P02: Cancer Vaccines

E356 Pharmaceutical and Bio-Chem Supply Chain

Diploma in Supply Chain Management (DSCM)

E356 Topic Tree

Pharmaceutical and Bio-chem Supply Chain

- Introduction to Pharma and Bio-chem
- Classification of Dangerous Goods
- Best Practices (GMP/GDP)
- Clinical Supply Chain
- Cold Chain Management

Import, Packaging and Distribution

- Import and Distribution of Medical Devices
- Import of Pharmaceutical and Bio-Chem Products
- Local Transportation of Pharmaceutical and Bio Chem Products
- Packaging of Pharmaceutical DG for Air Transport
- Declaration of Pharmaceutical DG for Air Transport

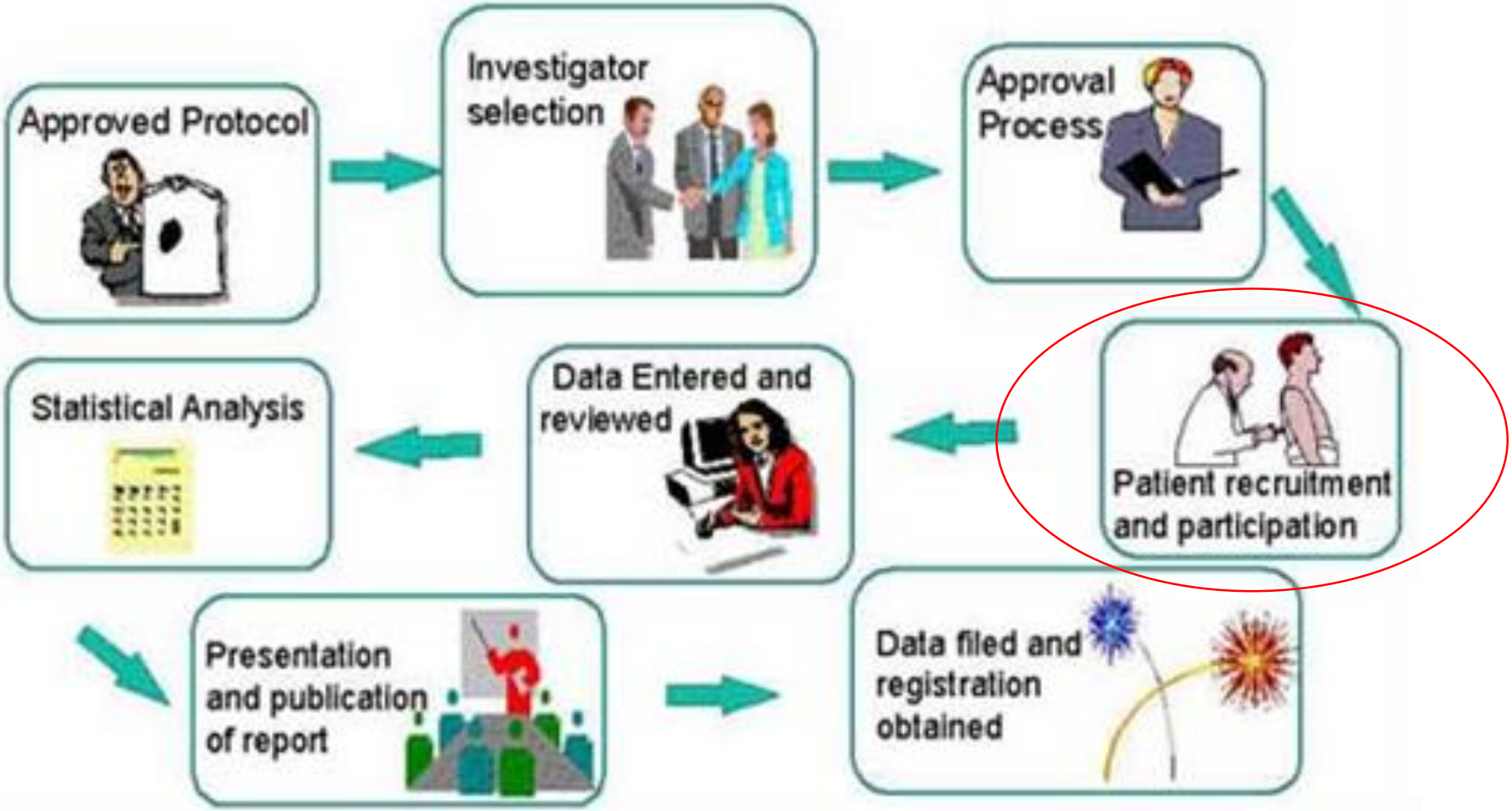
Product Tracing, Recall and Disposal

- Product Tracing
- Drug Recall
- Disposal of Bio-chem Products in Hospital Logistics

