Animal Pharmaceutical Supply Chain Interruptions

Why interruptions occur and best practices for mitigation

DISRUPTIONS

Major breakdowns in the production or distribution nodes that comprise a supply chain

Types of disruptions

- **Internal**
  - Breakdown of vital machinery (equipment qualification and validation)
  - Factory fires/explosion
  - Transportation and freight logistics
- **External**
  - Interruptions to flow of raw materials or components to your business
    - Natural disasters and extreme weather conditions
    - Price hikes
    - Mergers and acquisitions
    - Geopolitical Instability
  - Governmental regulations
    - Taxations, trade restrictions, border controls, and labor laws
    - Inspectional and non-compliance issues
    - State registration requirements

IMPACTS ON BUSINESS ACTIVITIES

There are an infinite number of factors in supply chain disruptions which may affect the cost, timing, or risk of a supply chain at any given time

Business impact

Degree of impact on your business will depend on the severity and length of the disruption, but most disruptions will have a financial effect.

- Supplier relations
- Inventory management of raw materials and finished goods
  - Ordering and purchasing
  - Safety stock levels
- Production
- Distribution
- Marketing aspects - customer relations and business reputation
  - Financial management
  - Sales and revenue

In reality, the best you can do is to make calculated decisions and actions that may reduce the occurrence of disruption events and to have systems in place to minimize their impact when they happen.

CHALLENGES

Challenges Industry faces when working with Contract Manufacturing Organizations (CMO) / Suppliers

Industry Challenges

- Identification/Qualification/Selection of quality CMOs / Suppliers (Sourcing)
  - Limited facilities that will handle animal health drugs
  - Business aspect (cost of goods, planning, supply)
    - ie. Secondary Qualified Supplier (volume satisfaction, cost to qualify)

- Regulatory aspect (Supply Chain and Regulatory Affairs)
  - Import alert
  - Changes in import requirements
    - Lack of understanding leads to blocks at the border
  - Inconsistency

- Compliance aspect (Quality and Regulatory Affairs)
  - Resources and people for oversight
  - GMP status
  - Location of foreign CMO/Supplier (remediation/support)
  - Resolving Drug Master File deficiencies (don't have access to DMF)
    - Lack of transparency between supplier and customer

MITIGATION

Every year, companies dedicate time, resources, and personnel to create strategies designed to reduce the likelihood of disruptions across the various points of the supply chain.

Mitigation Tactics

- Identification/Qualification/Selection of quality CMOs / Suppliers (Sourcing)
  - Minimize risk: Improve supplier audit process - always look forward and develop backup plan (proactive vs reactive)
    - Natural Disasters - Global Diversity
    - Geopolitical Instability - Cultural Research
    - Price hikes - Market Exploitation
  - Relationship building
    - Better communication among supply chain
  - Strike a balance between efficiency and effectiveness
  - Use of exercises to stress-test assumptions and plans
    - Start with top products
      - Made at multiple sites?
      - Safety stock of finished goods?
    - Look at Bill of Material
      - Single sourced? Dual sourced?
      - Vendor Managed Inventory – do the vendors keep stock on hand to cover production?

Mitigation Tactics

- Identification/Qualification/Selection of quality CMOs / Suppliers (Sourcing) – cont.
  - Develop business continuity plans, and protocols to address major concerns
    - Clearly defined corporate structure and coordinated departments with clear responsibilities
  - Work with suppliers to ensure they are similarly prepared and proactively mitigating the biggest risks.

