

**Group A**

# **SMALL SCALE COMPOUNDING FOR INDIVIDUAL PATIENTS**

Captopril Oral Liquid 1mg/ml (50ml)

---

# HOSPITAL A

---

- ✘ General hospital (adults & paediatrics) with 500 beds
- ✘ Compounding areas in Pharmacy Department
- ✘ Sterile Preparation
  - + Total parenteral nutrition, other aseptic preparations
- ✘ Non-sterile preparation
  - + Topical preparations, oral liquids, oral dosage forms, suppositories

# INDIVIDUAL PATIENT REQUEST

---

- ✘ 6 month old child with heart failure
- ✘ Requires titrating dose of ACEi
- ✘ Captopril is the ACEi of choice
  - + Short half life
  - + Clinical experience
  - + Pharmacokinetic experts
- ✘ Doctor requests advice from pharmacist

# TECHNICAL INFORMATION

---

- ✘ Captopril  $C_9H_{15}NO_3S$
- ✘ Molecular weight 217 (BP, 2007)
- ✘ Solubility 160mg/ml at 25°C (BP, 2007)
- ✘ pKa 3.7 (carboxyl group); 9.8 (sulfhydryl group)  
[Kadin, 1982]
- ✘ Optimum pH stability <3.5 (Kadin, 1982)



# OPTIONS

---

- ✘ Ward-based manipulation
  - + Dissolve a tablet and take an aliquot
- ✘ Compound in pharmacy
  - + Capsules
  - + Liquid
  - + Powders and papers
- ✘ Import from Australia (adult strength)

# WHAT SHOULD WE DECIDE TO DO?

	Advantages	Disadvantages
Ward-based manipulation	Quick	Inaccurate doses & safety, nursing time
Prepare capsules	Stability, generally accurate doses	Not easy to adjust doses, exposure to powder
Prepare liquid	Titration of doses, easy to swallow	Stability concerns
Prepare powder/paper	Quick	Exposure to powder, inaccurate, unstable
Import from Australia	Assurance of quality	Adult strength, excipients, cost, indication

# PRODUCT DESIGN

---

- ✘ API – Captopril powder
- ✘ Concentration 1mg in 1ml
- ✘ 1:1 Ora-Sweet:Ora-Plus
- ✘ (Or Unpreserved Syrup in newborn child)
- ✘ 50ml volume
- ✘ Amber glass bottle (Type III) with clear label
- ✘ Label –strength per ml
- ✘ Child-resistant closure (polyethylene)
- ✘ Oral syringe
- ✘ Shelf-life 7 days  
(Literature: 7-28 days)
- ✘ Life-cycle: In use but under development – possible addition of ascorbic acid to improve stability (antioxidant)
- ✘ Release criteria:
  - + Visual inspection & organoleptic control
  - + Label
  - + Volume

# SITE MASTER FILE

---

- ✘ Mission & Strategy
- ✘ Personnel
- ✘ Training & Competency
- ✘ Premises
- ✘ Equipment
- ✘ Quality Assurance & Quality Management System



# MISSION & STRATEGY

---

- ✘ “Right medicine, right patient, right time”
- ✘ We aim to provide medicines not available from industrial companies
- ✘ Provision of information for patients and healthcare professionals
- ✘ Continuing professional education of all members of staff with regard to compounding service

# PERSONNEL

---

## Production Unit

- ✘ 1 Senior Pharmacist
- ✘ 4 Pharmacists
- ✘ 5 Technicians
- ✘ 3 Operational Assistants
- ✘ 2 Student Pharmacists

## Non-Sterile

- ✘ 1 Pharmacist – Head of Non-Sterile Production
- ✘ 1 Pharmacist – Quality Assurance
- ✘ 2 Technicians
- ✘ 1 Operational Assistant
- ✘ 1 Student Pharmacist
- ✘ Support from quality control department

# TRAINING & COMPETENCY

---

## ✘ Pharmacists

- + Compounding legislation
- + Good Preparation Practice
- + Continuous professional education
- + Health & safety
- + Formulation & stability
- + Risk management
- + Product development
- + Quality management systems e.g. Standard Operating Procedures (SOP)

## ✘ Technicians & Assistants

- + Health & safety
- + Good Preparation Practice
- + Calculations
- + Continuous professional education



