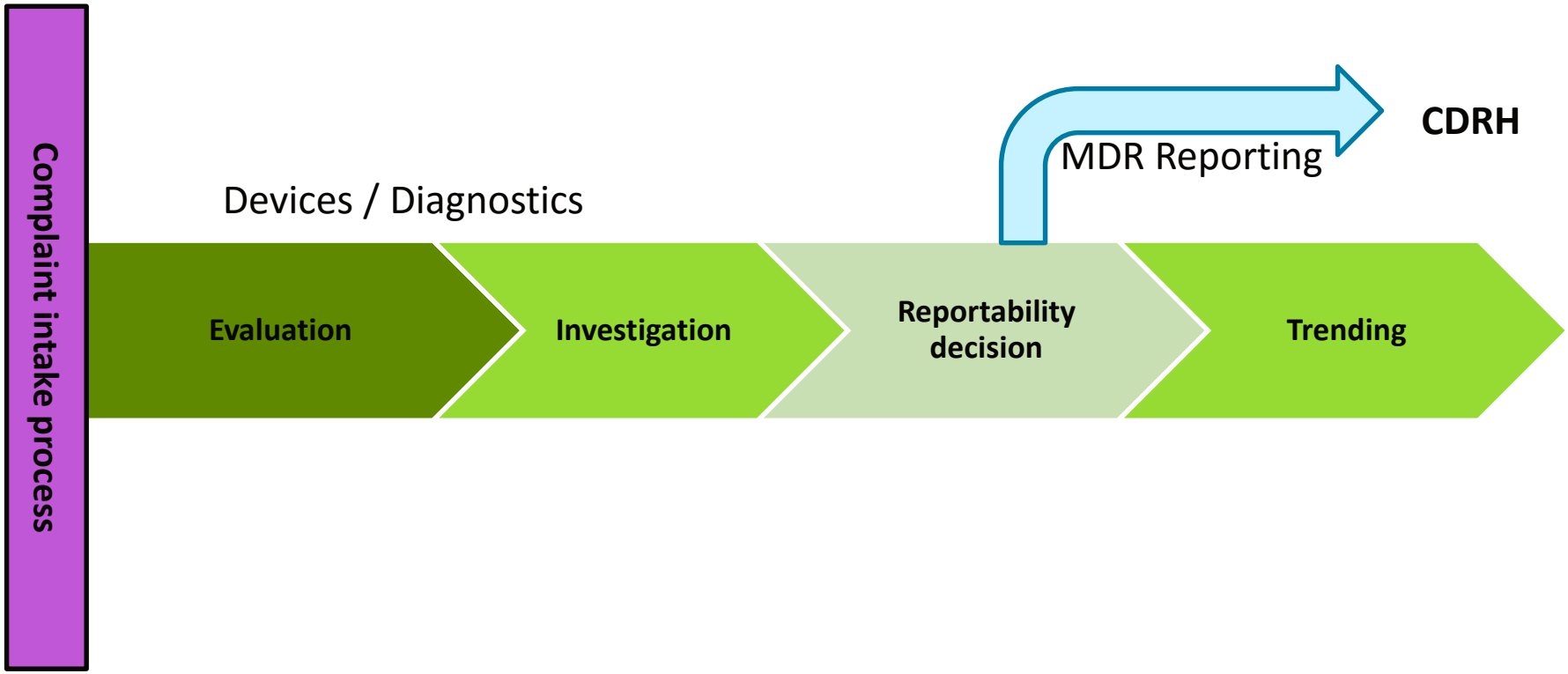
- A Single Report to minimize duplicate reporting.
- Based on Primary Mode of Action regardless of which constituent part was attributed to the reportable event
- Meet reportability criteria applicable to both / all constituent parts

Organizational Structure

- Company Size
  - Large / Medium / Small
- Teams - pharmacovigilance vs complaint
  - Single / Two or more teams
- Organizational Governance
  - Research & Development / Quality Assurance

