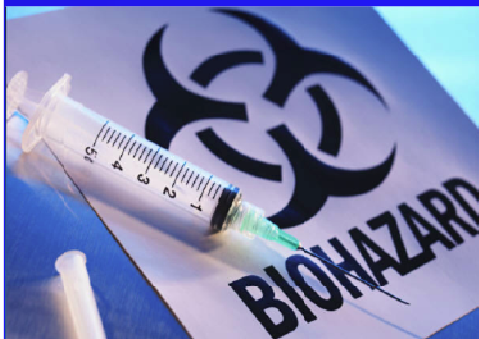




# ***CYTOTOXIC DRUGS***

## ***CYTOLAND***



**BEAM SUMMIT  
HAGUE 23-26 SEPTEMBER 2010**



# *Team members*

- Iben Larsson Denmark
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- Péter Csonka Hungary
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# ***Cytotoxic Drugs***

- Cytotoxic drugs are therapeutic agents intended for, but not limited to, the treatment of cancer.
- Cytotoxic drugs are toxic compounds and are known to have carcinogenic, mutagenic and/or teratogenic potential.
- Cytotoxic drugs are increasingly being used in a variety of healthcare settings. The toxicity of cytotoxic drugs dictates that the exposure of health-care personnel to these drugs should be minimized. At the same time, the requirement for maintenance of aseptic conditions must be satisfied.



# ***Mission***

- Provide safe, high quality cytotoxic drugs for individual treatment of patients
- Lower cost of chemotherapy
- Safe production and delivery of cytotoxic formulations



# *Safe cytotoxic drugs*

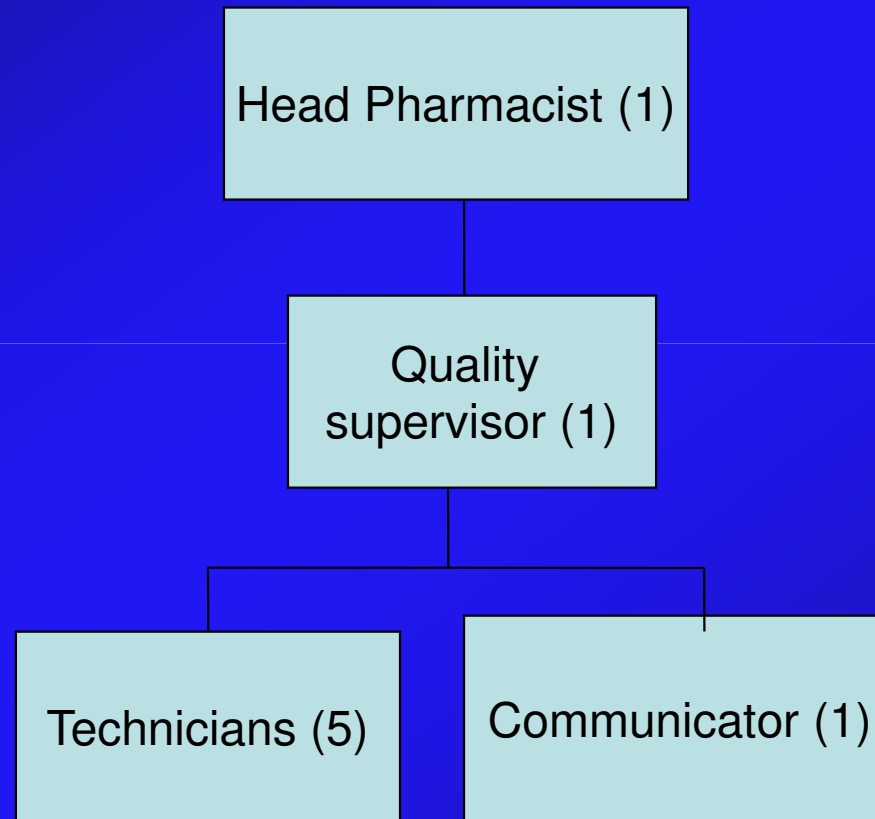
- Safe for patient
- Safe for staff
- Safe for environment
- Safe during transportation



# *Strategy*

- Prepare cytotoxic drugs for individual hospital patients.
- Delivery of right drugs for right patient in right time.

