APEC GMP Toolkits

APEC AHC – USP Center of Excellence (CoE) for Product Quality & Supply Chain Pilot Program: “Securing Medical Product Quality Through the Supply Chain”

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http://www.nifds.go.kr/apec/SupplyChain/APEC_SupplyChainToolkit_190217_external%20drive%20links.pdf

Good Manufacturing Practices (GMP)

Appropriate manufacturing is essential for global medical product quality and supply chain security. The materials below identify best practices related to medical product supply chain security, providing current good manufacturing practices (CGMP) recommendations for stakeholders. These recommendations for best practices are intended to minimize divergent practices and opportunities for the introduction of substandard, spurious, falsely-labeled, falsified, or counterfeit medical products into the global supply chain.

The information and materials below are intended for industry stakeholders and National Medical Regulatory Authorities (NMRAs)-

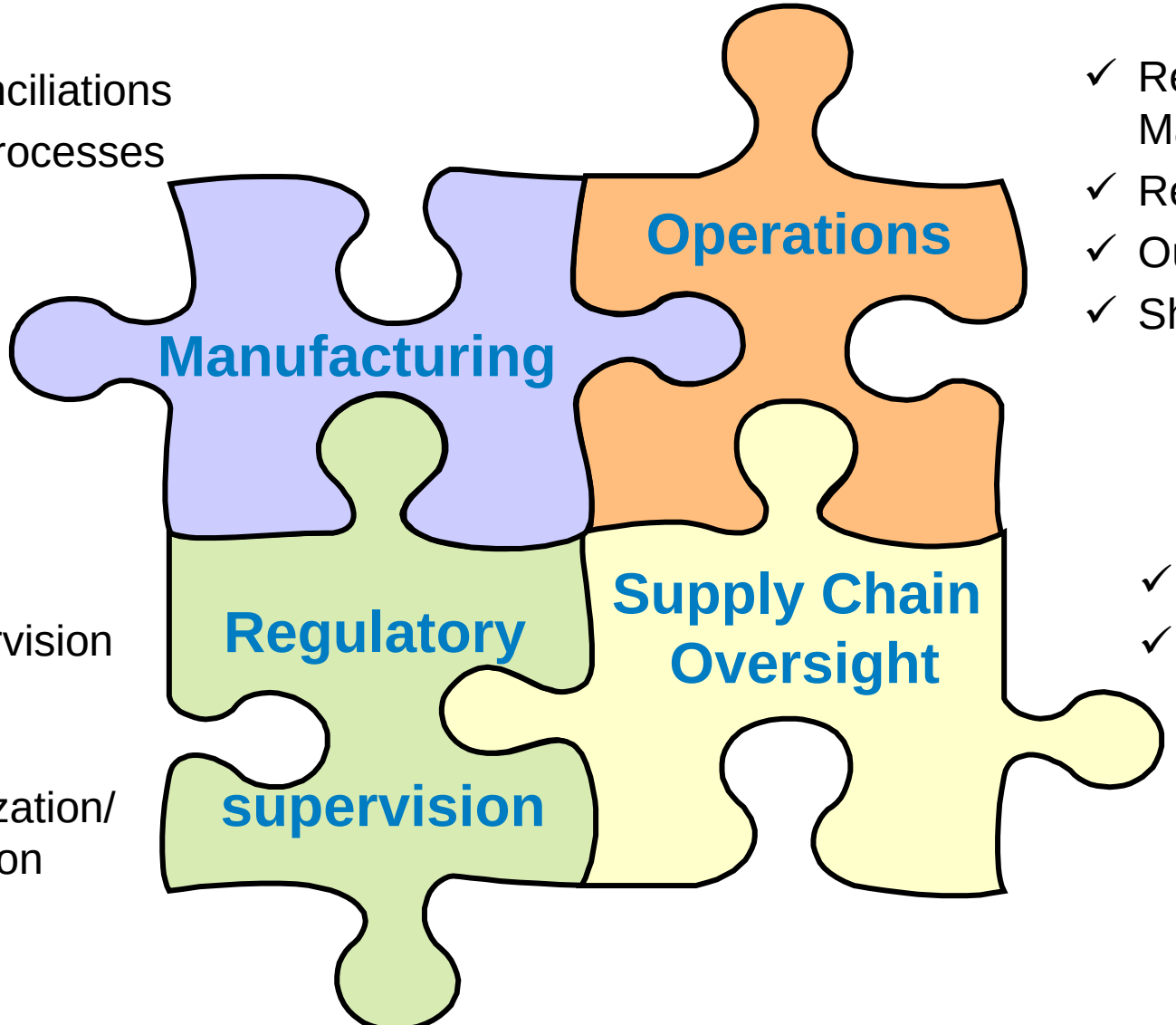
1. Industry may use this information to adopt best practices;
2. NMRAs may use this information to strengthen laws and regulations; and
3. Industry and government may use for training purposes.