Clinical Trials

- **After the discovery phase, pre-clinical trials are performed on animals to test new therapies or procedures. With more conclusive results, clinical trials are performed to gather more information on an experimental treatment, its risks and how well it may or may not work on humans.**
- **Clinical Trials are generally considered to be biomedical or health-related research studies in human beings that follow a pre-defined protocol. Carefully conducted clinical trials are the safest and fastest way to find treatments that work in people, and new ways to improve health.**

Clinical Trials



http://www.thecountymedicalexaminers.com/clinical-trials/

Two main types of clinical studies

- **Observational studies**
  - Researchers collect data by observing groups of participation
  - Participants not assigned to specific interventions by researchers
  - Eg, observing a group of participants on the effects of their lifestyle on their liver health.

- **Interventional studies (clinical trial)**
  - Participants receive specific interventions.
  - Interventions may be medical products such as drugs or devices
  - Placebo is required so that comparisons can be made
  - Participants will not know they are taking the placebo

Purposes of clinical trials

1. Treatment trials test experimental treatments, new combinations of drugs, or new approaches to surgery or radiation therapy.
2. Prevention trials look for better ways to prevent disease in people who have never had the disease or to prevent a disease from returning. These approaches may include medicines, vaccines, vitamins, minerals, or lifestyle changes.
3. Diagnostic trials are conducted to find better tests or procedures for diagnosing a particular disease or condition. This usually include people who have signs or symptoms of the disease or condition being studied.
4. Screening trials test the best way to detect certain diseases or health conditions.
5. Quality of Life trials (or Supportive Care trials) explore ways to improve comfort and the quality of life for individuals with a chronic illness.

Treatment Trial

PARTICIPANTS WANTED
for Electromagnetic Therapy Clinical Trial for
URINARY LEAKAGE
in Female

Adventist urology clinic is conducting a clinical trial to investigate the efficacy of transpelvic magnetic stimulation (using QRS®-1010 PelviCenter) as a potentially beneficial non-surgical option for female patients with Stress Urinary Incontinence.

QRS Pelvicenter Electromagnetic Therapy
- non-invasive (no probes, no cones, etc)
- No need for drugs or medications
- Fully automated pelvic floor muscle exercise
- Simply sit on a hair, wearing normal everyday clothing
- Pain free

Qualified participants will receive electromagnetic therapy for Urinary Leakage at minimum or no cost.

Inclusion criteria
- ✓ Diagnosis: Stress Urinary Incontinence
- ✓ Malaysian only
- ✓ Age: 21 -70 years old
- ✓ Sex: Female
- ✓ Urine leak because of cough sneeze, laugh, exercise or stand up from sitting

Exclusion criteria
- ✗ Metal heart implant
- ✗ Previous treatment with magnetic stimulation
- ✗ Previous surgery for Stress Urinary Incontinence

- Treatment trial – To treat Incontinence

Prevention Trial

- Prevention trial to reduce dust allergy (allergic disease)
- To prevent the allergic disease from returning

Diagnostic Trial

Diagnostic Trial in Patients Who Are Undergoing Surgery for Early Stage Mouth Cancer

A Trial Of Lymphatic Mapping And Sentinel Node Lymphadenectomy For Patients With T1 or T2 Clinically N0 Oral Cavity Squamous Cell Carcinoma

RATIONALE: Diagnostic procedures to detect cancer cells in sentinel lymph nodes may help plan effective cancer treatment.

PURPOSE: Diagnostic trial to study the effectiveness of lymph node mapping and sentinel lymph node lymphadenectomy in patients who are undergoing surgery remove early-stage cancer of the mouth.

OBJECTIVES:

- Determine whether a negative hematoxylin and eosin finding from the lymphatic mapping and sentinel node lymphadenectomy procedure accurately predicts t negativity of the other cervical lymph nodes in patients with stage I or II squamous cell carcinoma of the oral cavity.
- Determine the extent and pattern of disease spread in the nodal bed in these patients.
- Obtain data on the use of immunohistochemistry to assess nodes in these patients.