- Regulatory aspect (Supply Chain and Regulatory Affairs)
  - Sponsor import broker
  - Harmonize documentation requirements
  - Contact CVM for assistance
  - Start state registration process early

Mitigation Tactics

- Compliance aspect (Quality and Regulatory Affairs)
  - Audit the facilities early and often
  - Vendor quality metrics
  - Audit open part of DMF – early
  - If not submitted yet, be a partner with your supplier on submission:
    - Ensure they are aware of requirements (USP, Parenteral Drug Association (PDA), Ph. Eur., etc.)
    - Common Technical Document (CTD) format / eSubmitter for VMF/DMF helps point out what may be missing
    - Understanding contracted facilities

CONSIDERATIONS

Submission Considerations

Information needed to support requirements of the CMC supplement can be found in:

- Guidance for Industry (CVM/FDA and VICH/ICH)
- External standard setting organizations (USP, PDA, Ph. Eur.)
- Common Technical Document (CTD) format
- Question Based Review format in eSubmitter
- Alternate approaches are acceptable, if supported by scientific justification

Facility Considerations

All facilities must have an acceptable GMP status at the time of approval.

- For foreign facilities, cannot approve if Official Action Indicated (OAI) status and import alerts
- Data integrity issues can lead to unacceptable GMP status
- Master file deficiencies
- Facilities contracted to produce the significant portions of the API process

Research Considerations

When looking for alternate/backup sources or suppliers, do your homework:

- Basic Internet Search

https://www.google.com, etc..

- Drug Master Files (DMFs)

https://www.fda.gov/drugs/forms-submission-requirements/drug-master-files-dmfs

- Veterinary Master Files

https://www.fda.gov/animal-veterinary/development-approval-process/veterinary-master-files

- Drug Establishments Current Registration Site

https://www.fda.gov/drugs/drug-approvals-and-databases/drug-establishments-current-registration-site

- Inspection Classification Database Search

https://www.accessdata.fda.gov/scripts/inspsearch/

- FDA Warning Letters

https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/compliance-actions-and-activities/warning-letters

Research Considerations

- Import Alerts

https://www.fda.gov/ForIndustry/ImportProgram/ActionsEnforcement/ImportAlerts/default.htm

- Recalls, Market Withdrawals, & Safety Alerts

https://www.fda.gov/safety/recalls-market-withdrawals-safety-alerts

- Drugs@FDA: FDA Approved Drug Products

https://www.accessdata.fda.gov/scripts/cder/daf/

- Animal Drugs@FDA (and Green Book reports)

https://animaldrugsatfda.fda.gov/adafda/views/#/search

- Electronic Animal Drug Product Listing Directory

https://www.fda.gov/industry/structured-product-labeling-resources/electronic-animal-drug-product-listing-directory

- Dailymed

https://dailymed.nlm.nih.gov/dailymed/index.cfm

Global Considerations

- Improving the availability of medicines authorized in the EU is a key priority for the European medicines regulatory network.
- Shortages or other problems with availability, creates challenges for supply chain, with a potentially serious impact on human and animal health.
    - Since 2016, task force set up by European Medicines Agency (EMA) and Heads of Medicines Agencies (HMA) look at availability issues and supply chain disruptions, to improve continuity of supply of human and veterinary medicines across Europe.
    - In EU, most medicine shortages are handled at national level by national competent authorities.

Guidance for marketing authorization holders

- Guidance on detection and notification of shortages of medicinal products for Marketing Authorisation Holders (MAHs) in the Union (EEA)

https://www.ema.europa.eu/documents/regulatory-procedural-guideline/guidance-detection-notification-shortages-medicinal-products-marketing-authorisation-holders-mahs_en.pdf

Global Considerations

Guidance for regulators on public communication

- Good practice guidance for communication to the public on medicines' availability issues

https://www.ema.europa.eu/documents/regulatory-procedural-guideline/good-practice-guidance-communication-public-medicines-availability-issues_en.pdf

Guidance for regulators on shortages due to manufacturing or quality issues

- Criteria for classification of critical medicinal products
- Decision tree on escalation from national to European level
- Points to consider for the overall assessment of a supply shortage of a medicinal product due to GMP Non-compliance /quality defects
- Closing report on assessment of a supply shortage of a medicinal product due to manufacturing and quality problems
- Resources for issuing treatment recommendation during shortages of medicinal products
- Risk indicators for Shortages (Manufacturing and Quality)

https://www.ema.europa.eu/en/human-regulatory/post-authorisation/availability-medicines

Thank You