GMP Tools

Introduction (PPT)	Good Regulatory Practices (PPT)	Supply Chain Verification (PPT)	Outsourcing (PPT)
Show and Shadow Factories (PPT)	Incoming Material Checking (PPT)	Yield and Reconciliation (PPT)	Repackaging (PPT)
Product Release Procedure (PPT)	Rejected and Returned Material (PPT)	GMP GAP Assessment (DOC)	

Elements of Managing Supply Chain Risk

- ✓ Yields and Reconciliations
- ✓ Batch Release Processes



- ✓ Rejected and Returned Materials
- ✓ Repackaging and Relabelling
- ✓ Outsourcing
- ✓ Show and Shadow Factories

- ✓ Licensing & Supervision of Manufacturers, distributors
- ✓ Marketing Authorization/ Product Registration

- ✓ Qualification and Verification
- ✓ Checking of Incoming Goods

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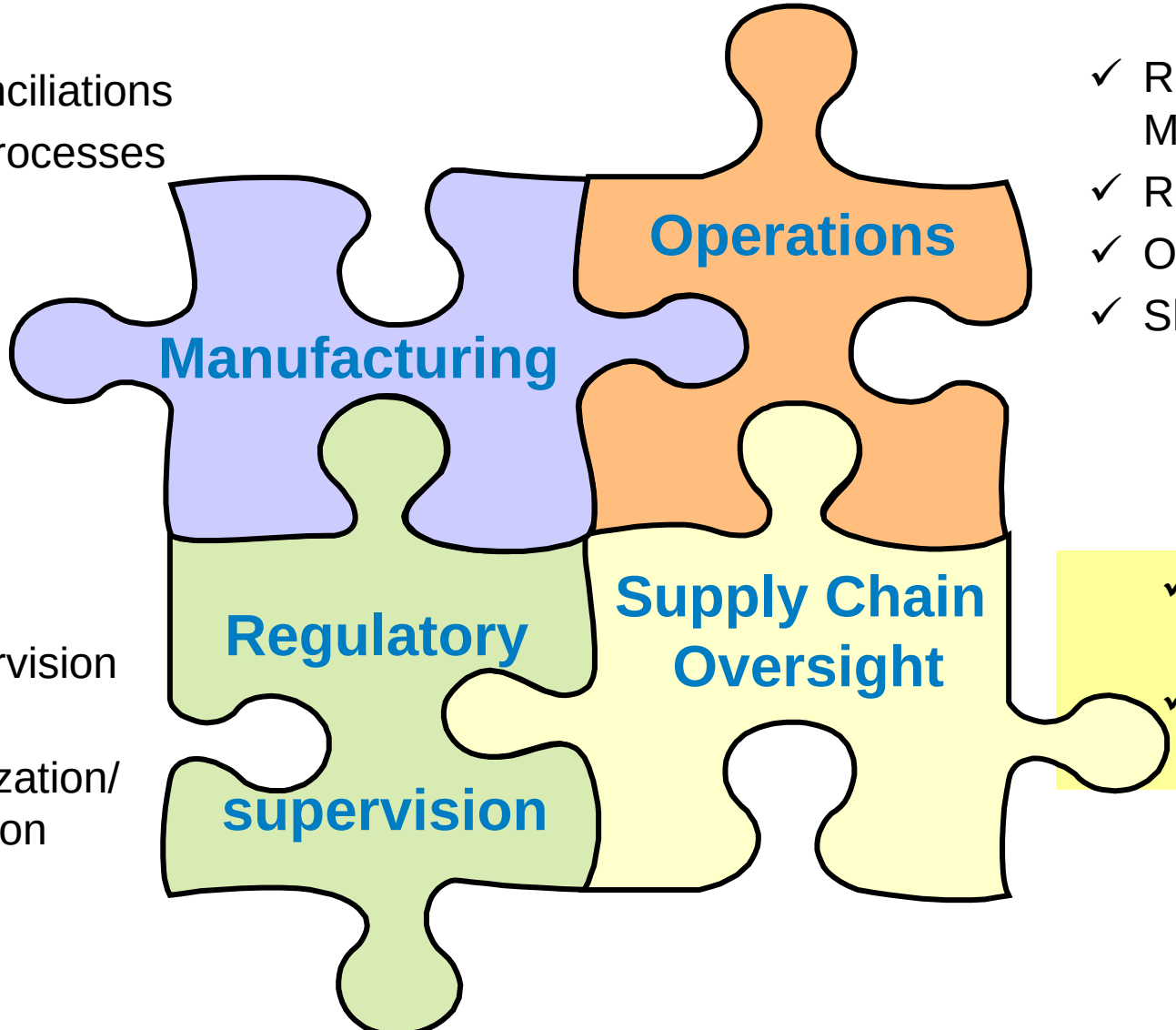

