CONTROL ACTIVITIES IN THE PHARMACY PRACTICE

WHO CONTROLS WHAT?

Control activities in the pharmacy

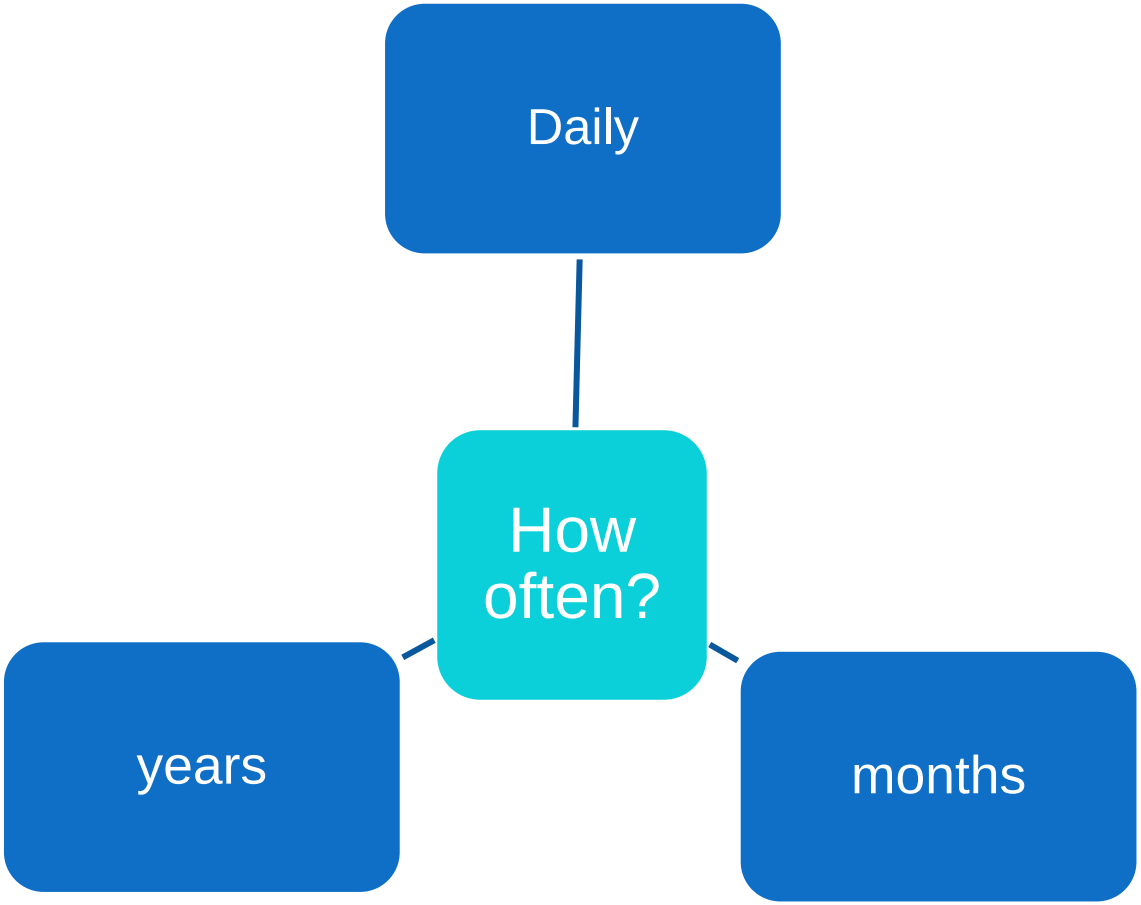
Inspections

1. CONTROL ACTIVITIES IN THE PHARMACY

Pharmacy, equipment

Medicinal products, treatment

CONTROL ACTIVITIES IN THE PHARMACY



A. PHARMACY AND EQUIPMENT

Condition of storage - temperature, humidity,…

Equipment – certificate - validation

Viz Introduction to the pharmacy (1th year)

B. MEDICINE, TREATMENT

Delivered pharmaceuticals

Substances before preparing

Clinical trials

Pharmacovigilance, additional monitoring

Treatment - Medication errors

Product problems

WHO AND PATIENT SAFETY

patients are harmed caused by a range of errors or adverse events

may result in serious injury or death.

the economic benefits of improving patient safety

DEFINITION - ADR

Adverse Drug Reaction (abbreviated as ADR) – shall mean an adverse and unintended response to the product administration which occurs at doses normally used for the prophylaxis, therapy or diagnosis of a disease or for the restoration, correction or other modification of physiological functions; where clinical trials on medicinal products are concerned, it shall mean an adverse and unintended reaction to any administered dose.