Common Organizational Setup – Devices / Diagnostics

Single Systems / Organization / Process / Procedures

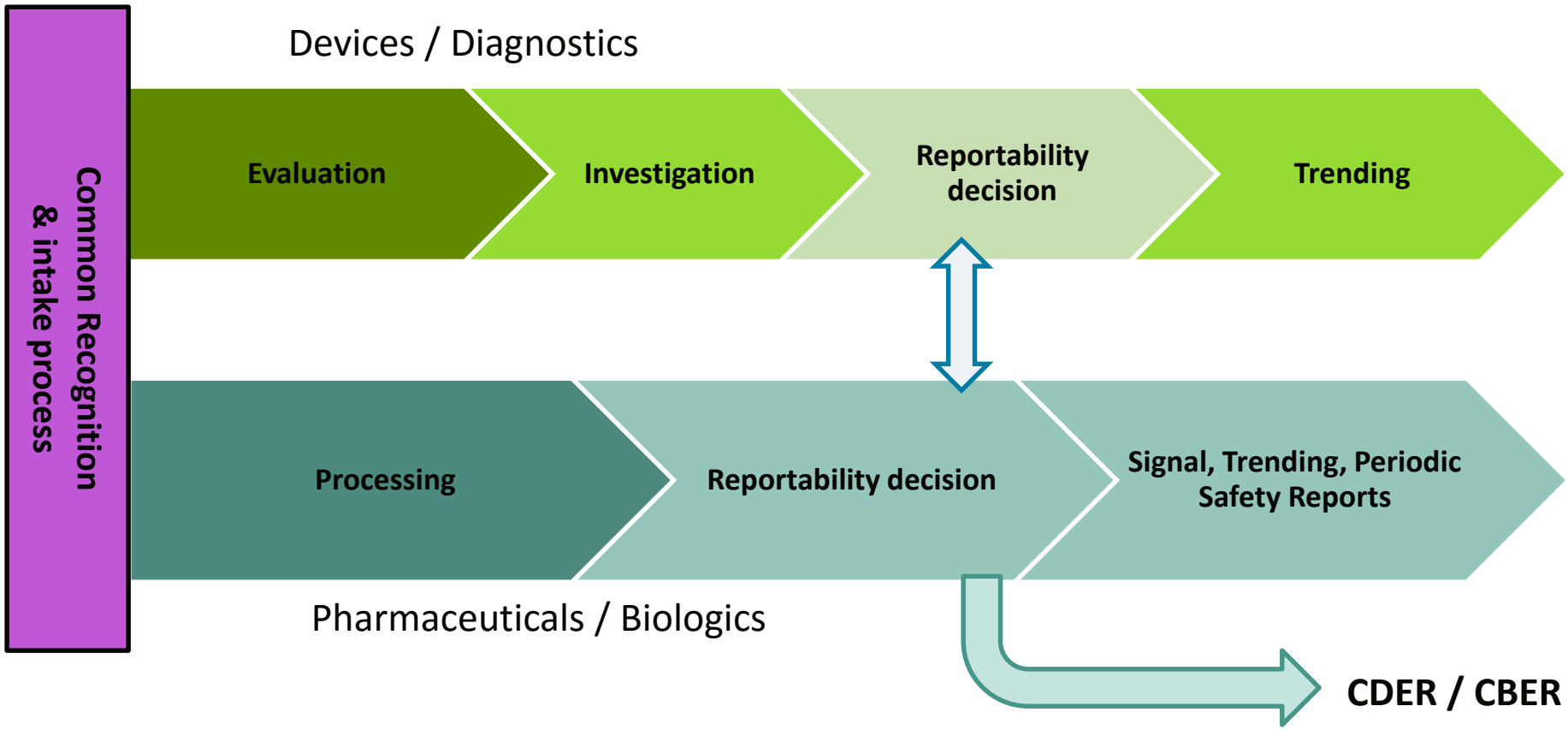


Best Practices – Devices / Diagnostics

- Intake and follow-up – information for both constituent parts
- Criteria to ascertain causality (preliminary)
  - **Device (Caused / Contribution)**
  - Drug or Biologic – Labeled
  - Both / Neither
  - Other - Procedure / Underlying condition / alternative etiology
- Risk based approach – Device class
- Investigation – assessment for malfunction
- Reporting Timelines - 5-Day OR 30-Day SAE / Malfunction
- Product lifecycle management
- Coding – FDA Device codes even for AEs (Not MedDRA)
- A drug related SAE may be reported against the device