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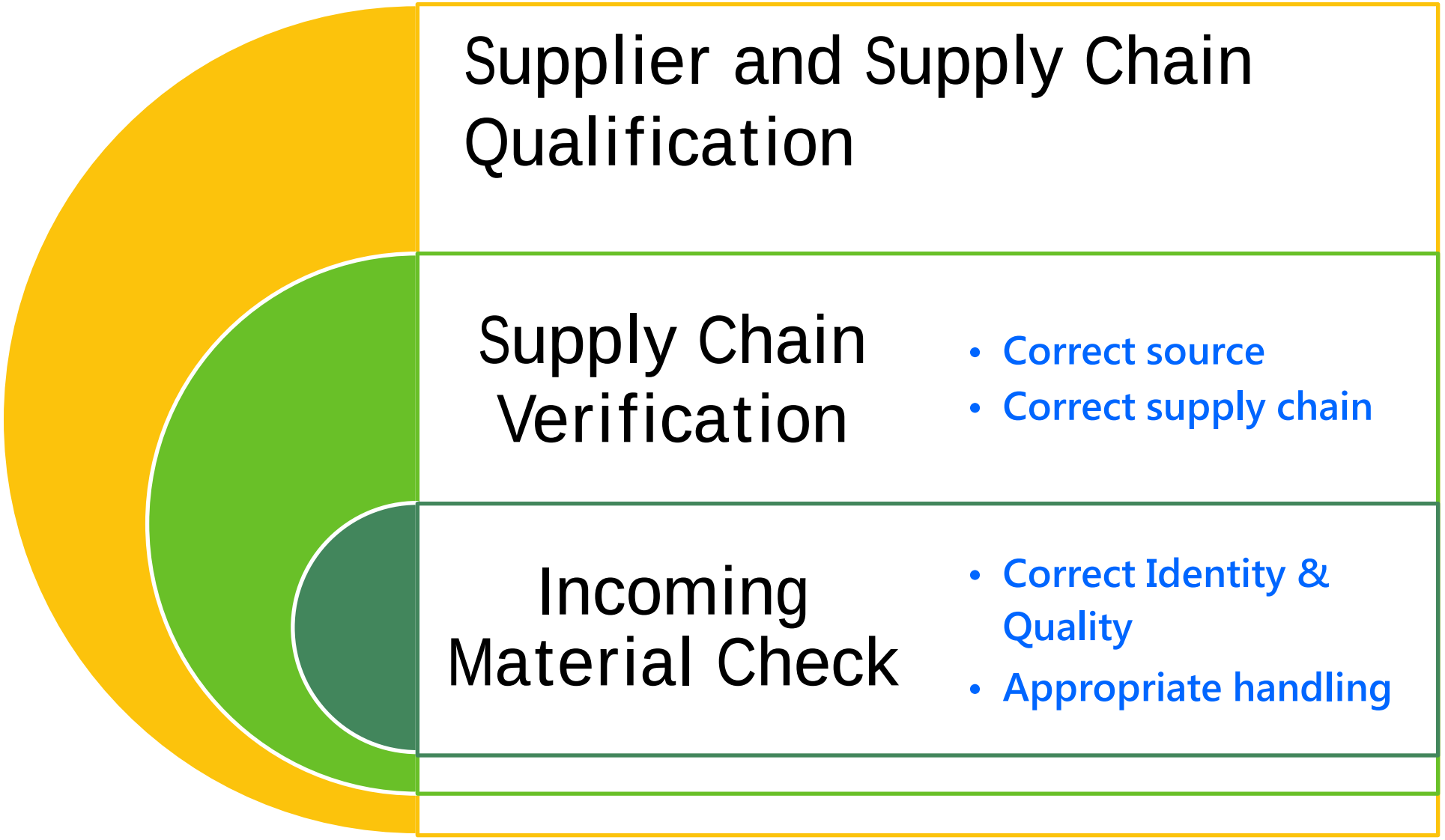
Supply Chain Oversight



