



Australian Government  
Department of Health  
Therapeutic Goods Administration

# Regulating the manufacture of therapeutic goods





# Overview

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- The basis of Good Manufacturing Practice
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# Checking the quality of therapeutic goods



The TGA monitors and assesses manufacturers to ensure that therapeutic goods supplied in Australia are manufactured to a high standard



The emphasis and depth of manufacturer inspections, as well as the frequency of inspections, are guided by the inherent risks of the product and the method of manufacture. We also take into account the compliance and inspection history of the manufacturer



# How do we do this ?



On-site inspections of manufacturers and compliance verifications (paper-based assessments)

Australian and overseas manufacturers are assessed prior to supply of goods and are then regularly reviewed

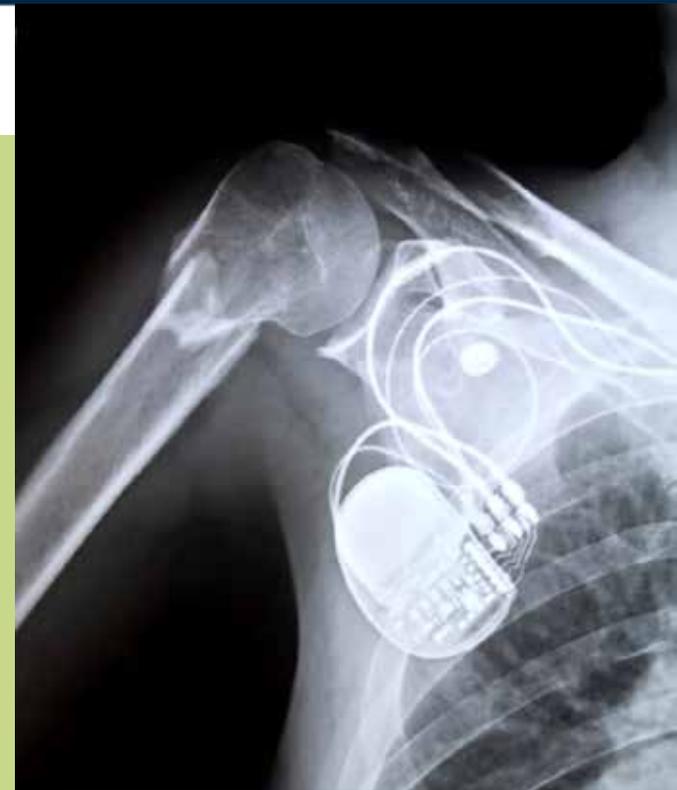
Inspections against the relevant Code of Good Manufacturing Practice (GMP) or Standard (for devices) which describes the range of conditions required for the safe, sterile production of goods

Quality manufacturing



# Higher risk products

- Sterile medicines, including active pharmaceutical ingredients
- Single step sterilisers
- Non-sterile medicines containing antibiotics, steroids or antineoplastics
- Primary collection, processing and storage sites for blood, including human haematopoietic stem cells
- Tissue banks with complex processing
- Cellular therapies
- Medical devices - [Class III and Active Implantable Medical Devices \(AIMD\)](#)



Pacemakers are regulated as AIMDs



Plasmapheresis

## Medium risk products

- Non-sterile medicines, including herbal products
- Secondary blood collection and separation sites (including sites collecting plasma only or platelets)
- Tissue banks with low manipulation
- Other medical devices



# Lower risk products

- Minerals, vitamins, fish oils and other supplements
- Sunscreens
- Medicinal gases
- Other blood collection sites including mobile units
- Homeopathic medicines

