

# Small Scale Compounding Facility

NONSTERILE LIQUID PRODUCTS

Group D



# Introduction

- ◉ Small scale compounding of nonsterile oral solution
- ◉ Formulation
- ◉ Design of suitable pharmacy
- ◉ Business plan

# Mission & Strategy

Name : Hilton Hospital Pharmacy



- Mission

to provide good pharmaceutical care for pediatric patients

- Strategy

Preparation and delivery of individual nonsterile liquid products



# Assessment of necessity for compounding

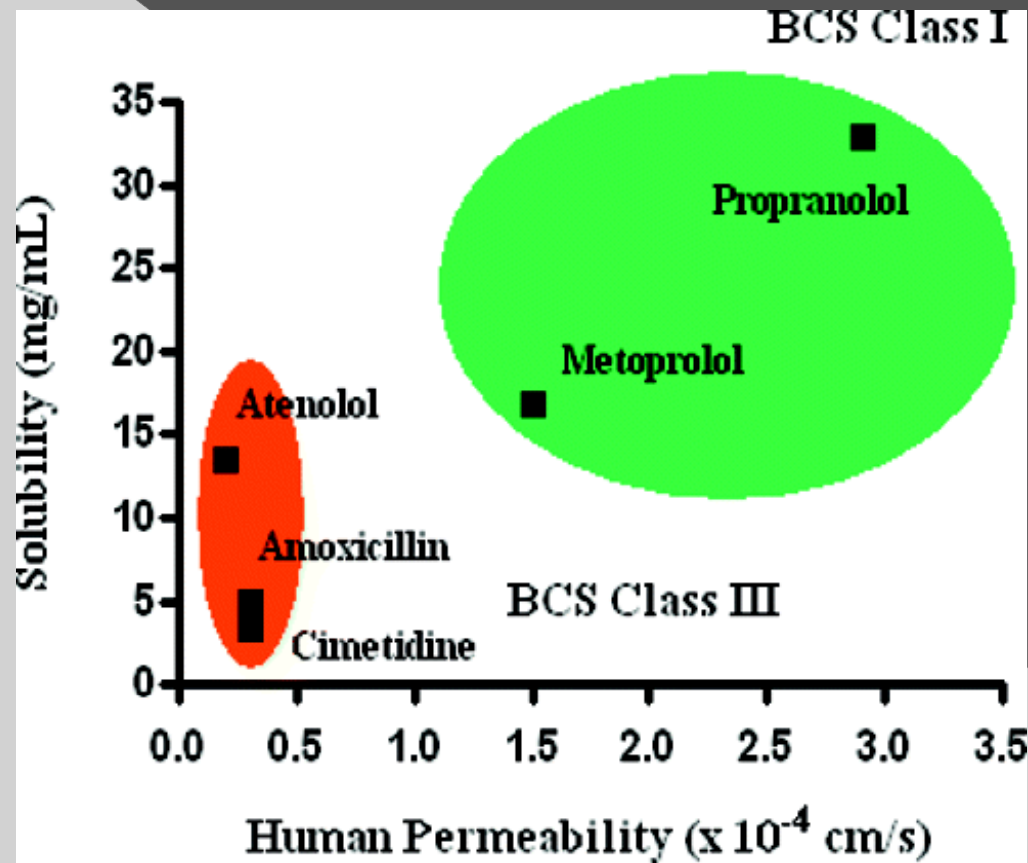
- PREPARATION: Propranolol oral solution

To be used:

- Pediatric population (individual dosage)
- In patients with difficulties to swallow

Those patients cannot be safely treated with available propranolol formulations

# BCS class of propranolol



# Biopharmaceuticals

## Absorption

Bioavailability

In children, no differences in the bioavailability of solution versus a tablets

(Wilson et al, 1976).

Conventional tablets are rapidly and completely absorbed with approximately 16% to 60% of the drug reaching systemic circulation.

## Distribution

Protein Binding-approximately 93% (Schneider et al, 1981).

Vd-approximately 6 L/kg (Borgstrom et al, 1981).

Metabolism- LIVER, Extensive; 50% -70% of an oral dose during its first pass (Cleveland & Shand, 1972)

Excretion – Kidney; Renal Excretion (%) Less than 1% of a dose is excreted as unchanged drug in the urine (Nace & Wood, 1987).

Elimination Half-life 3 to 4 hours (Lowenthal et al, 1974; George et al, 1972; Shand & Rangno, 1972; Riopel & Walle, 1980).