- **Diagnostic trials in Patients with condition**

Screening Trial

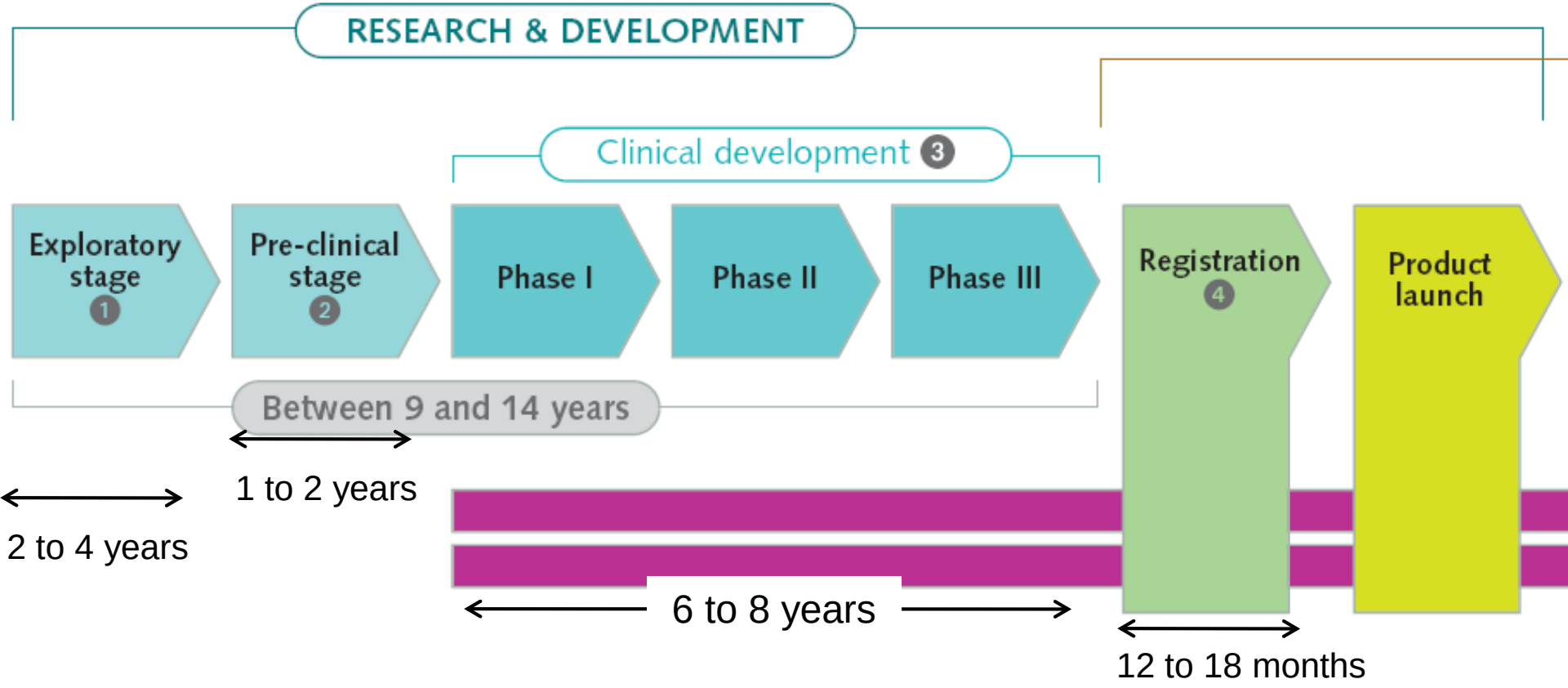
- The purpose of screening is to check your lungs while you are feeling healthy and to look for any changes from year to year. If there's something unusual in the lungs, a screening may be able to find it at an early stage.