Adverse reaction to veterinary medicinal product …..

This definition shall not apply to transfusion products.

ADR CLASSIFICATION

Shall be classified as:

a) **serious adverse reactions** which result in death, are life-threatening, require hospitalisation or prolongation of existing hospitalisation, result in persistent or significant disability or incapacity or are demonstrated as a congenital anomaly or birth defect in offsprings;

b) **unexpected adverse reactions -** the nature, severity or consequences of which are not consistent with the information laid down in the summary of the product characteristics for an authorised medicinal product or which are not consistent with available information,

c) human adverse reactions related to the use of a veterinary medicinal product, which are noxious and unintended and which occur in a human being following exposure to a veterinary medicinal product.

DEFINITION - AE

Adverse event (abbreviated as AE) –shall mean an adverse change to the health affecting a patient or trial subject who is the recipient of a medicinal product, even if it is not known whether a causal relationship with the treatment by this product exists.

(with the exception of transfusion products)

AE

Serious Adverse Event (abbreviated as SAE) - shall mean such adverse event that results in death, is life-threatening, requires hospitalisation or prolongation of existing hospitalisation, results in persistent or significant disability or incapacity or is demonstrated as a congenital anomaly or birth defect in offsprings, irrespective of the administered dose of the medicinal product

DEFINITION

Risk associated with the use of a medicinal product:

- a risk to the health of a human being, to public health or to the health of an animal associated with the quality, safety, and efficacy of the medicinal product, or
- a risk of adverse environmental impact.

Risk-benefit ratio shall mean the evaluation of positive therapeutic effects of the medicinal product related to the defined risks.

The risk-benefit ratio is favourable, if the benefit of use of the medicinal product outweighs the risk associated with its use.

Type of reaction	Mnemonic	Features	Examples	Management
A: Dose-related	Augmented	• Common • Related to a pharmacological action of the drug • Predictable • Low mortality	• Toxic effects: Digoxin toxicity; serotonin syndrome with SSRIs • Side effects: Anticholinergic effects of tricyclic antidepressants	• Reduce dose or withhold • Consider effects of concomitant therapy
B: Non-dose-related	Bizarre	• Uncommon • Not related to a pharmacological action of the drug • Unpredictable • High mortality	• Immunological reactions: Penicillin hypersensitivity • Idiosyncratic reactions: Acute porphyria Malignant hyperthermia Pseudoallergy (eg, ampicillin rash)	• Withhold and avoid in future
C: Dose-related and time-related	Chronic	• Uncommon • Related to the cumulative dose	• Hypothalamic-pituitary-adrenal axis suppression by corticosteroids	• Reduce dose or withhold; withdrawal may have to be prolonged
D: Time-related	Delayed	• Uncommon • Usually dose-related • Occurs or becomes apparent some time after the use of the drug	• Teratogenesis (eg, vaginal adenocarcinoma with diethylstilbestrol) • Carcinogenesis • Tardive dyskinesia	• Often intractable
E: Withdrawal	End of use	• Uncommon • Occurs soon after withdrawal of the drug	• Opiate withdrawal syndrome • Myocardial ischaemia (β-blocker withdrawal)	• Reintroduce and withdraw slowly
F: Unexpected failure of therapy	Failure	• Common • Dose-related • Often caused by drug interactions	• Inadequate dosage of an oral contraceptive, particularly when used with specific enzyme inducers	• Increase dosage • Consider effects of concomitant therapy

SSRIs=serotonin-selective reuptake inhibitors.

Table 1: **Classification of adverse drug reactions**

CLINICAL TRIAL AND PAHRMACY PRACTICE

- **SOPs**
- **GCP**
- **Register**
- **https://www.clinicaltrialsregister.eu/**

PHARMACOVIGILANCE

Pharmacovigilance shall mean supervision over medicinal products aimed at ensuring maximum safety and the best practicable risk-benefit ratio of the medicinal product.