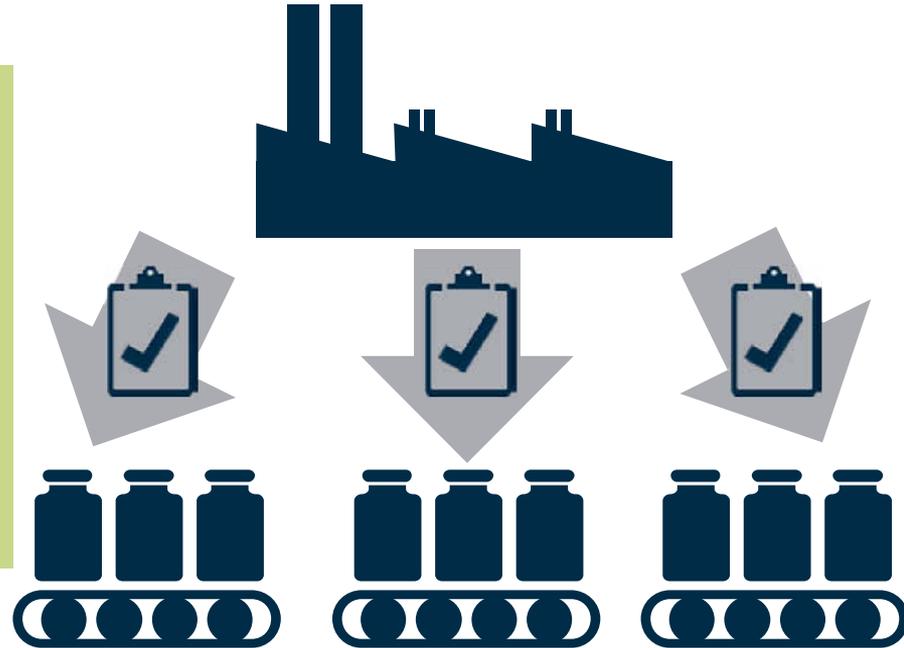




# The basis of Good Manufacturing Practice

A basic tenet of GMP is that:

- Simply testing a product after manufacture is not sufficient to ensure product quality
- Quality must be built into each batch of a product during all stages of the manufacturing process





# Looking at the actual product

GMP requirements cover:

- How products are manufactured, packaged, labelled and stored
- How therapeutic goods are tested to ensure that products are of a suitable quality, including the final evaluation and approval for use by the manufacturer of each batch made



# The manufacturer must:



Have a quality management system in place under which manufacturing activities are controlled



Include in the system personnel involved in the control of therapeutic goods manufacturing and how they are trained



Provide information on how premises used in the manufacture of goods are designed, operated, maintained and controlled



Control manufacturing activities through the use of written procedures and instructions



Record manufacturing events through comprehensive record keeping practices



# Inspections include verification that:

All manufacturing processes are clearly defined and regularly reviewed

Critical manufacturing processes and changes are validated

Written instructions for all tasks are developed and available

Records of all manufacturing activities are kept

All starting materials and finished products are sampled, tested and approved for use using appropriate methods

Batches are certified as fit-for-purpose prior to distribution





# Inspections ensure quality of therapeutic goods

- Planned and unplanned inspections are undertaken to assess compliance with GMP standards, both domestically and overseas
- The emphasis, depth and frequency of inspections for a particular manufacturer are guided by the inherent risks of the product and the method of manufacture as well as:
  - manufacturer size
  - complexity of their products
  - compliance history

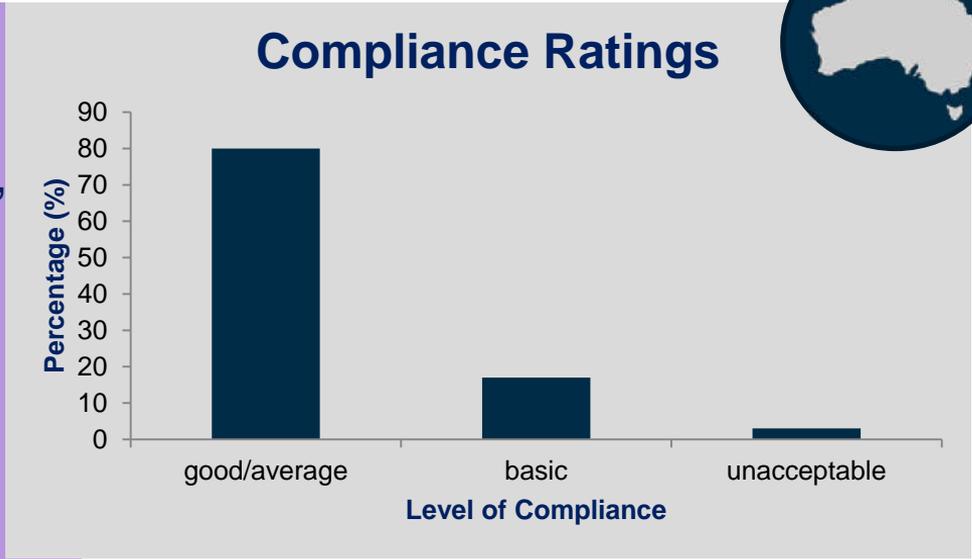




# Inspecting Australian manufacturers

In Australia, the TGA manages annually:

- ~400 licences for manufacturing, supply and distribution sites
- ~450 sites
- ~250 inspections of sites



\*statistics per annum, current as of July 2013



# Manufacturers who receive a basic rating

- Where 'basic' is considered just acceptable, the TGA applies a specific strategy to each manufacturer to enforce improvement by a combination of the following:
  - follow up and close out inspections where required
  - a letter to outline any concerns where required
  - inspections every 12 months



# Which countries supply to Australia?

Therapeutic goods are manufactured and supplied in a global market

This includes both finished goods and ingredients

Countries who manufacture or supply to Australia include:

Sites:

- Europe
- India
- China
- US/Canada
- Other

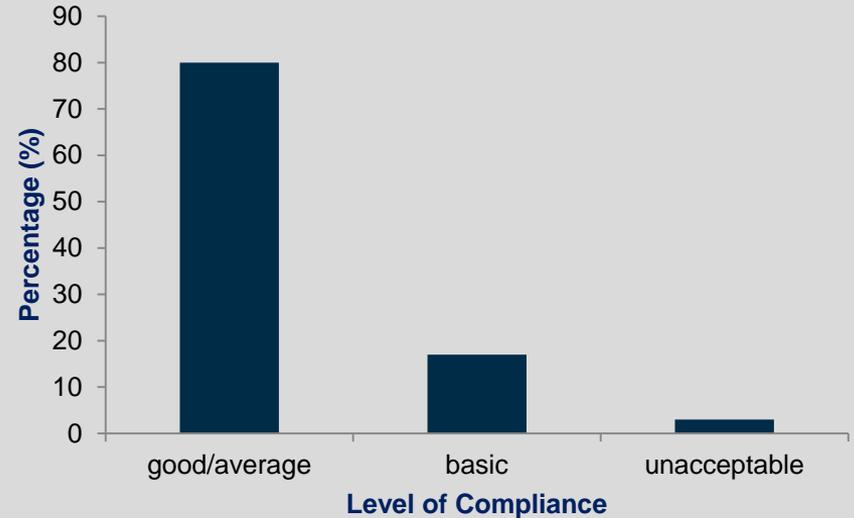


# Inspecting international manufacturers

TGA inspection and certification of overseas sites

- ~2,000 manufacturers > 2,500 sites
- ~3,500 clearances
- 150-200 on-site inspections
- Increasing number of compliance verifications (using inspection reports from other agencies)