# Organization



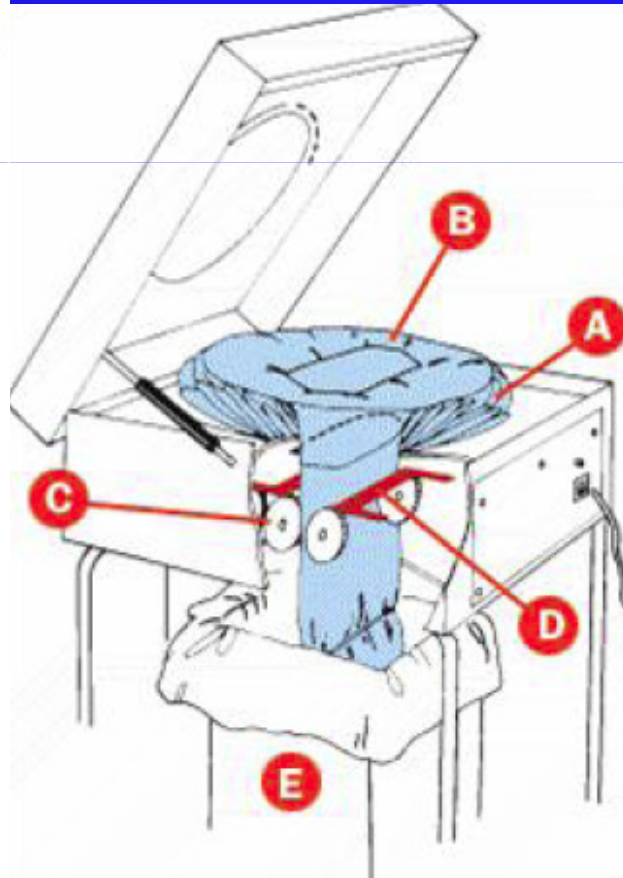
# Facility





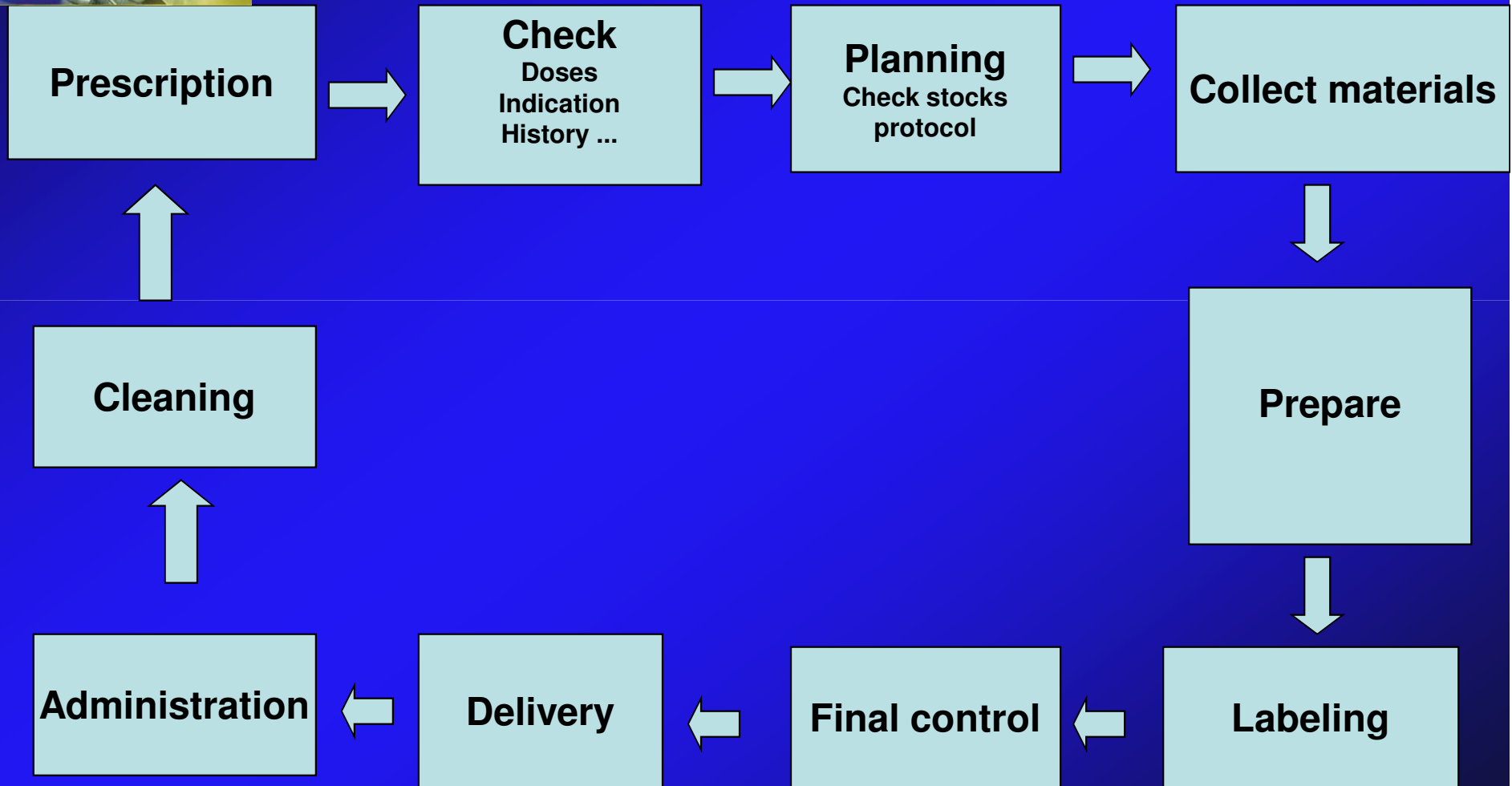


# Waste disposal





# *Product preparation*



# *Business plan*

- Facility 100m<sup>2</sup>
- 8 employees
- Output: 250 preparations a day
  - 50 IV bags
  - 200 syringes



# ***Business plan: expenses***

- Personnel costs per year: 84.000 euro/year
- Facility and equipment: 30.000 euro /year
- Drugs and medical devices : 1.562 million euro
  - 25euro/preparation
  - 250days/year
  - 250 preparations/day



## ***Business plan: profit***

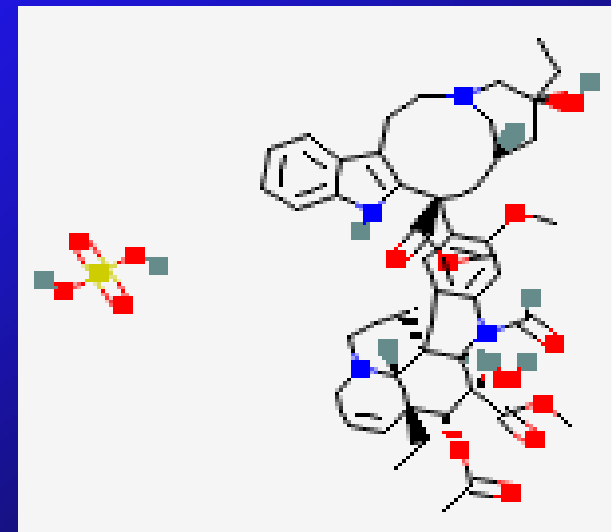
- Insurance reimbursement: 1.470.000
- Benefit from centralization: 120.000

# Vincristine

## Chemical properties

- Commercial vial is water based solution
  - Vincristine sulphate 1 mg/ml Injection
  - Solution for injection is a sterile, colorless solution
- Vincristine sulphate
  - $C_{46}H_{56}N_4O_{10}$
  - Average Molecular Weight 824.9576
  - Water solubility 3.00e-02 mg/mL

*Mannitol, benzyl alcohol (9 mg per ml), Water for Injections*





# ***Pharmacokinetic properties***

- Poorly absorbed orally.
- The clearance of the drug after rapid intravenous injection follows a triphasic decay pattern: a very rapid steep descent (alpha phase); a narrow-middle region (beta-phase) and a much longer terminal region (gamma phase).
- The terminal phase half-life of the drug varies from 15-155 hours.
- Dosing with the drug more frequently than once weekly is therefore probably unnecessary.
- Vincristine is primarily excreted by the biliary route.
- Patients with impaired hepatic or biliary function, as evidenced by a raised serum alkaline phosphatase, have been shown to have a significantly prolonged vincristine elimination half-life.



# *Way of administration*

*FOR INTRAVENOUS USE ONLY  
FATAL IF GIVEN BY ANY OTHER ROUTE*

## *Dosage*

**Adults:** I.V. at weekly intervals, 1.4 to 1.5 mg/m<sup>2</sup>  
Maximum weekly dose of 2 mg.

**Children:** 1.4 to 2 mg/m<sup>2</sup>

Maximum weekly dose of 2 mg.

For children weighing 10 kg or less the starting dose should be 0.05 mg/kg administered as a weekly intravenous injection.





## ***Packaging material for vincristine***

- **Type Sample:** Syringe 20ml (B. Braun)
- **Material:** Polypropylene, Ph.Eur grade



# *Vincristine stability*

Only to be mixed with 0.9% sodium chloride injection or 5% dextrose injection; the drug should not be diluted in solutions that raise or lower the pH outside the range of 3.5–5.5.

