Inspection/audit at the Hospital Pharmacy

General aspects

- The audit of the Hospital Pharmacy is conducted during the audit at the Investigator site and is foreseen in the agenda.
- The audit is focused on the study that is audited in the investigator's site and on general management of IMPs
- The Head of the Pharmacy or 1 pharmacist delegated by her/him must take part in the audit
- The pharmacist must be on duty at the Hospital Pharmacy and must be aware of the Investigational Medicinal Product(s) management

General aspects

- The IMP is always delivered at Hospital Pharmacy in Italy.
- Then, it can be forwarded to the investigator's department, where it should be maintained at the same conditions of custody and environment (temperature, light and humidity) guaranteed by the pharmacy
- If this is the case, one person of the site staff must take the responsibility of IMP control.

General aspects

The audit is composed in three parts:

1. Meeting with the pharmacist(s) and possible other personnel involved in the IMP management
2. Review of the documentation related to the trial subject of the audit
3. Visit of the Pharmacy

1. Introductory Meeting

The purpose of this meeting is to:

- Introduce the auditor(s) to the auditee(s).
- Confirm that the resources, documents and facilities needed by the auditor(s) are available.
- Have information about the IMP management into the hospital pharmacy (receipt, storage, distribution and destruction)

Furthermore....

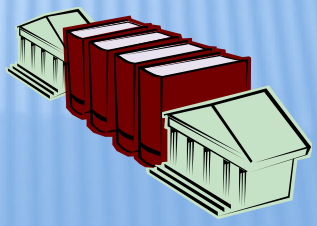
... the auditors have to:

- Confirm if the management of the IMP is in compliance with GCP, verifying registrations, electronic or on paper;
- Confirm if there are SOPs in place;
- Confirm that there is a sufficient number of pharmacists compared to the number of clinical trials conducted in the hospital.

2.Review of the documentation

The auditors verify all the documents related to the IMP used in the clinical trial.
Points to be considered are:

- Drugs shipment notes from the Sponsor with the corresponding receipts. The notes should contain batch numbers, expiry date and patients code numbers (if applicable);
- evidence of the correct conditions at arrival
- Drugs shipment notes from the pharmacy to the Investigator and, if necessary, drugs shipment notes from Investigator to the pharmacy about unused drugs.
- EC approval
- CT Protocol



2.Review of the documentation

- Accountability form

  → IMP amount delivered to the pharmacy, amount dispensed at the investigator's site and, if it is the case, IMP amount returned to the pharmacy (including batch numbers, expiry date and code numbers)

  → Documentation related to re-labelling (if applicable)

  → IMP amount returned to the Sponsor, if applicable, (including batch numbers, expiry date and code numbers)

- Documents of drug destruction (if applicable)

3. Visit to the Pharmacy

Points to be considered are:

- if the IMP is maintained in a cabinet accessible only to the hospital pharmacy personnel and if it is identified as IMP and is separated from other drugs;
- if the IMP is maintained at appropriate conditions, separated from other drugs, in appropriate fridge or freezer;
- if the fridge/freezer temperature is continously monitored and recorded
- if there is an alarm system in case of derangements
- whether there is a quarantine section for expired drugs to be returned or destroyed

Closing meeting

At the end of the audit, the auditor(s) should hold a closing meeting with the auditee(s).

The main purpose of this meeting is to present audit findings to the auditee(s) and to ensure that the results of the audit are clearly understood and that there are no misunderstanding by either the auditor(s) or the auditee(s).

