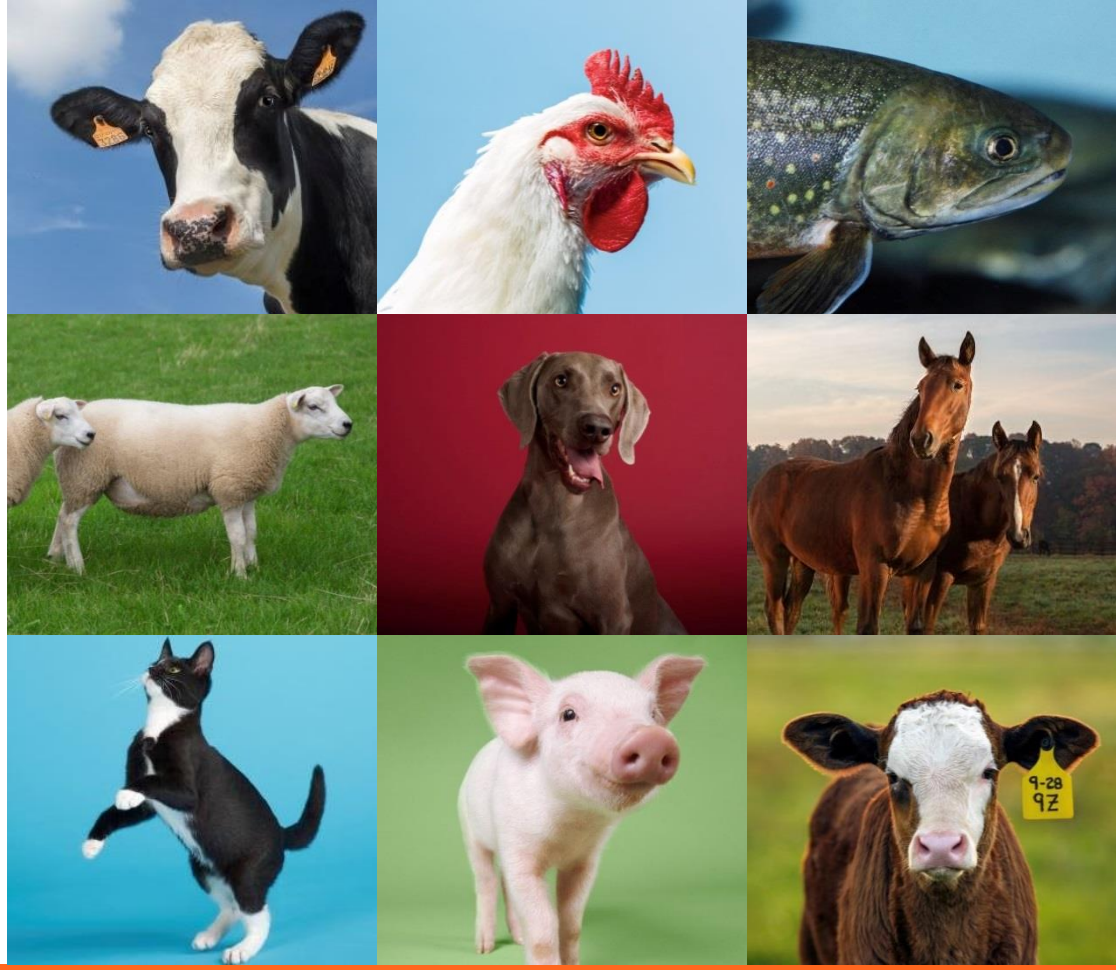
Veterinary Medicine Requirements for Distribution (GDP)



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What is GDP?

For all Pharmaceutical products including Biological products for both Human and Animal Health there are requirements to maintain and protect the Product Quality, Safety and Efficacy as manufactured until it reaches the Patient and is used.

– For Manufacturing and site storage facilities Good Manufacturing Practice (GMP) exists to manage and assure Product Quality.

– Once it leaves the Manufacturing process and enters Distribution networks, the product still needs Standards to ensure the Quality, Safety and Efficacy of a Product is maintained throughout its Distribution described as Good Distribution Practice (GDP).