Doses of 0.5, 1, 2, or 3 mg of vincristine sulfate diluted in 25 or 50 mL of 0.9% sodium chloride solution in small-volume IV bags (i.e., minibags) or in 20 mL of 0.9% sodium chloride solution in a 30-mL syringe remained stable when stored for 7 days at 4°C followed by 2 days at 23°C.

# ***Requisition Form***

The prescription is checked in the pharmacy in accordance with s. 7 *Apothekenbetriebsordnung* (pharmacy regulations) and the preparation is authorised by the pharmacist responsible.

The prescription must be unambiguous and must include at least the following information:

- name and gender of the patient
- patient's date of birth and/or admission number
- body weight, height and/or body surface area
- ward / department / therapeutic unit or section thereof
- cytostatic prescribed (INN)
- regular dose and the resulting dosage for the patient
- adapted dosage according to clinical chemical and pharmacokinetic parameters as target value
- correction factor for an indicated dose reduction or dose increase
- pharmaceutical form
- type of carrier solutions
- volume of the ready-to-administer solution
- required administration time
- signature of doctor, date.



# ***Labeling***

**Patient name**

**Ward**

**Name of the drug**

**Total amount and volume of the preparation,**

**Infusion time**

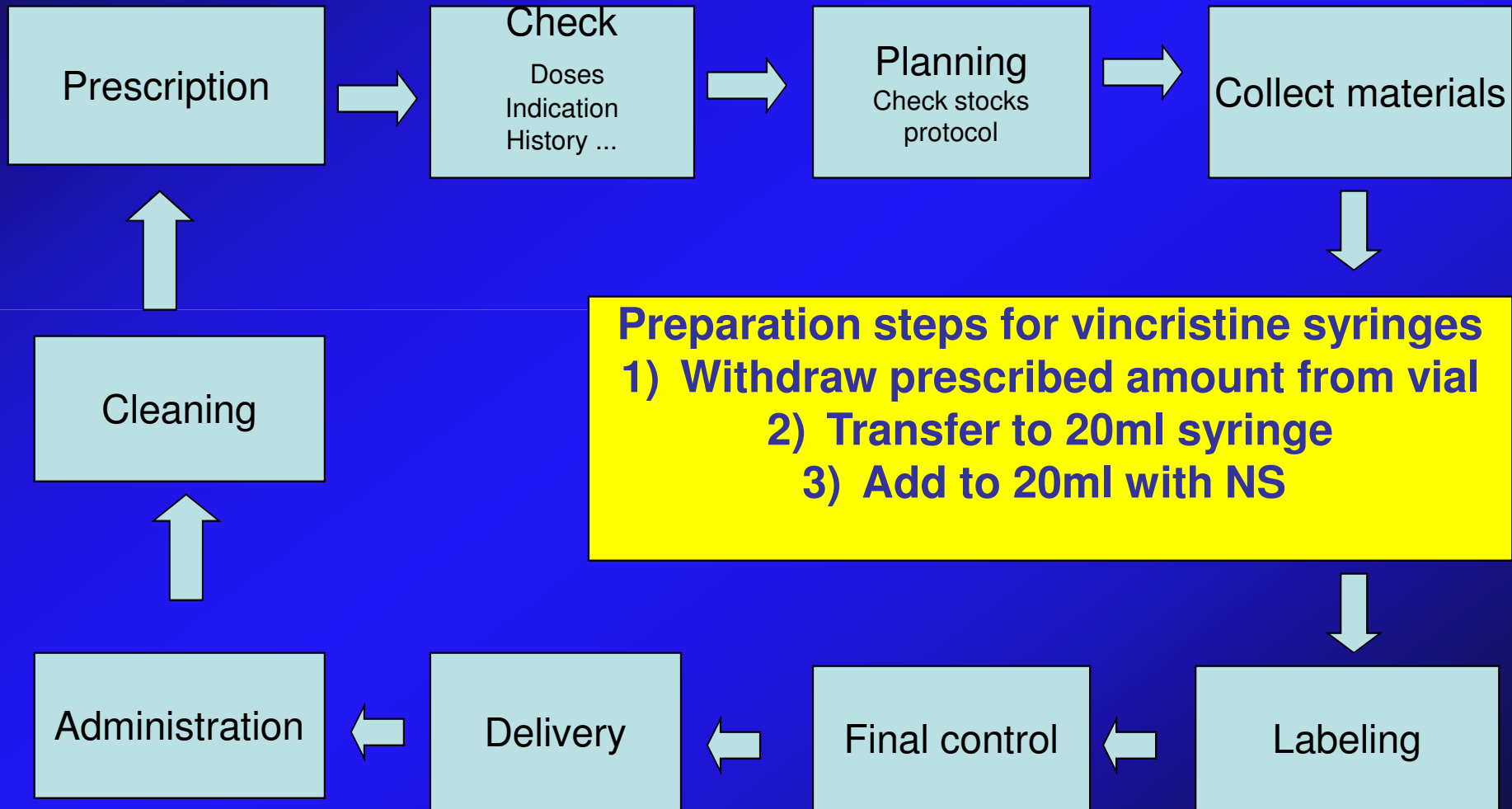
**Route of administration (colored label)**