-Feedback
-Issues
-Observations
-Recommendations for corrective actions

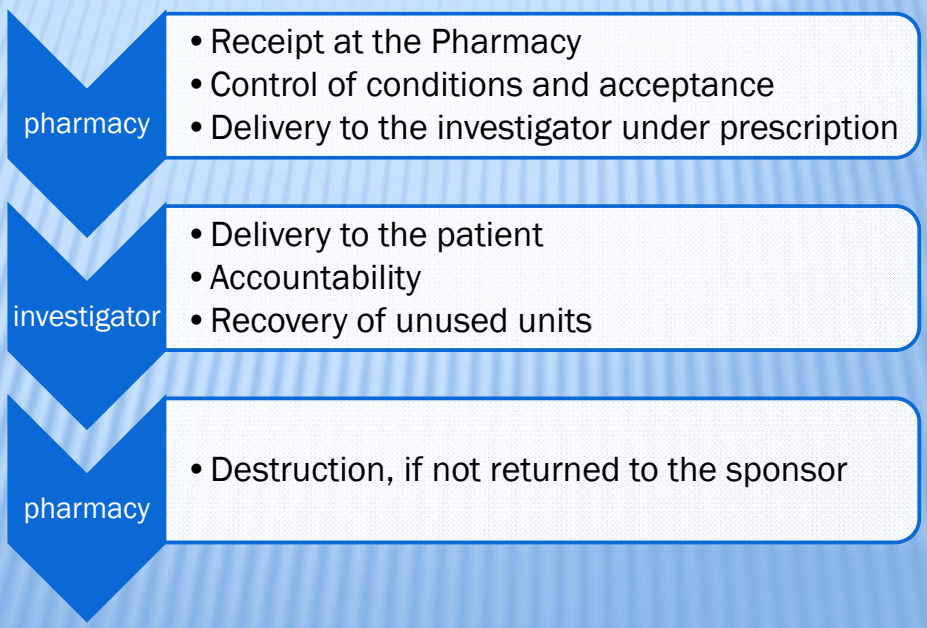
common audit findings of Investigational Medicinal Product

- Labelling not compliant with GMP Annex 13
- Inadequate records to track the IMPs during the transport
- Missing or unsigned documentation - accountability, dosing, shipping & no alternative mechanism to verify protocol compliance
- Queries in underlying pharmacy systems & procedures e.g. action in the event of out of specification temperature storage
- Failures in accountability - difficulty in determining who was dosed, when, and with what

common audit findings of Investigational Medicinal Product

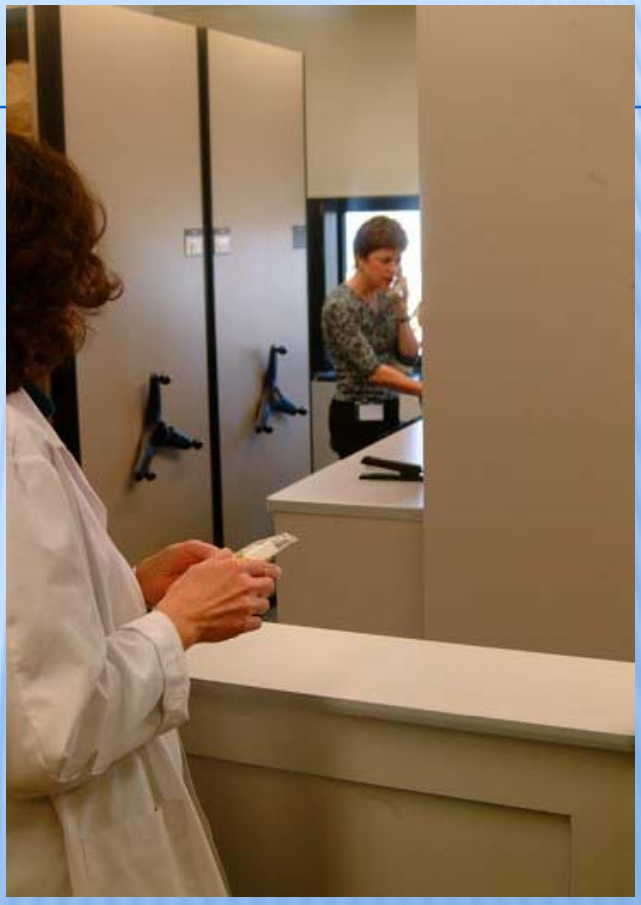
- No IMP shipment notes from the Sponsor
- IMP shipment notes without key elements
- No IMP internal shipment notes between investigator and pharmacy
- IMP delivery directly to the investigator
- IMP stored mixed with other drugs
- IMP storage without T° monitoring (when required)
- IMP storage at the wrong T°
- Local drug destruction without documentation/SOP

IN SUMMARY, THE JOURNEY OF THE IMP AT THE HOSPITAL SITE IS ....