## Compliance Ratings



\*statistics are per annum, current as of July 2013



# The future of manufacturing

Manufacturing is being expanded to developing countries

Faster access to products for Australians

Multi-step manufacture of products is common

Complex supply chains which may span many different countries

Challenges with different languages

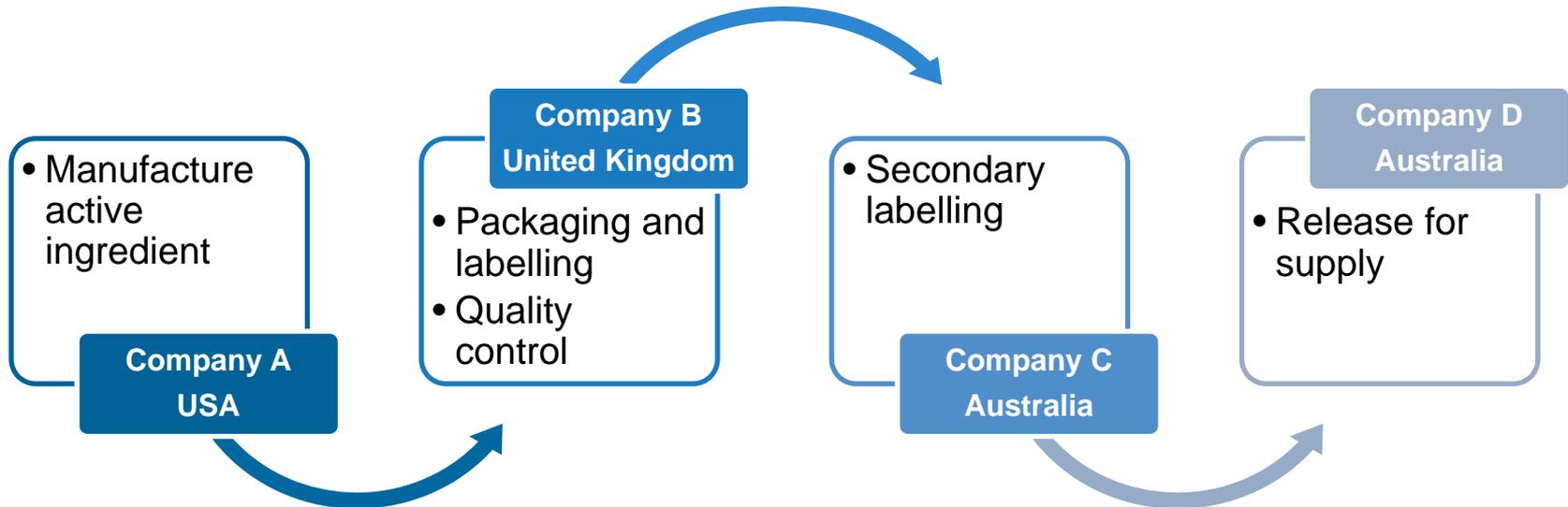




# Multi-step manufacturing process

## Example of an over-the-counter medicine

The manufacturing process for medicines may occur in stages. In the following real world example, an over-the-counter medicine may be handled by four different companies across three countries before it reaches the market.

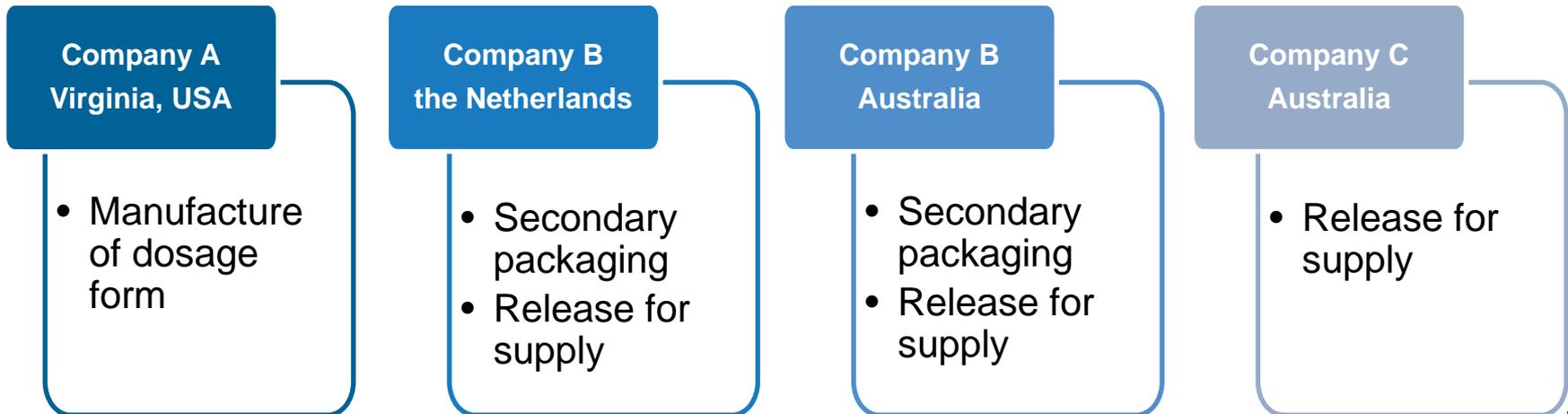




# Multi-step manufacturing process

## Example of a prescription medicine

Company A – in Pennsylvania, USA – may complete every stage of the manufacturing process OR it may only manufacture the active ingredient, with the following stages being completed in one of a number of alternative sites



# International harmonisation



- International harmonisation of standards and inspections allows for a shared workload with regulators in other countries
- It may include:
  - joint inspections with overseas partners
  - shared inspection scheduling
  - sharing of information, reports and manufacturer information
  - mutual recognition of codes of GMP and standards



# Other education modules include:

Introduction to the TGA

Medicines

Biologicals

Medical devices

Postmarket monitoring