Common Organizational Setup - Pharmaceuticals / Biologics

Two - Systems / Organizations / Processes / Procedures



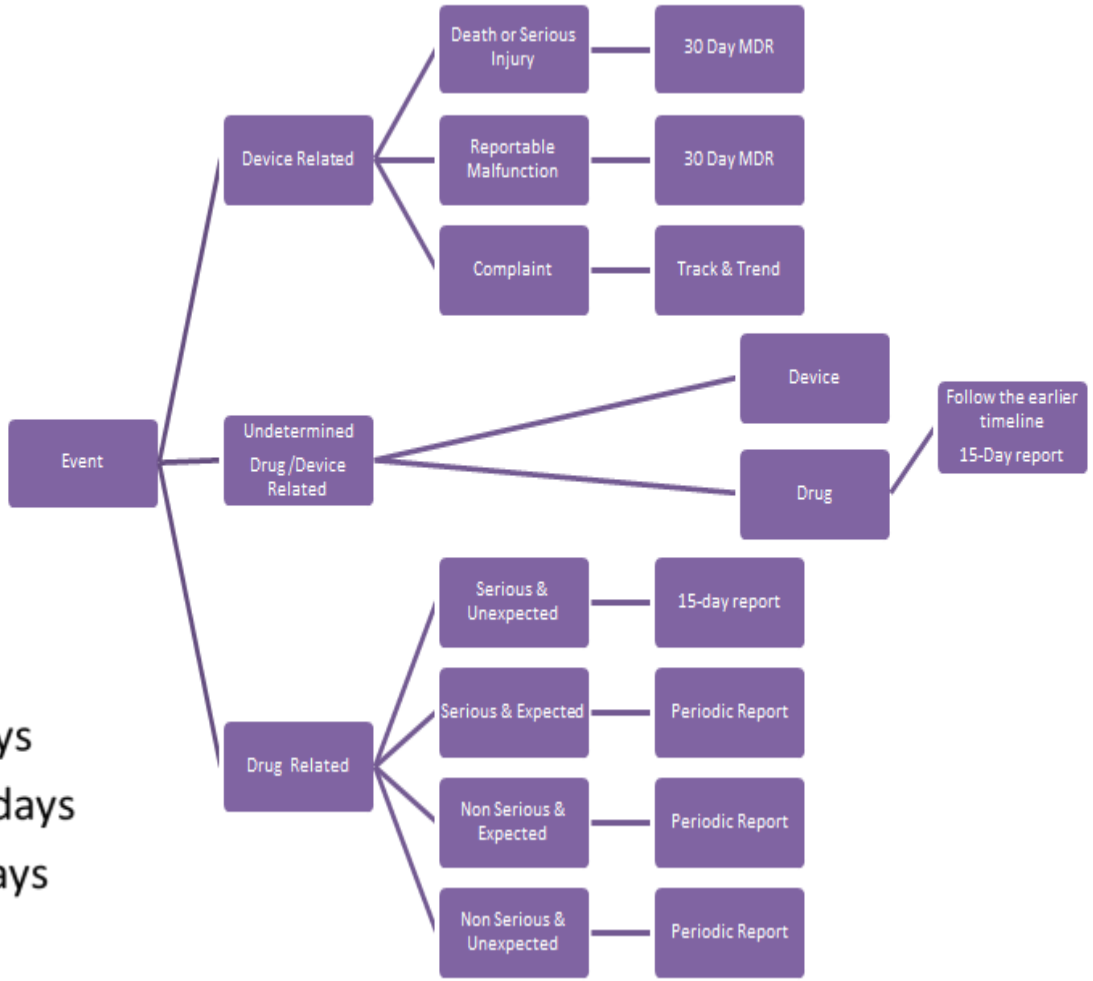
Best Practices – Pharmaceuticals / Biologics

