3G SYSTEM IN PHARMACY WITH VIGILANCE

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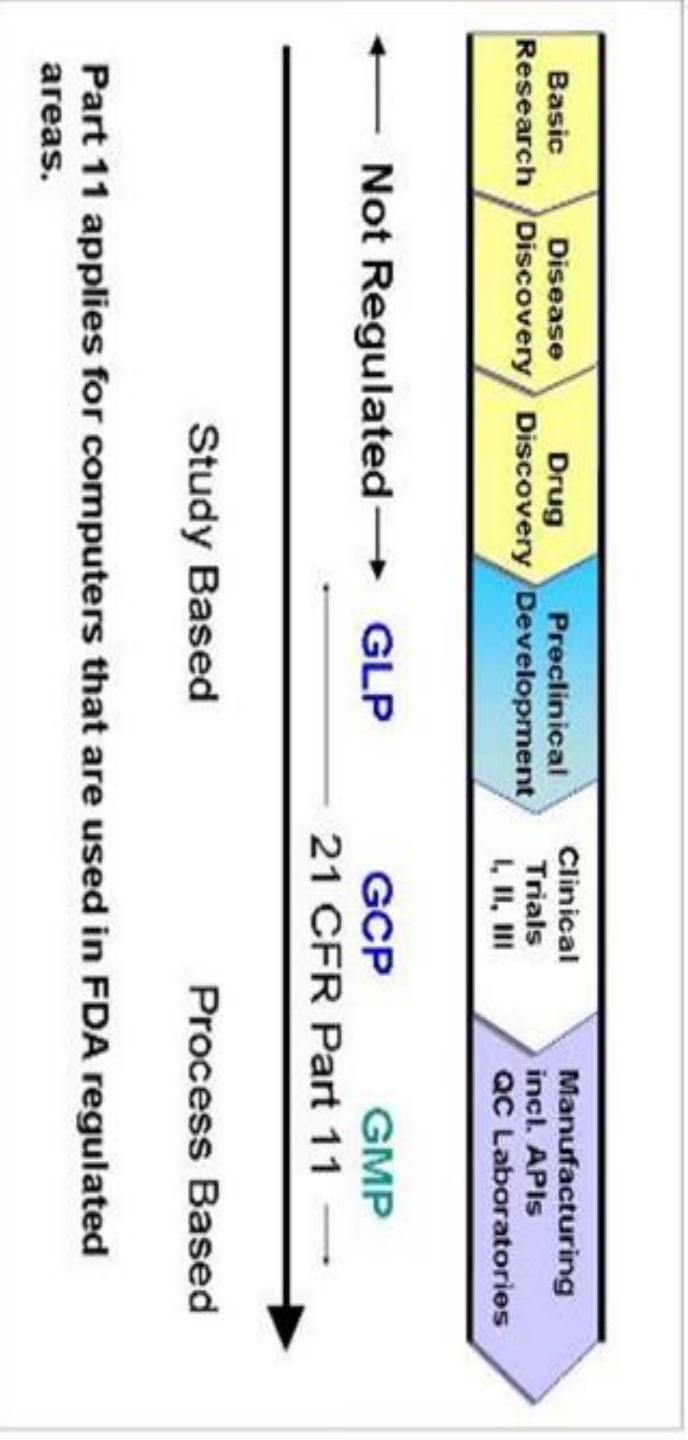
INTRODUCTION

- No drug which is pharmacologically active is without side-effect. Furthermore not all adverse effect can be known before a drug is marketed.
- Once put onto the market, a medicine leaves the secure and protected scientific environment of clinical trials and is legally set free for consumption by the general population.
- Experience has shown that many adverse effects, interactions (i.e. with foods or other medicines) and risk factors come into light only years after release of the drug.

Development of Current 3G System

1. GOOD MANUFACTURING PRACTICE
2. GOOD LABORATORY PRACTICE
3. GOOD CLINICAL PRACTICE



3G SYSTEM

GMP: Good Manufacturing Practice

GMP is a system for ensuring that products are consistently produced and controlled according to quality standards.

GMP is concerned with both production and quality control

GLP: Good Laboratory Practice

GLP is a system, which has been evolved by Organisation for Economic Co-operation and Development (OECD) to ensure the generation of high quality and reliable test data related to the safety of industrial chemical substances and preparations.

GCP: Good Clinical Practice

GCP is an international quality standard that is provided by ICH, an international body that defines standards, which governments can transpose into regulations for clinical trials involving human subjects.

Importance of Vigilance

HUMANITARIAN CONCERN

– Insufficient evidence of safety from clinical trials.

– Animal experiments

– Phase 1 – 3 studies prior to marketing authorization

MEDICINES

– Medicines are supposed to save lives.

– Dying from a disease is sometimes unavoidable; dying from a medicine is unacceptable. It has been suggested that ADRs may cause 5700 deaths per year in India.