**Time and date after which it should not be used**

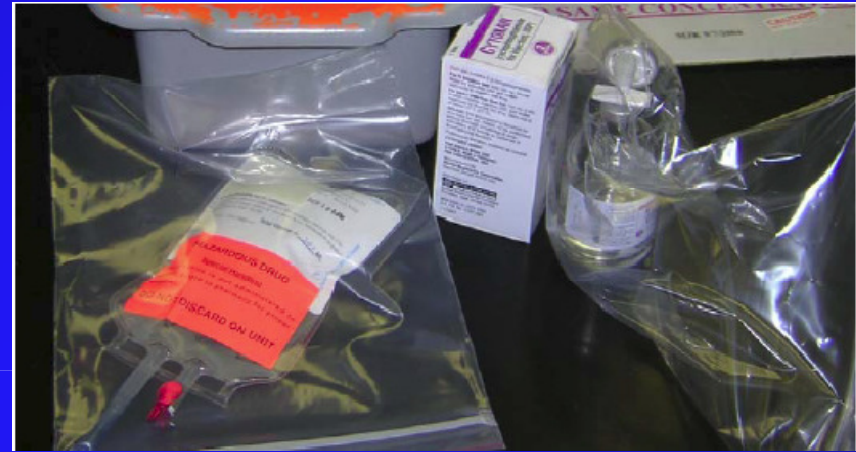
**Storage recommendations**



# *Vincristine preparation*



# Packaging-Transportation



# *Risk analysis*

- **Biggest risk** Personnel
- Consists of: labeling, mix-up, cross contamination, microbiological contamination, dosage error, spilling
- **Other risks:** ventilation

# Quality Risk Management

	score
Severity	3
Occurrence	1/1500
Detection	0,9

$$\text{Risk} = S \times O \times D$$

$$\text{RISK} = 0,0018$$



# *Quality Risk Management*

**Ways of detection:** ex. Monitor the rate of production of the preparations daily

**Solution:** Staff rotation  
Competency checking  
Auditing once a year

# Spill kit



# *Quality control*

- Registered product: no routinely quality control
- Syringes: CE marking

# *Monitoring*

- Twice a year microbiological testing
  - Swabs
  - Settle plates 3 times a week
- Air pressure
  - Every day
- Particles
  - External twice a year
- Cytotoxic contamination
  - External company (swabs and exhaust filters)

# ***Auditing and self inspection***

- **Internal audits : 3 times a year**
- **External audits: once a year**

# *Complain policy*

- Complains are being investigated, answered, and classified
- Special sheets for internal and external customer satisfaction
- ISO 9001:2008

# *Pharmacy versus Ward*

## Pharmacy preparation

- Controlled environment
- Knowledge, skills & experience
- Quality assurance / controls
- Systematic documentation
- Ongoing risk management
- Smaller risk of environment contamination
- Safety for the staff
- Smaller risk of product microbiological contamination
- Financial profit