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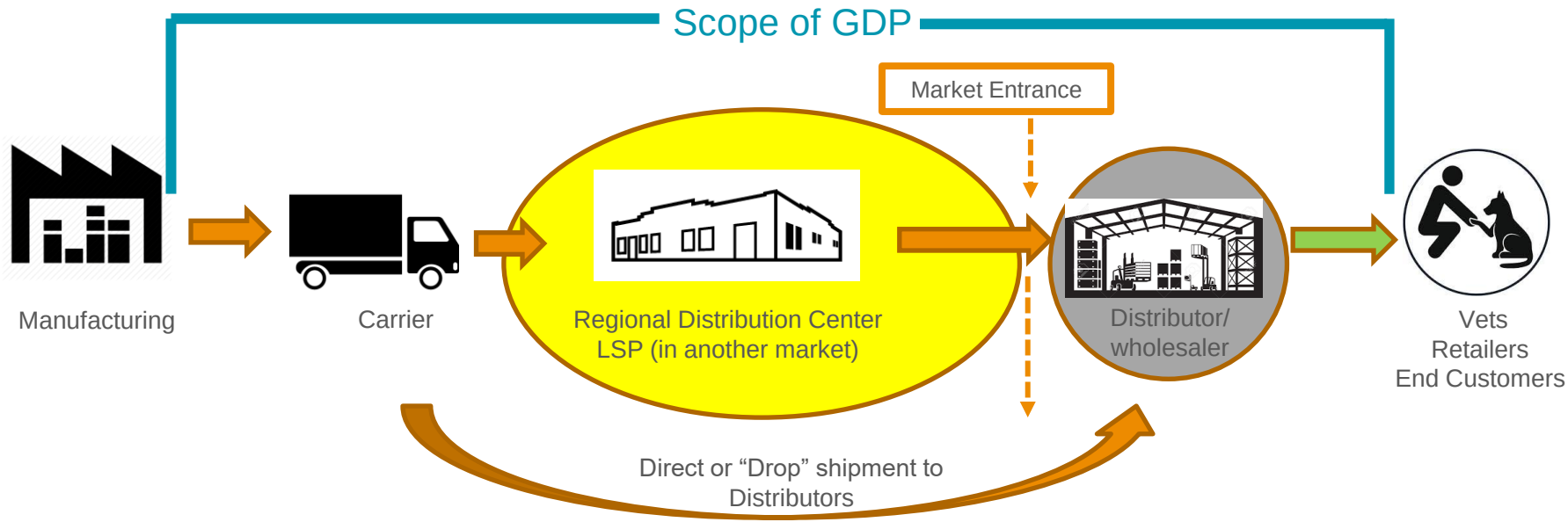
Example of a Simplified Supply flow to Distributor Markets



Definitions and Goals

GDP applies to both Human and Veterinary Medicinal and Biopharmaceuticals Product in the US and EU based on regulations and directives.

- EU 2019/6 Article 4 defines distribution as covering "*all activities consisting of procuring, holding, supplying or exporting veterinary medicinal products whether for profit or not, apart from retail supply of veterinary medicinal products to the public*"
- US FDA *has the **goal** of GDP described as "to **encourage sound business practices** that help deter interference and manipulation by bad actors and also to provide effective means to detect adulterated drug components and drug products to prevent them from entering the supply chain" The GDP regulations are codified into Title 21 of CFRs*
- *The World Health Organisation has a GDP guidance for Pharmaceuticals Products (WHO Technical report No. 957,2010 Annex 5) distribution based on US and EU Human pharmaceutical GDP. There is within the Scope an expectation distributors would use for Veterinary Pharmaceutical GDP in countries following WHO GMDP for Human pharmaceuticals*

These are MINIMUM standards to ensure that the quality and integrity of medicines is maintained in distribution networks.

EU VETERINARY GDP

EU GDP for Veterinary Products

The European Union (EU) has recently harmonized Veterinary Pharmaceutical Rules under EU Regulation 2019/6, including veterinary GDP for finished Products.

- European Member States historically applied their national laws based on Human GDP Directives 2013/C 343/01 or 94/C 63/03.
- EU Regulation 2021/1248, and implementing regulation of 2019/6, sets out detailed pan-European Veterinary GDP regulations for Finished Vet Med Products.

Any Individual / Company that performs any activities consisting of procuring, holding, supplying, exporting, collection, transportation, warehousing, distribution, payment and/or ownership (MAH) of veterinary medicinal products whether for profit or not, must hold wholesale license issued by the Competent Authority.

A Manufacturer may perform distribution of its own products under the scope of its Manufacturing Licence.