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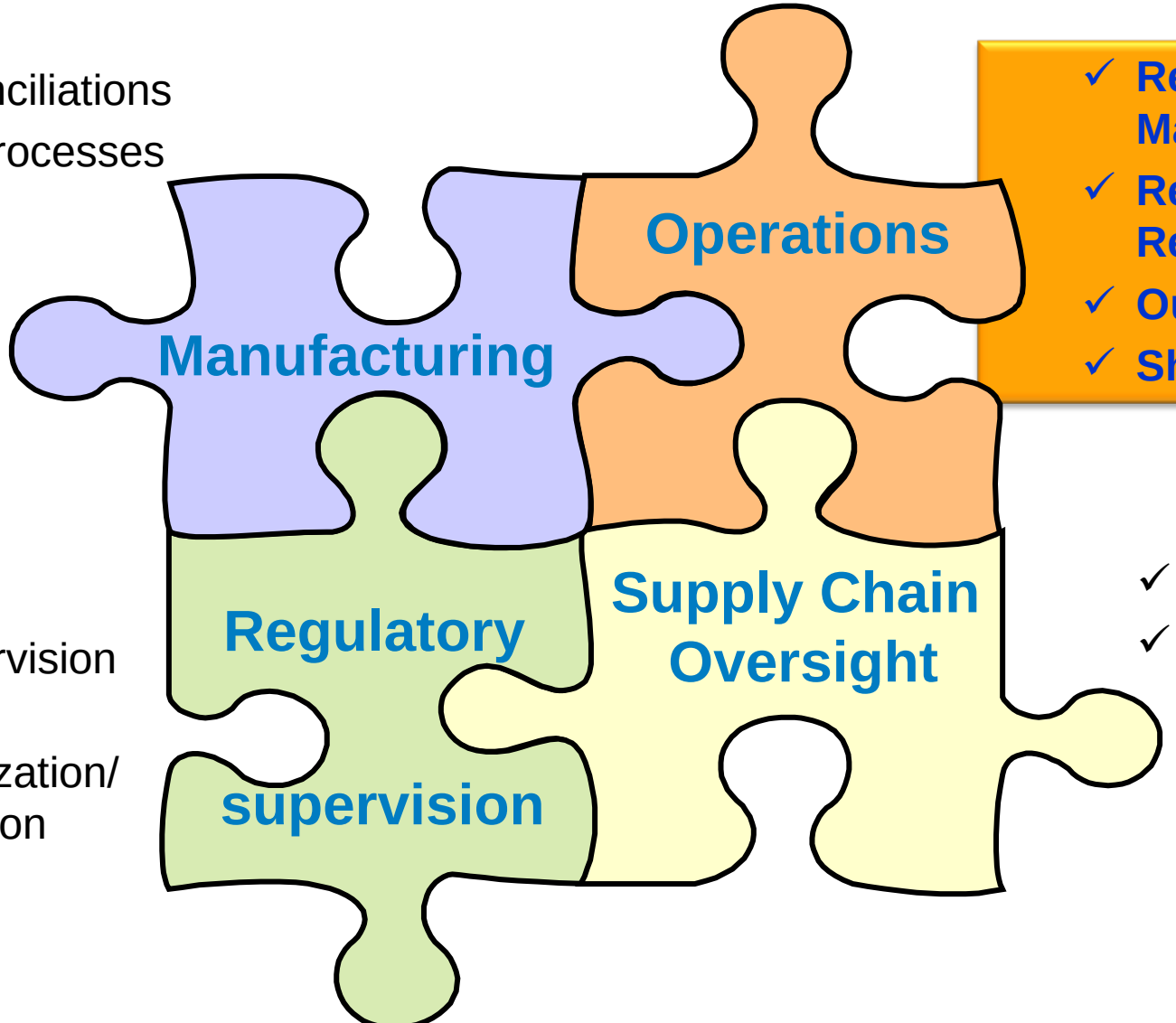