Pharmacovigilance represents namely the collection of information relevant to the safety of the medicinal product, including any information obtained from clinical trials, their evaluations and adoption of appropriate measures.

PHARMACOVIGILANCE

New medicinal product - all available information on its safety and efficacy - from clinical trials.

The conditions in clinical trial may not necessarily reflect the way medicines are used in public.

It is very important to monitor the safety of medicinal products also AFTER their marketing = pharmacovigilance.

PHARMACOVIGILANCE

Risk management system:

a set of pharmacovigilance activities and interventions for identification, description, prevention or mitigation of risks related to the medicinal product, including assessment of the level of efficacy of these activities and interventions.

HAEMOVIGILANCE

Haemovigilance shall mean a set of organised surveillance procedures over transfusion products and raw materials from blood and its constituents for further production relating to serious adverse or unexpected events or reactions in donors or recipients, and the epidemiological follow-up of donors.

PHARMACOVIGILANCE SYSTEM IN THE EU

operates with the management and involvement of:

regulatory authorities in Member States,

the European Commission

the European Medicines Agency.

(In some Member States, regional centres are in place under the coordination of the national competent authority.)

EUROPEAN MEDICINES AGENCY

decentralized agency of the European Union

located in London

The Agency is also responsible for developing and maintaining EudraVigilance and EudraVigilance Veterinary,

(the EU reporting and data-storage systems for side-effect reports, and for supporting signal-identification activities in the EU, including coordinating the EU rapid-alert and incident-management systems for responses to new safety data.)

EMA - PHARMACOVIGILANCE

Good pharmacovigilance practices (GVPP)

PHARMACOVIGILANCE – MARKETING AUTHORISATION HOLDER

Applicant for marketing authorisation has a qualified individual in charge of pharmacovigilance

Declaration signed by the marketing authorisation applicant saying that it disposes of the required means to discharge the tasks and ensure liability in pharmacovigilance;

Indication of the location where the basic document of the pharmacovigilance system for the relevant medicinal product is being kept;

PHARMACOVIGILANCE – NATIONAL AUTHORITIES

a) encouraging doctors, pharmacists, other healthcare professionals and patients to report to the national authority any suspected adverse reactions;

b) facilitating patient reporting through the provision of alternative reporting formats in addition to web-based formats;

c) publishing information on pharmacovigilance concerns as regards the use of medicinal products

PHARMACOVIGILANCE – NATIONAL AUTHORITIES

Prohibition of the supply or use of a medicinal product or order the recall of a medicinal product if:

a) the medicinal product is harmful;

b) the medicinal product lacks therapeutic efficacy;

c) the risks prevail over benefits;

d) the qualitative or quantitative composition of the medicinal product does not comply with the composition stated in the marketing authorization;

e) controls of the finished medicinal product or its components and intermediate product inprocess controls have not been performed by the manufacturer or marketing authorisation holder;

f) an obligation implied by the manufacturing authorisation has been breached by the marketing authorization holder;

PHARMACOVIGILANCE – NATIONAL AUTHORITIES

Confine the prohibition on supply of a medicinal products or its use or withdrawal from the market solely to determined production batches.

Repeal from the decision to prohibit the dispensing or use ..

In its decision to prohibit the dispensing or use of a medicinal product or from an order to recall the medicinal product from the market, in exceptional cases and for the necessary period of time, permit the dispensing or use of such products by patients who are already being treated by the medicinal product in question.

RECORDING AND REPORTING OF SUSPECTED ADVERSE REACTIONS

Recording and reporting of suspected adverse reactions

The marketing authorisation holder shall record and make accessible at a single point within the European Union all reports of suspected adverse reactions to its authorised medicinal products made in the European Union or in third countries, that were reported, regardless of the form and method of submission

a) by patients;

b) by healthcare professionals;

c) from medical literature which it is obliged to monitor;

d) in the context of a post-authorisation study, except for reports made in the context of a clinical trial.