Regulation 2019/6: https://eur-lex.europa.eu/legal-content/AUTO/?uri=CELEX:32019R0006&qid=1643616093155&rid=1
Regulation 2021/1248: https://eur-lex.europa.eu/legal-content/AUTO/?uri=CELEX:32021R1248&qid=1643616125424&rid=1

What does GDP cover/ require ?

Examples of Key areas (1 of 3)

- Quality Management Systems (ISO/ ICH Q10)
  - Documentation/ Records/ Schedules
  - Change Control
  - Qualification/ Validation
  - Audit/Self-inspection
  - Complaint Management
  - Deviations and CAPA management
  - Management Review and monitoring
- Responsible Person/ Management Representative for Quality
- Good Facility Management
- Temperature Control/ Environmental Control
- Warehouse Management Systems (Inventory Control, Prevention of expired product entering market)

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What does GDP cover/ require ?

Examples of Key areas (2 of 3)

- Outsourcing activities
- Training and knowledge
- Shipment protection (Packaging)
- Recall management
- Hygiene, Cleaning and Pest Control
- Security of Products
  - Prevention of falsification/ counterfeit/ adulteration/ Contamination
  - Segregation of Pharmaceutical products from other products
  - Status control and Segregation.
  - Theft

What does GDP cover/ require ?

Examples of Key areas (3 of 3)

- Receiving/ Dispatch Controls
- Supplier and customer verification and Management
- Returns management.
- Transport
- Risk Management Approach (ICH Q9)
- Prevention of Damage/contamination
- Controlled Substances
- Destruction of obsolete Products
- Authority interaction
  - Inspection to GDP Compliance and licence to operate (Wholesale Dealer)
  - Other

Temperature Management

Temperature management is not only recording that the storage area meets the Product Labelled Storage conditions.

- Transport delivering Product has to maintain the labelled Storage Conditions, both to and from the distributor.
- Temperature mapping is used to determine the correct locations for monitoring in both transport and Storage. Any out of range results to be investigated and product quality assessed by Manufacturer/ supplier.
- For Transport - Passive or Active temperature control is used according to decisions from a ***shipping lane validation study*** taking into account Seasonal temperature challenge, the time and distance in transit and the Product stability and protection.

Distributors should

- If a delivery comes with temperature monitors, check for alarms and upload to sender's site as soon as the delivery comes under distributor's control.
- If a logger is in alarm status; a shipment in passive packaging arrives after its certified controlled period; or the protection is damaged: Place the shipment in Quarantine and contact the sender to confirm if the product is still OK for further supply

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Falisified/ Adulterated Products

- Individuals and companies trading in Pharmaceutical Products have to take special care and actions to ensure that counterfeit or poor quality products do not enter the supply chain.
- In the EU, product is not eligible for return to saleable inventory after it has left the traceable supply chain, or it is suspected of being stolen or tainted in any way.
  - Lost in transit is automatically ineligible for further use, if recovered.
  - Recovered stolen Pharmaceutical products are ineligible for further use.
  - Checks (e.g. supplier certification) must be in place to assure the sources of products are genuine and the product has not been tampered with.
  - Product must only be delivered to valid certified customers eligible to use the product, i.e. Customer certification.
  - Returned Product must be verified to ensure that no defective or falsified products have been introduced; it must be genuinely what was shipped to the customer.

Outsourcing

- Outsourcing distribution arrangements can take many forms and for various reasons.
- When outsourcing, the Contract Giver is responsible for assuring that Contract Acceptor is capable and qualified
  - Audit is one risk assessment tool for a snapshot
- The Contract Acceptor's performance should be monitored on a periodic basis.
- When delegating control to a 3rd party it is always good practice to use a Quality Agreement alongside the Commercial agreement.
  - Under EU Regulation 2021/1248, where the *product owner or an operator* has outsourced responsibilities and delegations in distribution to 3rd parties, a contract is required detailing Quality responsibilities.
- Quality Agreements are signed by the Quality Management and Legal/ Commercial
- Quality Agreements may be called Technical agreements and assign detailed responsibilities for GDP activities between parties including Contacts, Locations and Product Quality Processes such as Recall and Product Assurance Guarantees to the next layer of distribution.