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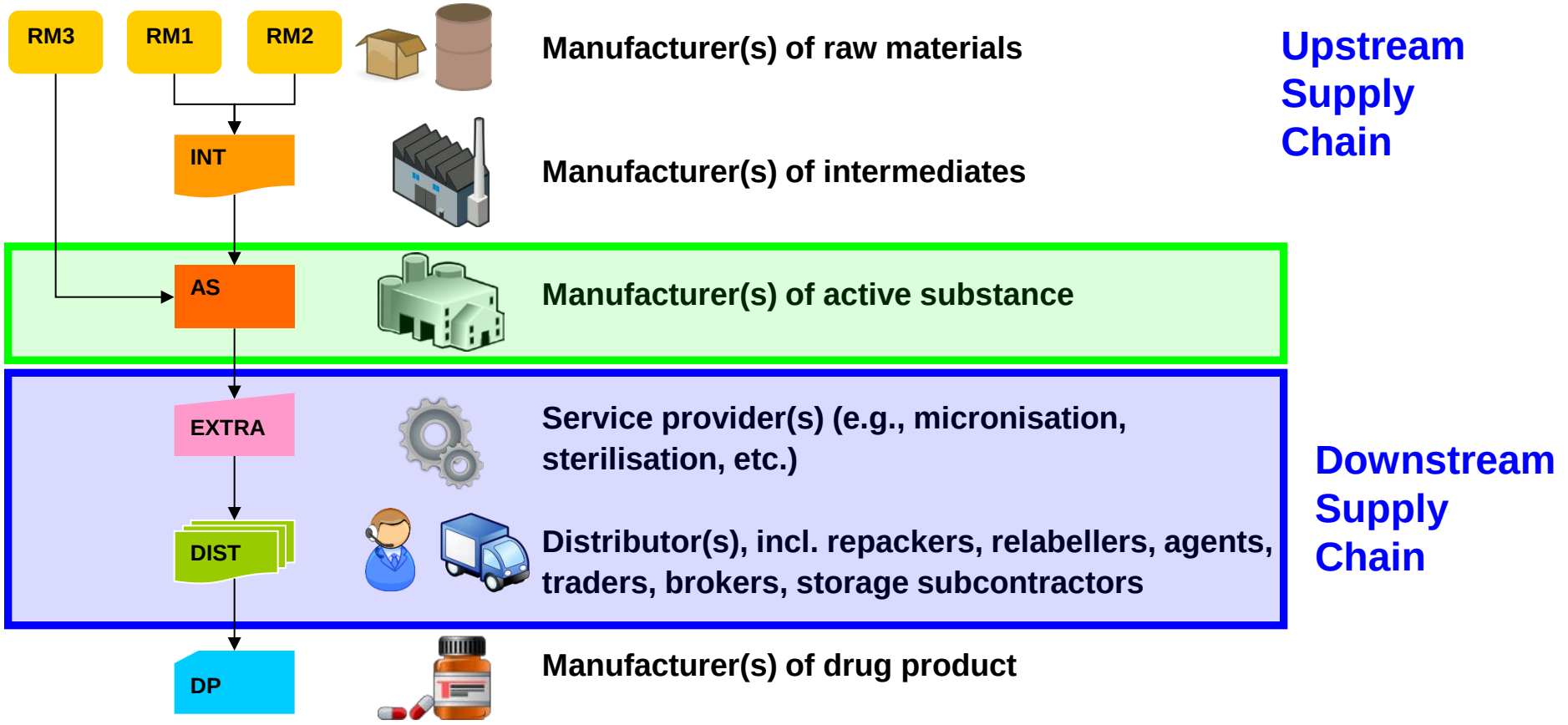
Rejected and Returned Materials

Considerations

- Any rejected material should be clearly identified and securely stored (restricted area) to prevent inadvertent use
  - Final disposition of rejected material (e.g. return to supplier, destroy material or material may be reprocessed or reworked (in exceptional cases) should be documented
- Any returned material should be clearly identified and securely stored in a restricted area to prevent inadvertent use
  - *Extreme care should be used before releasing any returned material for resale*

Main goal is to prevent rejected or substandard material from being introduced into the supply chain

Repackaging and Relabelling



Repackaging and Relabelling

Associated risks

- Maintaining the quality of APIs or products
  - Complex supply chain involving several brokers, traders and distributors in different countries
  - Outsourcing of re-packaging & re-labelling operations
  - Traceability to the 'original manufacturer' and all parties that are involved in the re-packaging & re-labelling activities
  - Transfer of Information (e.g., restricted release)
  - Risk of Contamination
  - Low margins → economically motivated adulteration

Who is responsible for securing the global supply chain ?