Quality of life Trials

Approved For Period: 3/28/2014 - 3/27/2015

Clinical Supply Chain- Research & development Phase

Average development time : **12 years**



Phases of Clinical Trials

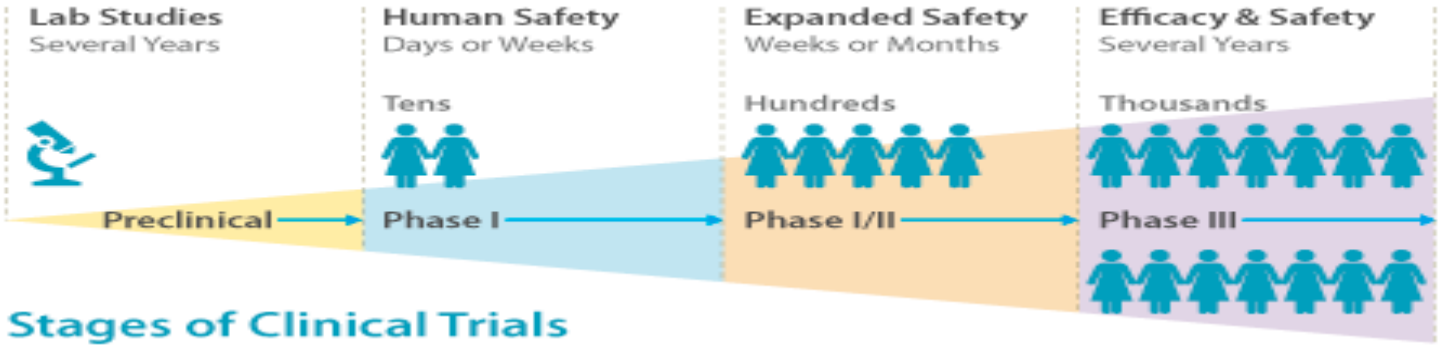
Clinical trials are conducted in phases. The trials at each phase have a different purpose and help scientists answer different questions:

- **In Phase I trials, researchers test an experimental drug or treatment in a small group of people (20-80) for the first time to evaluate how a new drug should be given (by mouth, injected into the blood, or injected into the muscle), how often, what dose is safe, and identify side effects. Testing on toxicity and safety on 10 to 100 subjects.**
- **In Phase II trials, the experimental study drug or treatment is given to a larger group of people (100-300) to see if it is effective and to further evaluate its safety. Evaluation of the immune response.**

Phases of Clinical Trials

- **In Phase III trials, the experimental study drug or treatment is given to large groups of people (1,000-3,000 to 40,000 subjects) to confirm its effectiveness, monitor side effects, compare it to commonly used treatments, and collect information that will allow the experimental drug or treatment to be used safely. Large scale tests of the vaccine efficacy and tolerance on 3k-40k subjects.**

- **In Phase IV trials, post marketing studies delineate additional information including the drug's risks, side effects, benefits, and optimal use.**



Stages of Clinical Trials

Who are involved in Clinical Trials?

- **Regulatory authority e.g. HSA (Singapore), FDA (USA)**
- **Investigator e.g. Specialist doctor, physician**
- **Sponsor - organizations such as medical institutions, voluntary groups, and pharmaceutical companies, in addition to government/ statuary agencies e.g. SingHealth group, NHG (National Healthcare group) and DSTA in local context.**
- **Clinical Research Organization (CRO) - An organization contracted by the sponsor to perform one or more of a sponsor's trial-related duties and functions including clinical-study and clinical-trial management for drugs and/or medical devices.**
- **Clinical Research Associate - Representative from the sponsor company or CRO.**
- **Site Staff / Trial Team - Personnel in contact with the participants who monitor the participants carefully during and after the trial. e.g. Doctors, nurses**
- **Participants e.g. Patients, healthy volunteers**

Guidelines for Clinical Trials Management

- **With increased clinical research activities in Singapore and the need to accord appropriate protection to ensure the safety and well-being of trial subjects, the Singapore Guideline for Good Clinical Practice (SGGCP) was implemented on 1 Aug 1998.**
- **The SGGCP, which was adapted from the International Conference on Harmonization (ICH) Guideline for Good Clinical Practice (GCP), sets standards for the conduct of clinical trials.**
- **GCP guidelines require the receipt, storage, dispensing and destruction records for an IP / IMP to be maintained.**
- **The information that needs to be maintained include date, quantities, serial number, expiry dates.**

Managing Clinical Trial Supply Chain

Clinical supplies management services are often managed by Clinical Research Organizations (CROs). These services often include clinical supplies demand projection, inventory management from depot to site, tracking from depot to site to patient and expiry date management.

Samples of biological fluids from participants may also need to be sent back to site and laboratories for analysis.