RECORDING AND REPORTING OF SUSPECTED ADVERSE REACTIONS

The marketing authorisation holder shall submit electronically to the database and data-processing network referred to in the directly applicable regulation governing marketing authorisation procedures and surveillance over medicinal products

"Eudravigilance database"

- information on all suspected adverse reactions,
- in the case of suspected serious adverse reactions that occur in the European Union and in third countries within 15 days following the day on which the marketing authorisation holder concerned gained knowledge of the suspicion;
- suspected non-serious adverse reactions that occur in the European Union within 90 days following the day on which the marketing authorisation holder concerned gained knowledge of the suspicion.

REPORTING

A **medical doctor, a dentist, a pharmacist** or other healthcare professional who has noticed **a suspected serious or unexpected adverse reaction** and other facts that might affect the health of the treated persons in association with the use of a medicinal product shall be obliged to:

a) immediately report these facts to the National authority, even when the medicinal product has not been used in compliance with the summary of the product characteristics or when it has been abused;

b) cooperate in the verification of facts associated with suspected serious or unexpected adverse reaction and provide access to documentation to the Institute upon request, including documentation containing personal data.

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EUDRAVIGILANCE

EudraVigilance is a web-based information system designed to manage information on safety reports.

http://eudravigilance.ema.europa.eu/highres.htm

EUDRAVIGILANCE

EudraVigilance is a web-based information system designed to manage information on safety reports.

launched EudraVigilance in December 2001

EudraVigilance data are analysed at least every month.

For some medicines this is done more frequently (every two weeks.)

EUDRAVIGILANCE

The Committee for Medicinal Products for Human Use (CHMP)

Pharmacovigilance Risk Assessment Committee (PRAC)

evaluate signals from EudraVigilance and may recommend regulatory action as a result.

guide on the interpretation of spontaneous case reports of suspected adverse reactions to medicines.

MEDICINES THAT ARE SUBJECT TO ADDITIONAL MONITORING

Medicinal products authorised after 1 January 2011 that contain:

new active substance;

biological medicines for which there is limited post-marketing experience;

medicines with a conditional approval or approved under exceptional circumstances;

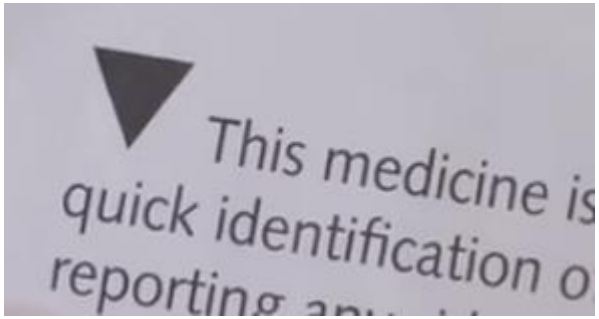
medicines for which the marketing-authorisation holder is required to carry out a post-authorisation safety study

Other medicines can also be placed under additional monitoring, based on a recommendation from the European Medicines Agency's Pharmacovigilance Risk Assessment Committee (PRAC).

BLACK TRIANGLE

If a medicine is labelled with the inverted black triangle, it does not mean that it is unsafe;

Actively encourage healthcare professionals and patients to report any suspected adverse reactions observed with the medicine



BLACK TRIANGLE

The inverted black triangle will start appearing in the package leaflet and SmPC, PIL, box.. of the medicines concerned from the autumn of 2013.

REPORTING - SUMMARY

ADRs that have caused death or a serious illness

Any ADR, however minor, if associated with a new medicine or one that is under continued monitoring (with a ▼)

Any ADR, however minor, if associated with a child (under 18 years of age) or in pregnancy

Details of reporting – in seminar

FDA

protecting the public health by assuring the safety, efficacy and security of:

- human and veterinary drugs,
- biological products,
- medical devices,
- nation’s food supply,
- cosmetics,
- products that emit radiation.

FDA

FDA plays a significant role in the Nation's counterterrorism capability. FDA fulfills this responsibility by ensuring the security of the food supply and by fostering development of medical products to respond to deliberate and naturally emerging public health threats.

FDA

FDA receives some adverse event and medication error reports directly from health care professionals (such as physicians, pharmacists, nurses and others) and consumers.

Healthcare professionals and consumers may also report these events to the products' manufacturers.