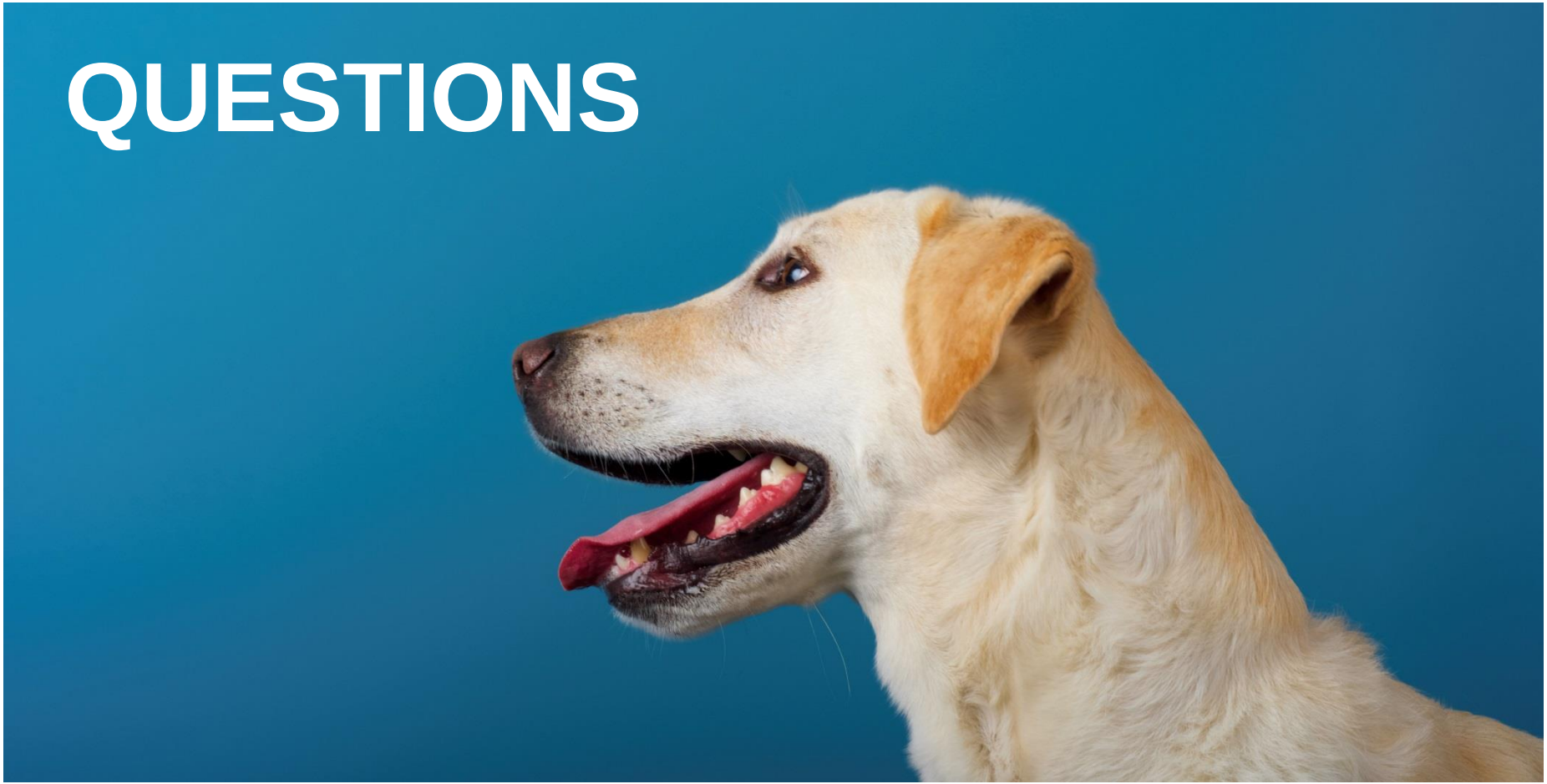
Supplier/ Customer Verification in EU

Supplier/ Customer verification can take many forms depending on regulations and resources.

- Involves checking the supplier/ customer is who they say they are
- Supply and retention of Certifications to Manufacture or Distribute the products and any special licences (Controlled substances) and ensuring they are current.
- European Union is expanding its Eudra GMDP database* to include all Wholesale Dealers Licences (WDA) and GDP Certificates of Inspections issued in EU.
  - Only entities on that database will be eligible for supply to, or purchase from, for EU distribution.
  - Non-EU entities sourcing from EU based partners should check the database to ensure their partner is certified to source/ supply the product and export it out of EU.

* http://eudragmdp.ema.europa.eu/inspections/displayHome.do

QUESTIONS



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