# PREMISES

---

- ✘ Compliance with national guidelines for room specifications
- ✘ Dedicated room for small scale preparation
- ✘ Uni-directional workflow
- ✘ Separate weighing area with minimum draughts and vibration
- ✘ Easy to clean
- ✘ Monitoring of temp, humidity and lighting – comfortable and limit degradation (less than 25 degrees)
- ✘ Compounding Unit:
  - + Storage Room (raw material and packaging materials)
  - + Preparation Room
  - + Administrative Room
  - + Washing Room



# EQUIPMENT

---

- ✘ Calibrated balances & measuring cylinders
- ✘ Glassware inspected regularly and free from cracks and chips
- ✘ Separate glassware for internal and external products
- ✘ Fridges with controlled temperature monitoring
- ✘ Dedicated garments, gloves, mask and hair covers during preparation
- ✘ Anti-vibration table
- ✘ Secure storage with ventilation

# QUALITY MANAGEMENT SYSTEM

---

- ✘ Standard Operating Procedures - SOP
  - + Weighing and measuring
  - + Labelling
  - + Producing worksheets
- ✘ Change control
  - + E.g. change of starting materials
- ✘ Worksheets & records
- ✘ Non-conformity Policy
- ✘ Complaints & Errors Policy
- ✘ Validation & calibration of critical processes & equipment
- ✘ Computerised systems for labelling

# QUALITY CONTROL OF PROCESS

---

- ✘ No testing of captopril or packaging (purchase from certified supplier – Certificates of Analysis/Conformity)
- ✘ No chemical analysis – but visual inspection
- ✘ Verification of balances
- ✘ Completed worksheet check (date, batch numbers, signatures for key steps)
- ✘ Release check