## Ward Preparation

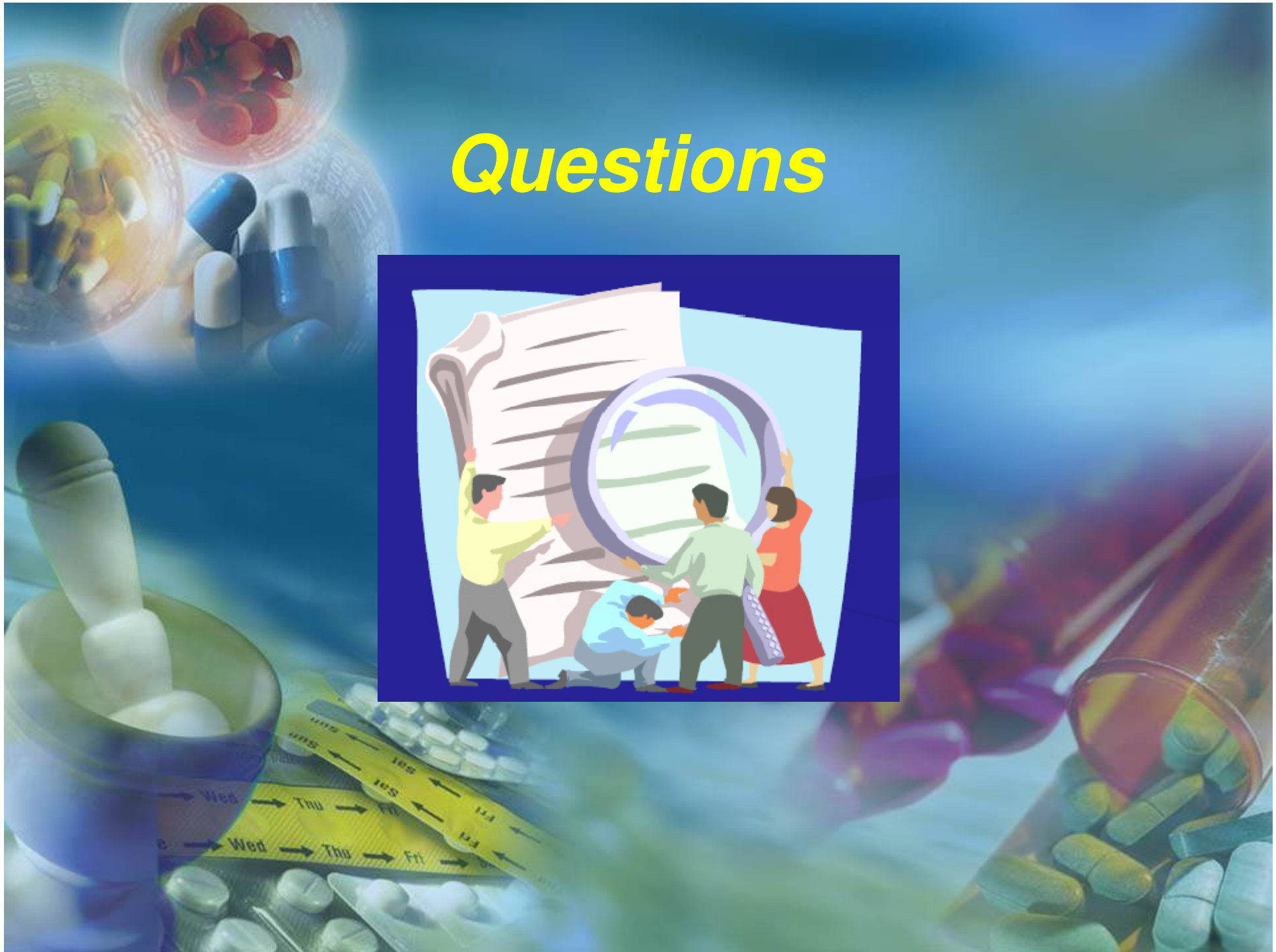
- Uncontrolled environment
- Variable skills, limited knowledge
- Little / no quality assurance
- Minimal documentation / checks
- Variable risk management
- Environmental contamination
- Staff in danger

# *Team members*





# Questions



# *Incompatibilities*

It is not recommended that vincristine sulphate should be mixed with any other drug and should not be diluted in solutions that raise or lower the pH outside the range 3.5 to 5.5. Furosemide both in syringe and injected sequentially into Y-site with no flush between, results in immediate precipitation.

# *Contamination*

- (a) In the event of contact with the skin or eyes, the affected area should be washed with copious amounts of water or normal saline. A bland cream may be used to treat the transient stinging of skin. Medical advice should be sought if the eyes are affected.
  
- (b) In the event of spillage, operators should put on gloves and mop the spilled material with a sponge kept in the area for that purpose. Rinse the area twice with water. Put all solutions and sponges into a plastic bag and then seal it.

# ***Personal protective equipment***



- overall or protective gown (possibly in combination with cuffs)
- protective gloves
- and in special cases
- respiratory protective equipment
- protective eyewear
- overshoes.



## **Special cases include:**

- cleaning tasks inside the safety workbench which extend beyond simply wiping the work surface
- clearing up spilled cytostatic material
- filter replacement in the safety workbench