# Production Size

## General

- Number of different liquid products:  
30 from 1 mL up to 1000 mL

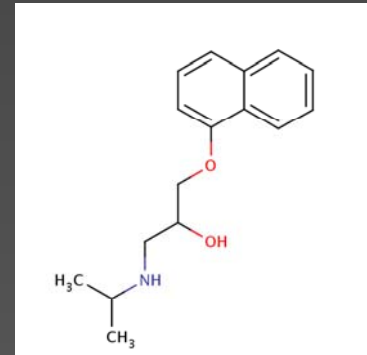
Number of batches per year:  
500

## Propranolol oral solution

- Batch size: 20 bottles à 50 mL
- Number of batches per year: 4

# Product Design

LIFE CYCLE: Compounding of an existing API



## MATERIAL

API: propranolol

## EXCIPIENTS

- taste corrector (cherry taste, saccharine)
- Preservative (MOB/POB)
- solvent (WFI)

## PACKAGING MATERIALS

plastic bottles



# Preparation Process



## Preparation

- Step: line clearance
- Step: weight propranolol and saccharine
- Step: dissolve in 2/3 of the total quantity of the WFI
- Step: add MOB/POB solution
- Step: filling to the final volume with WFI and mix
- Step: filling into bottles and closure of the bottles
- Step: labeling of the bottles

## IPC:

- step: /
- Step: /
- Step: visual
- Step: visual
- Step: check volume
- Step: extracting of samples (1<sup>st</sup> and last bottle)
- Step: visual

# Preparation Process

## Risk Assessment

### RISKS

- Weighing (5x1x1)
- Dissolving (3x1x1)
- Mixing (5x3x1)
- Interaction between plastic and product (5x3x1)

### PREVENTIVE MEASURES

- analytical control (API, preserving agent) & control from the 2<sup>nd</sup> person
- Training of the technician

# Pharmacy Design

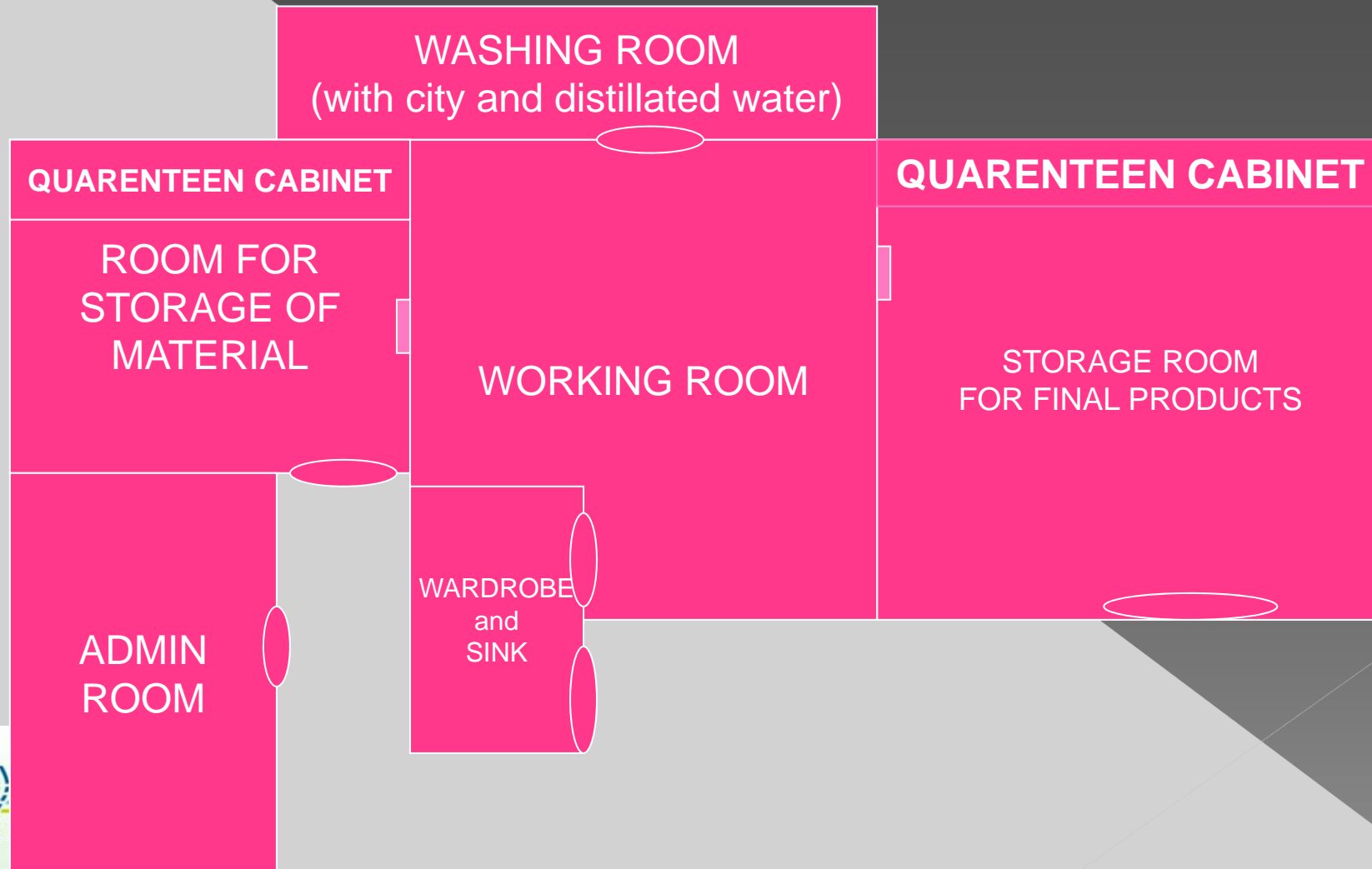
- ◉ QA (Quality Assurance)
- ◉ Premises & Equipment
- ◉ Personnel
- ◉ Materials
- ◉ QC (Quality Control)