If a manufacturer receives an adverse event report, it is required to send the report to FDA as specified by regulations.

Reporting of adverse events:

Voluntary

Mandatory

MedWatch site

FDA

may take regulatory action(s) to improve product safety and protect the public health:

updating a product's labeling information,

restricting the use of the drug,

communicating new safety information to the public,

removing a product from the market.

FDA

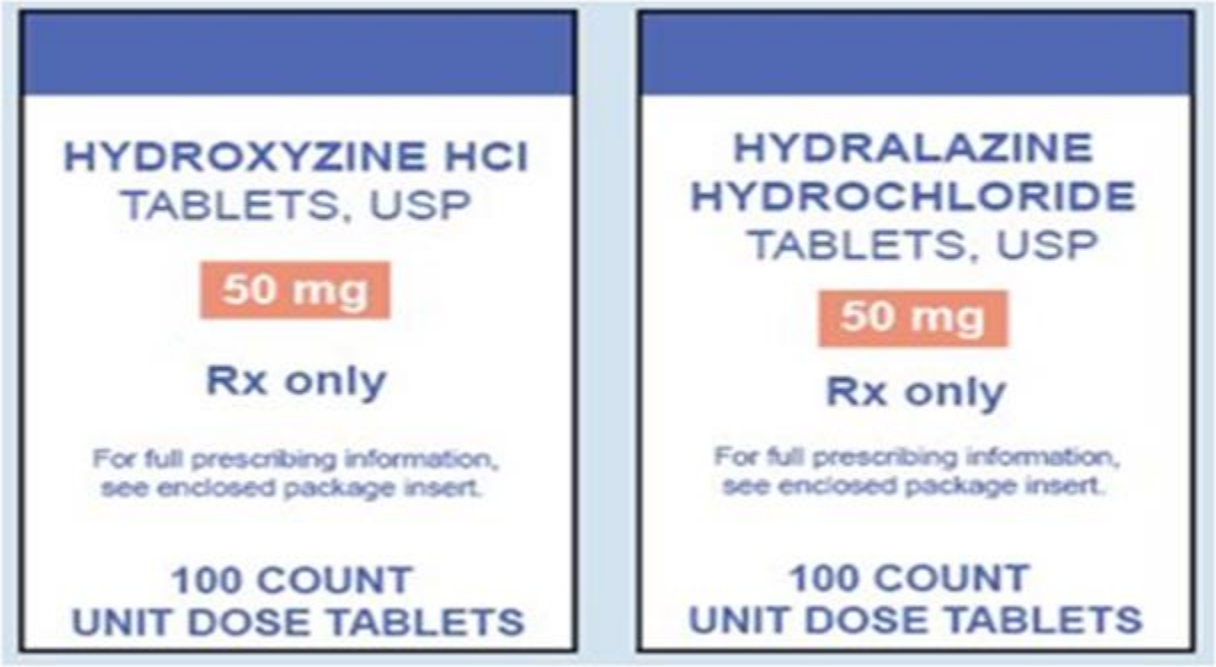
Adverse Event Reporting System data do have limitations:

there is no certainty that the reported event was actually due to the product.

FDA does not receive all adverse event reports that occur with a product.

Many factors can influence whether or not an event will be reported, such as the time a product has been marketed and publicity about an event.

MEDICATION ERRORS



MEDICATION ERORRS

can be defined as a failure in the treatment process that leads to, or has the potential to lead to, harm to the patient

"any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer. „

MEDICATION ERROR

Such events may be related:

to professional practice,

health care products, procedures, and systems,

(including prescribing; order communication; product labeling, packaging, and nomenclature; compounding; dispensing; distribution; administration; education; monitoring; and use.)

MEDICATION ERROR

Medication errors are mishaps that occur during prescribing, transcribing, dispensing, administering, adherence, or monitoring a drug.

Misreading or miswriting a prescription.

“near misses” “close calls”

MEDICATION ERROR

Prescribing faults, prescription errors, and balanced prescribing

irrational prescribing, inappropriate prescribing, underprescribing, overprescribing, and ineffective prescribing.

This leads to the distinct concepts of ‘prescribing faults’ and ‘prescription errors’.

PRODUCT PROBLEMS

Classificaton – in the seminar

Communication procedures