- Intake and follow-up – all information for both constituent parts
- Criteria to ascertain causality (preliminary)
  - Device (Caused / Contribution)
  - **Drug or Biologic – Labeled / Expected**
  - Both / Neither
  - Other - Procedure / Underlying condition / alternative etiology
- Risk based approach – Indication
  - All Adverse Events in one system
  - Device related AE / SAE in the device related system
- Data Exchange and Reconciliation process
- Investigation – assessment for malfunction (as applicable)
- Reporting Timelines - 3-Day OR 15 OR 30 Day BPDR / SAE / Malfunction
- Product lifecycle management
- Coding – MedDRA - SOC 27 maybe for devices
- A device only related SAE / Malfunction may be reported against the drug

Key Considerations - General

- IT Infrastructure – Industry & Agency
- The seriousness criteria utilized to determine if a reported event qualifies as a Serious Injury (SI) vs. Serious Adverse Event (SAE) differ.
  - Malfunction "likely" to cause death or Serious Injury if it recurs
- Review of product complaint reports to determine if they meet criteria of a **reportable malfunction** is required for Medical Devices but not for Drugs/Biologics.
- Expectedness/Relatedness: Medical Device Products do not include an assessment of expectedness to determine reportablity.
- Lot Numbers – Drug vs Device Constituent part

Reporting Timelines



- Medical Devices – 5 & 30 calendar days
- Prescription Drugs – 3 & 15 calendar days
- Monograph Products – 15 business days
- Biologics – 15 & 45 calendar days
- Blood Fatality Report – 7 calendar days

Other Considerations

- Follow-up Reports:
  - Medical Device Follow-up submissions only require that new information is reported. That is not the case for the other regulatory classes.
- Coding nomenclature:
  - Prescription/Monograph products require reporting of MedDRA coding of events while Medical Devices utilize FDA codes.
- Additional data requirements:
  - Medical Devices reporting requires inclusion of the quality investigation method, results, conclusions (section H6 of FDA3500A MedWatch).
  - Same or similar: For medical devices, reportable malfunctions that occur outside the US require reporting to the FDA for same or similar products, while this is not the case for drugs/biologics.

Challenges

- When drugs, biologics and devices are combined it may be difficult to determine which component caused or contributed to the safety event.

- Globally, a combination product may be approved with different designations (regulatory class)in different geographies.

- In addition, FDA's regulations require notification of reportable events outside the US. Further clarification will be needed to comply with the FDA requirement for combination products.

Best Practices - Risk Based model

- Remove redundant entry of data when possible
- Risk based decision
  - Device Class and Indication
  - Evaluation vs Investigation
  - Right population
  - Risk due to component interaction
- Attribution – Risk management done right
- All AEs - safety evaluation
- Non AEs - safety oversight – process
- Define system of record . Automate reconciliation
- PSUR – Device Annex
- Platform approach
- Develop Talent

Solution options - Pharmaceuticals / Biologics

ICSR E2B schema does not include device fields and for a complete submission these data are required.

Potential solutions to submit a complete report are:

- **Include the additional device information as free text in the narrative (B5)** – currently viable option
- Submit MDR related information as an attachment to the ICSR.
- Submit the drug constituent through the NDA/BLA and submit the device constituent through the device gateway (if a device MFR # exists)

Implementation Challenges

- The work around does not utilize structured data and manual signaling processes would need to be developed.
- Most common safety databases can accommodate both drug and device products. Organizations may need to validate their systems for use of both drug and device in one report.
- The FDA system receiving data into various centers may not be able to accommodate the combined data.
- This may not effectively alert the market authorization holder and/or FDA to issues related to devices in a timely manner as information may be buried within unstructured data fields making it hard to analyze.

Drivers for Establishing Linkage

- Appropriate level of safety and compliance oversight
- Risk Management of product as a whole
- Product life cycle management
- Effective use of resources
- **It adds up to safe use of product**
- Benefit / risk – holistic view
- Unified face to customer
- Enhanced data quality (Initial & follow-up) and compliance

Product as a "System"

- Appropriate level of safety and compliance oversight
- Risk Management of product as a whole
- Product life cycle management
- Benefit / risk – holistic view
- Unified face to customer

Product as a whole