# Quality Assurance – QA

## Quality management system:

- SOP`s on responsibilities, organizational procedures, cleaning procedures, complaints, recalls, audit
- VMP
- Quality Risk Management
- Training plan

# Premises & Equipment (1)



# Premises & Equipment (2)

## PREMISES

- No air classification
- Washable walls, doors, ceiling and floor

## EQUIPMENT

- Balances (in weighting cabinets)
- Glassware
- pH measurement
- Mixing
- Heating device
- Refrigerator (one for raw materials, second for final product)
- Labeling equipment with computer

# Premises & Equipment

## Risk Assessment

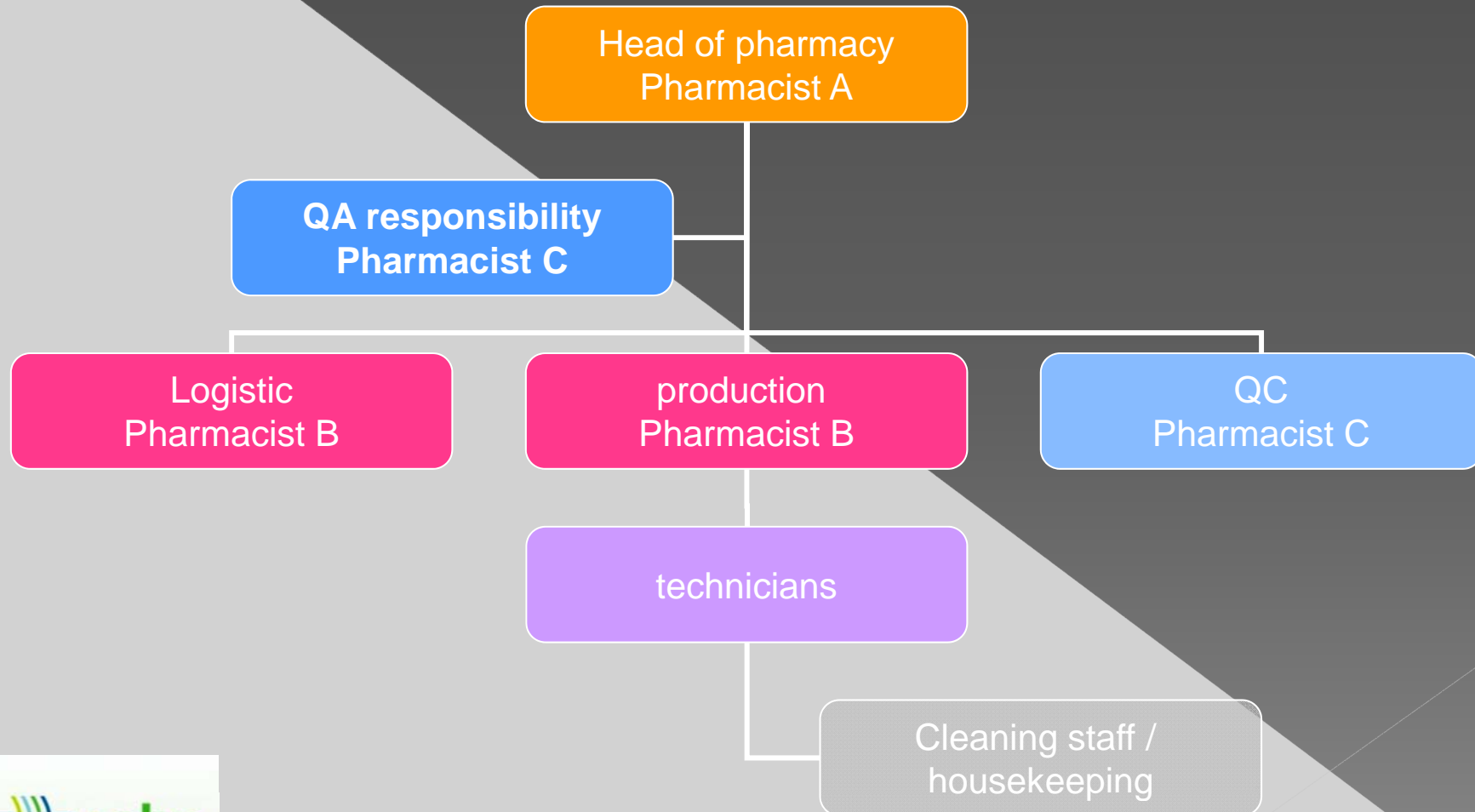
### RISK

- balances is not calibrated (5x1x1)
- pH meter is not calibrated (5x1x1)
- glassware are not clean (5x3x1)
- refrigerator is not cooling properly (5x1x1)

### PREVENTIVE MEASURES

- make the calibration every time you use the balance and pH meter
- educate the cleaning staff and improve SOP
- check the refrigerator performance with termo sonda every day

# Personnel





# Personnel Risk Assessment

## RISK

- not educated according to GMP/hygiene (5x3x3)

## PREVENTIVE MEASURES

- education regarding GMP

# Materials (1)

- ◉ API (EP quality with CoA)
- ◉ EXCIPIENTS (EP quality with CoA)

## RISKS

- ◉ wrong identity (5x1x1)
- ◉ purity (5x1x1)

## PREVENTIVE MEASURES

- ◉ identity check
- ◉ certificate or purity check



# Materials (2)

## PACKAGING MATERIALS / LABELLING RISKS

- ◉ interaction with product (5x3x3)
- ◉ quality system of wholesaler (5x3x3)
- ◉ wrong text on label (5x3x3)
- ◉ quality of ink (wiped off) and glue (peal off) (3x1x1)

## PREVENTIVE MEASURES

- ◉ identity check and certificate
- ◉ check of final product



# Quality Control

## Outsourcing

### RISKS

- the transportation condition of the samples (3x1x3)
- analysis (false positive/false negative) (5x1x1)

### PREVENTIVE MEASURES

- Audit before outsourcing, repeat every 3 yrs
  - > Report incl. description of quality system, which analysis etc
- Validation report for each new analysis
- Certificate of Analysis of control of final product