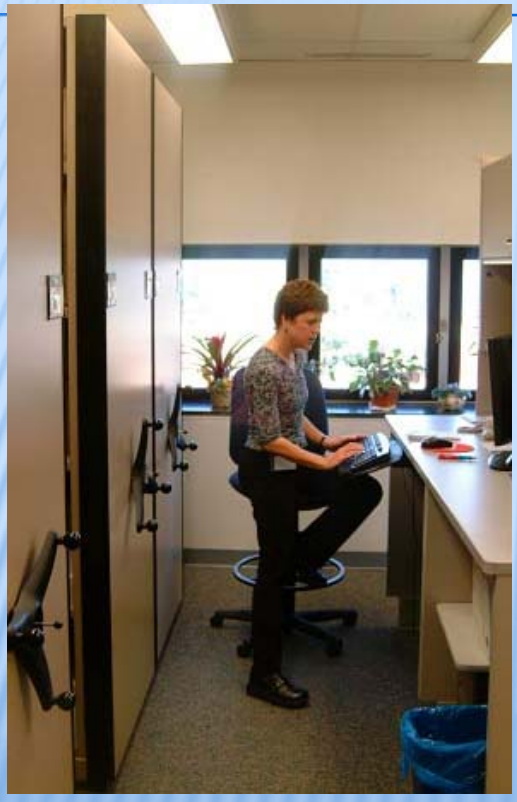


THE FRONT OFFICE OF THE PHARMACY 1ST STEP OF CONTROL

HALF DOOR KEEPS UNAUTHORIZED PERSONNEL AWAY FROM MEDICATIONS



WORKSTATIONS



QA AUDITING TOOL

- Standards/Elements Reviewed
  - ✓ Policies/procedures for handling drugs
    - × Receipt
    - × Storage
    - × Security
    - × Dispensing
    - × Disposition of Unused Stock
  - ✓ Drug maintained under custody of Investigational Pharmacy

QA AUDITING TOOL (CONT)

- ✓ Investigational drug is kept locked with limited access
- ✓ Storage conditions are documented per protocol
- ✓ Temperature logs maintained
  - ❖ Room temp
  - ❖ Refrigerator temp
  - ❖ Freezer temp

ROOM TEMPERATURE LOG

INVESTIGATIONAL PHARMACY							
DAY	JUL	AUG	SEP	OCT	NOV	DEC	CORRECTIVE ACTION
1							
2							
3							
4							
5							
6							
22							
23							
24							
25							
26							
27							
28							
29							
30							
31							

ROOM TEMPERATURE LOG
RANGE: 15-25 DEGREES CELCIUS (59-77 DEGREES F)

REFRIGERATOR WITH AUTOMATIC TEMPERATURE LOG

QA AUDITING TOOL (CONT)

- ✓ Investigational drugs separated from other drug stocks
- ✓ drugs require signed prescription
- ✓ monitoring visits also to the pharmacy, if appropriate

QA AUDITING TOOL (CONT)

- ✓ Pharmacy File contains:
  - ❖ Approved protocol & amendments
  - ❖ Investigator Brochure
  - ❖ Drug dispensing logs
  - ❖ Drug Study Summaries

DISPENSING LOG

Protocol # / IRB ID / Approval Date:_____

Drug:_____

Sponsor / Manufacturer:_____

PI / Coordinator(s):_____

Date	RX #	Patient Name/ Last Four	Pt Initials/ ID#	Med ID	Lot#/Exp	Amt Disp/Rec	Balance	Prescriber	Disp RPh	Date Rtn to Pharm	Qty Rtn	Rtn RPh