Outsourcing

Key issues in the Owner / Contractor Relationships

Quality Agreement
Template developed by the Manufacturing Practices Work Group
as part of the APEC program Roadmap for Global Medical Product Integrity and Supply Chain Security
August 2015

QUALITY AGREEMENT FOR
((ADD FIELD OF COLLABORATION))

Made between:

OUR COMPANY
Country
(hereinafter referred to as "OUR COMPANY")

and

Company Name Counterpart
Country
(hereinafter referred to as "XXX")

- Responsibilities of the contract facility must be clearly defined
  - Assure all aspects of GMP compliance are addressed by standard operating procedures (SOPs)
- Quality Agreement
  - Define, establish, and document the responsibilities of the parties involved in the contract
  - Define products and/or services
  - Use clear language
  - Define communication (incl. change control), expectations (e.g., Regulations / GMP requirements) and points of contact
  - Awareness: inter-company agreements might be required

Shadow and Show Factories

Definitions

- Show factory
  - Identified as the source, but does not actually manufacture the product that it claims to manufacture
  - Falsely named in the dossier (or other regulatory correspondence) as the site of manufacture
  - Generally an impressive facility in excellent state of repair (meant to “show” well)
  - Intended to mislead clients and regulators

- Shadow Factory
  - Product is identified as being manufactured by another site
  - Show factory or product owner *secretly contracts out* (or sub-contracts) work to the shadow factory that perform the operation
  - Uses equipment and possibly materials intended for or belonging to its client to manufacture an “identical” product

Shadow and Show Factories

Risks

- Real manufacturing site not assessed for its capability
- Products coming from real manufacturing site not produced under GMPs and consequently
- Unknown risks in regulatory systems
- Unreliable, unaudited, and uninspected sites
- Intolerable risk of poor quality and/or unsafe materials used in drug manufacturing

Note: not all shadow and show factories have been identified and one should vigilantly assess each facility to ensure they are the true manufacturer

Medicinal quality (and potentially safety) is compromised

Manufacturing: Yield & Reconciliation, Batch Release Process

Elements of batch release

The person, who decide, is accountable for adhering to compliance

A Holistic Approach To Manage Risk

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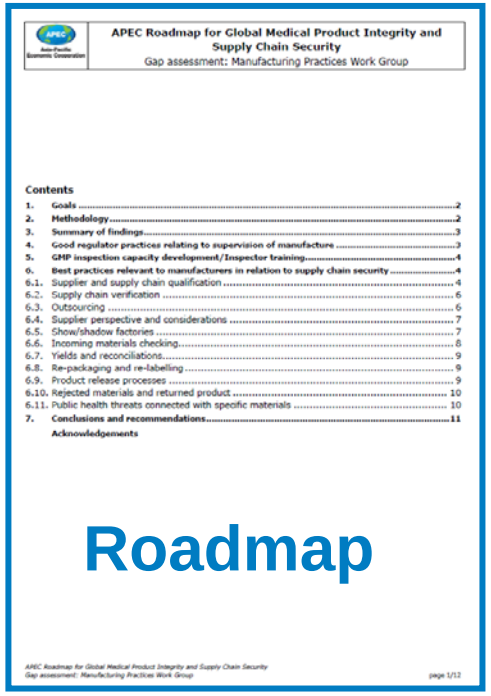
APEC Roadmap for Global Medical Product Integrity and Supply Chain Security
Gap assessment: Manufacturing Practices Work Group

Contents

Roadmap

- Supporting Material
  - ICH Q7 guideline & Q&A
  - Incoming Material check list
  - Q-Agreement template
  - Risk based procedure on inspections (PIC/S)
  - QMS for inspectorates (EU)
  - Guidance for inspection time on site

Details are available

- Manufacturing
  - Yields and Reconciliations
  - Batch Release Processes
- Supply Chain Oversight
  - Qualification and Verification
  - Checking of Incoming Goods
- Related operations along the Supply Chain
  - Rejected and Returned Materials
  - Repackaging and Relabelling
  - Outsourcing
  - Show and Shadow Factories
- Best practices for Regulators
  - Supervision of Manufacturers