# Summary of the risk assessment (1)

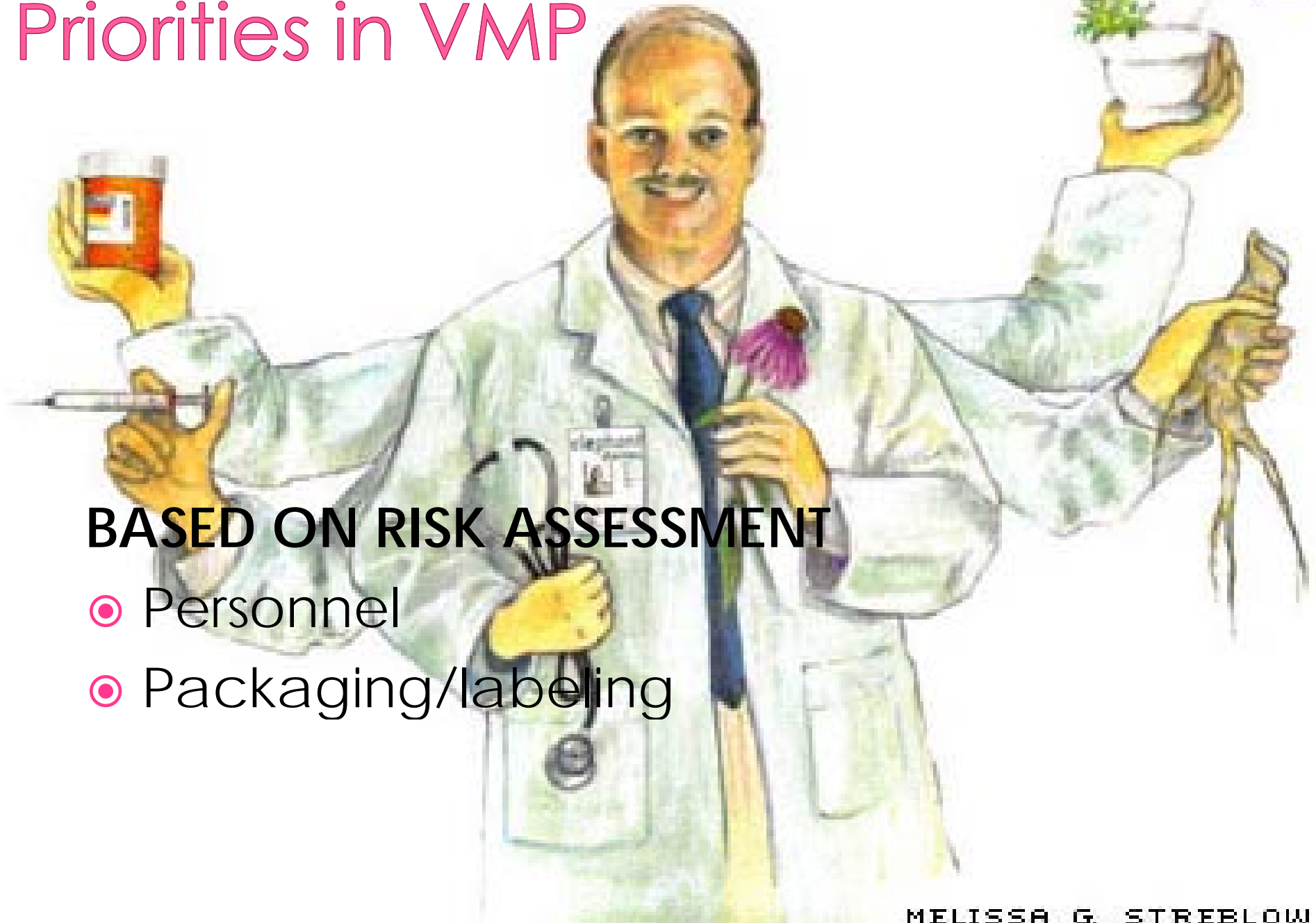
Topic	Description	Score
preparation	Weighing	5
	Dissolving	3
	Mixing	15
	Interaction	15
Premises/equipment	Balances	5
	pH meter	5
	Glassware	15
<b><u>Personnel</u></b>	<b><u>Knowledge GMP/hygiene</u></b>	<b><u>45</u></b>
QC	Transportation condition of samples	9
	analysis	5

# Summary of risk assessment (2)

Topic	Description	Score
Materials: API/excipients	Wrong identity	5
	purity	5
<u>Materials: packaging/labelling</u>	<u>Interaction with product</u>	<u>45</u>
	<u>Quality of wholesaler</u>	<u>45</u>
	<u>Wrong text</u>	<u>45</u>
	Quality of ink	3



# Priorities in VMP



## **BASED ON RISK ASSESSMENT**

- Personnel
- Packaging/labeling

# Business Plan (1)

## Business analyses

- The market: Preparation for hospital patients, sell to other hospital Pharmacies and Community Pharmacies on demand
- Customers needs: paediatrics and non swallowing patients
- Trends in area: only available tablets and iv solution
- Competitors: other hospital pharmacies





# Business Plan (2)

- **Facilities & Equipment** – non sterile room and simple laboratory material
- **Competences & Resources**– compounding expertise for liquid nonsterile products, available Quality management system (QMS); outsourcing the QC activity
- **Logistics** – Storage condition (available); Traceability (available); Environment Issues (n/a); Lead Times (12h-1 week in week days);
- **Procurement** – wholesalers (audit according to QMS)
- **Pricing** – Costs in the material, work and a margin
- **Financing** – investment from the hospital budget to improve the facilities, buy new **equipment**, staff education.  
Return investment by selling the product to other pharmacies

## Conclusion:

**Increasing the patients safety by preparing in controlled environment under controlled conditions with reasonable price.**