Managing Clinical Trial Supply Chain

Clinical trial supplies include :

- Investigational Product (IP) / Investigational Medicinal Product (IMP) / Trial Product – A trial product / drug that has not been approved for general use but is under investigation in clinical trials.
- Placebo - An inactive drug / product that has no treatment value, often used as a reference for comparison to assess the IPs effectiveness.
- Auxiliary Supplies other than trial product, e.g. all equipment such as needles, other medical devices and dummy packages, etc.

These items are often packed into a clinical trials kit.

Managing Clinical Trial Supply Chain

- **IPs are usually packed in an individual way for each participant before they are shipped and sent to the local sites.**
- **It is the Sponsor's responsibility to develop written instructions for handling and storage the IP i.e. IP shipment, IP receipt, IP storage, IP re-packaging, IP dispensing and accountability, IP return and / or destruction, and unblinding procedures. Blinding is where participants and/or study staff involved in the study do not know which study treatment they receive / give; 'blinding' is to prevent biases.**
- **Principles of GMP should be adhered to for IP re-packaging**
  - Line clearance: Pack one type of IP at a time.
  - In-process control checks: IP re-packaging should be performed and witnessed by delegated and trained unblinded study staff.
  - Label re-conciliation : No. of IP labels issued = No. of IP labels used + destroyed + remaining;
  - Documentation: The IP re-packaging process should be documented and signed off by the unblinded study staff

Managing Clinical Trial Supply Chain Globally

- **Clinical trials studies are increasingly conducted globally over wide geographical locations including India and China. This results in increased complexity of the clinical supply chain where researchers ship large volumes of temperature-sensitive IP worldwide.**
- **The primary concern of the trial team is to ensure that the correct medications are supplied to each site and each patient on time and within specification.**
- **CROs face many challenges distributing IPs to participants including regulatory requirements, importation procedures, duties and taxes and extreme weather climate.**

Anti-counterfeiting technologies in clinical trial

- **There has been increase in number of counterfeiting cases for comparator over the last few years, mostly due to inefficient clinical supply chain security.**
  - In 2010, 80 patients taking part in a clinical trial developed acute inflammation of the eye after using counterfeit version of Avastin drug in China
  - In 2013, a leading Indian drug maker was fined USD 500 million in the US for, misrepresenting clinical generic drug data and selling adulterated drugs to the US
- **Clinical trial supply players are now investing in anti-counterfeiting technologies for tracking of comparator drugs used in different phases of clinical trials. For example, nonClonableID technology by Bilcare is used in verifying the drug origin in the clinical supply chain.**

Today's Problem

- **Understanding the phases of clinical trial**
  - Different phase requires different amount of drugs to be delivered.
  - Phase 3 requires the most and phase 1 requires the least.
  - The difference between phases can be as high as tens of thousands of trial patients.
  - Amount to be shipped would be different

Today's Problem

- **Different strategies**
  - Outsource to a complete solution provider
    - One stop shop
    - One point of contact and handling
    - Accountability and traceability
    - Transport cost maybe lower especially during phase 1
    - Company should be GDP certified and have all the necessary expertise and knowledge to handle pharmaceutical products.
    - An example is to use World Courier. World Courier Clinical Trial Supply Chain Services (CTSCS) division operates GMP-compliant investigational drug storage facilities in 13 strategic locations in Asia Pacific, Latin America, Africa and Eastern Europe.
    - https://www.worldcourier.com/solutions-clinical-trial-logistics

Today's Problem

- **Different strategies (cont)**
  - Use own warehouse but outsource the transportation
    - Better control in terms of storage environment and condition
    - May not have the best equipment or latest technology
    - Transportation will be very expensive if Immno Scientific Biotech Centreis to ship only the small amount during phase 1 by themselves. No consolidation.
    - Cost may be better controlled because of own warehouse
    - For the same reason, if warehouse is not optimized, there will be wastages
    - For temperature sensitive drugs, will ship directly to clinic

Today's Problem

- **Different strategies** **(cont)**

Learning Outcomes

- Describe the different types and phases of clinical trials
- Identify the stakeholders in a clinical trial supply chain.
- Identify the supply chain requirement and challenges for clinical trial supply chain.
- Describe and apply the guidelines for clinical trials management.
- Suggest a suitable strategy for managing clinical supplies globally.