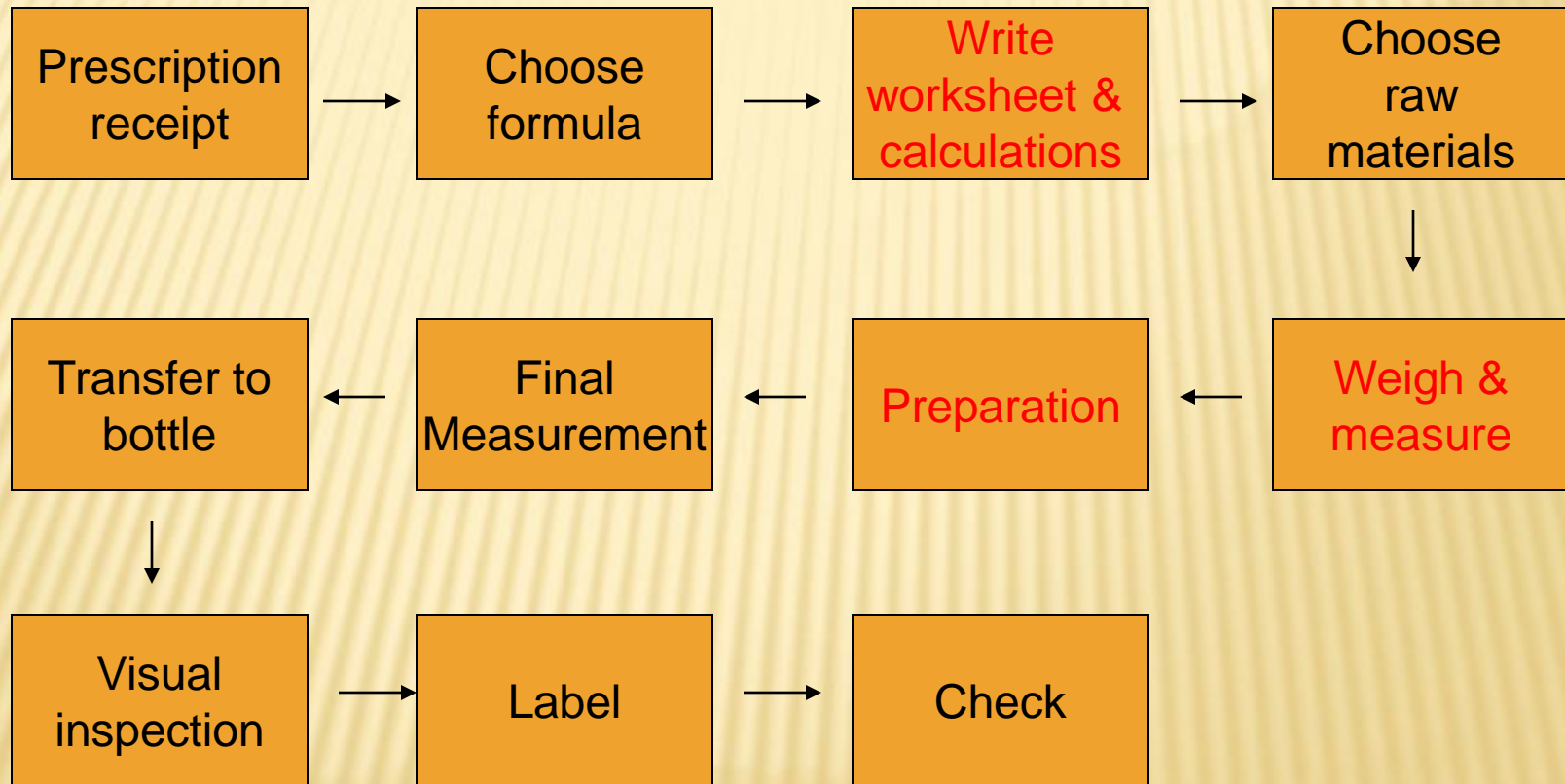


# BUSINESS PLAN – ORAL LIQUIDS

- ✘ Market – stroke patients, elderly, children, patients with swallowing problems and/or feeding tubes
- ✘ Competitors – imports, ward-based manipulations, batch manufacture
- ✘ Trends – increasing demand, shortages of licensed medicines
- ✘ Consequences of not delivering – treatment failure, morbidity, cost (to buy)
- ✘ Other options – buy from another source e.g. other hospital or pharmacy, specialist supplier



# PROCESS MAP



# RISK SCORING

---

Risk = S x O x D

✘ E.g. Calculations

$$+ 5 \times 1 \times 5 = 25$$

✘ E.g. Weigh/measure

$$+ 5 \times 3 \times 1.5 = 22.5$$

✘ E.g. Preparation

$$+ 1 \times 1 \times 5 = 5$$

Acceptable risk score – depends on the patient (consider risk of NOT preparing)

# RISK REDUCTION MEASURES

---

- ✘ Testing of raw materials
- ✘ Master worksheets
- ✘ One strength only
- ✘ Training packages
- ✘ Simple formulae
- ✘ Short shelf-life

# VALIDATION MASTER PLAN

---

- ✘ Staff
  - + Documented training plans (qualification)
  - + Continuing education
  - + Examination every year (revalidation)
- ✘ Process
  - + Dose concentration, particle size for oral liquids (outsource to laboratory)
  - + Cross-contamination check (outsource)
  - + Microbiological control
- ✘ Cleaning
  - + Cross-contamination check (outsource)
  - + Cleaning records
- ✘ Equipment
  - + Verification of balance
  - + Ventilation system (outsource)
  - + Temperature & humidity monitoring system



# POLICY ON PRODUCT DEVELOPMENT

- ✘ Scope - development of products for individual patients, including children (with possible expansion of use in time)
- ✘ Pharmacotherapeutic rationale (e.g. are other ACEi's available?)
- ✘ Facilities for making small scale products only (Magistral and officinal preparations)

# PROCUREMENT

---

- ✘ Raw materials – powder if available (tablets if powder not available), suspending agent
- ✘ Packaging materials – amber glass bottle with child-resistant plastic screw top, labels
- ✘ Equipment – pestle & mortar, balance, laboratory materials, magnetic mixer

# LOGISTICS

---

- ✘ Request from the ward
  - + Dispensing according to a prescription for an individual patient
- ✘ Preparation on Pharmacy
- ✘ Fridge storage (2 to 8 degrees)
- ✘ Lead time – 2-3 hours
- ✘ Delivered for patient
- ✘ Short shelf-life

# ISSUES FOR PRICING

---

- ✘ Cost of captopril & ora-sweet/ora-plus (or syrup)
- ✘ Packaging – bottles, tops, labels, outer bag, oral syringes
- ✘ Consumables used in preparation
- ✘ Lighting, heating, air handling unit
- ✘ Personnel costs (including training)
- ✘ Frequency and number of preparation



# SUMMARY

---

- ✘ The preparation of extemporaneous products are the highest risk area of pharmacy practice. But there is a clinical need.
- ✘ So our mission should be with minimal risk to do:

“Right medicine, right patient, right time”