PROMOTING RATIONAL USE OF MEDICINES AND ADHERENCES

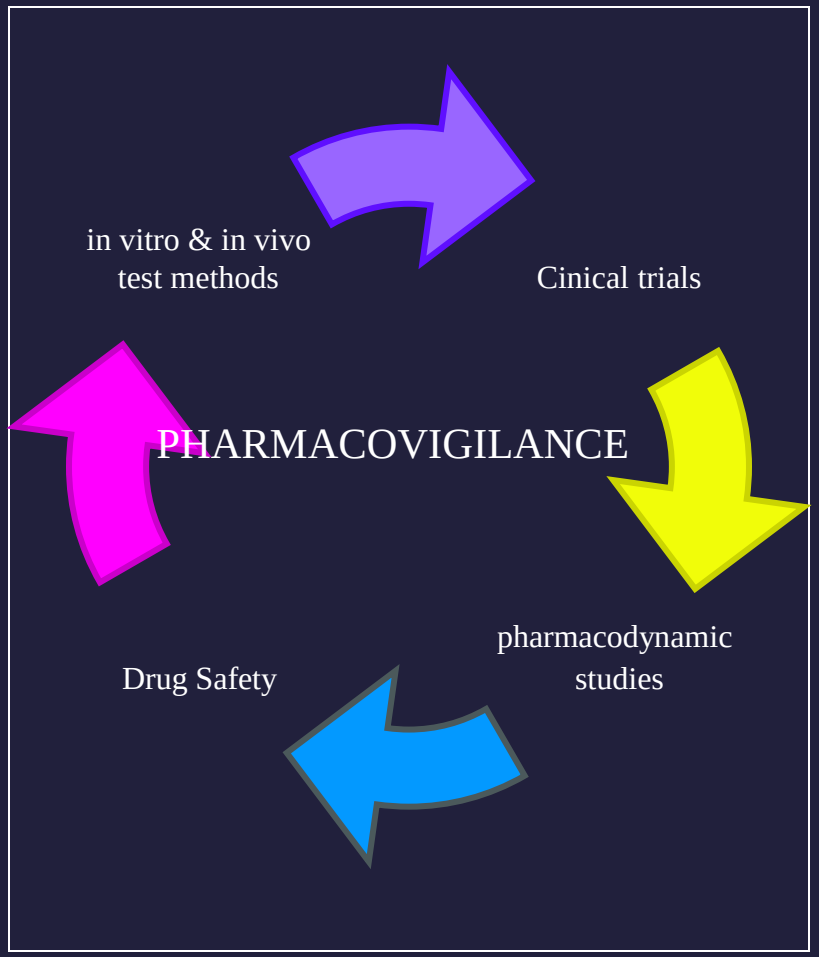
ADRs ARE EXPENSIVES!!!

ENSURING PUBLIC CONFIDENCE

ETHICS

PHARMACOVIGILANCE

- Pharmacovigilance the practice of monitoring the effects of medical drugs after they have been licensed for use, especially in order to identify and evaluate previously unreported adverse reactions.
- Related to the collection, detection, assessment, monitoring, and prevention of adverse effects with pharmaceutical products.



History

YEAR	ACTION
May 31, 1978	The Commissioner of the Food and Drug Administration sent a letter to officials of each state stating FDA's intent to provide a list of all prescription drug products that are approved by FDA for safety and effectiveness, along with therapeutic equivalence determinations for multisource prescription products.
January, 1979	The list was distributed (included only currently marketed prescription drug products approved by FDA through NDAs and ANDAs under the provisions of section 505 of the Act)
October 31, 1980	The final rule (includes FDA's response to the public comments on the proposal) was published in the Federal Register (45 FR 72582). The list incorporated appropriate corrections and additions.

Objectives

- To monitor Adverse Drug Reactions (ADRs)
- To monitor benefit-risk profile of medicines
- To Generate independent, evidence based safety of medicines.
- To Support CDSCO & To Create a national centre for global drug safety monitoring standards.
- To supply an additional form of user assurance

High-Alert Medications

Year	Medicine	Adverse Reaction	Resulting Action
1995	➢ Tramadol(Zydol)	Pyschiatric Reaction	Warning
1995	Cyproterone acetate(Cyprostat,Androcur)	Dose-related hepatotoxicity	Restricted indication,requirement for monitoring of Liver Function
1995	Quinolone antibiotics	Tendinitis,Tendon Rupture	Improved warning
1995	➢ Tacrolimus(Prograf)	Hypertrophic, Cardiomyopathy	Warning ,Dose reduction and monitoring Requirement
1996	➢ Alendronate(Fosamax)	Severe Oesopharangeal reaction	Warning and revised dosing instruction
1997	Clozapine(clozanl)	GI Obstruction	Improved Warning
1997	HIV Protease Inhibitor	Hyperlipidemia and fat redistribution	Improved Warning and monitoring redistribution
1998	Isotretinion(Roaccutane)	Psychiatric Reactions	Improved Warning
1998	**++**Sertindole(Serdolect)	Sudden Cardiac Death	Drug Withdrawal
1999	➢ Aristolochia in Chinese herbal remedies	Renal Failure	Aristolochia Banned
1999	Human Clottable Protein Conentrate	Neurotoxic reaction	Improved Warning
2000	**+++Cisapride(Prepuside)**	Serious Cardiovascular Reaction	Cisapride suspended in UK

Year	Medicine	Adverse Reaction	Resulting Action
2001	➢ Bupropoin(Zyban)	Seizures	Improved Warnings and revised dosing instruction
2003	Kava-Kava	Hepatotoxicity	Supply of Kava-Kava prohibited in UK
2003	Aspirin	Reye's Syndrome in children	Statutory Label Warning
2003	Warfarin	Interaction with cranberry juice leading to bleeding	Warning
2004	➢ Rosuvastatin(Crestor)	Rhabdomyolysis	Revised dosing instruction and improved warning
2005	➢ Atomoxetin	Hepatic Disorder	Warning
2006	➢ Linezolid(Zymox)	Optic neuropathy	Monitoring Recommended

Year	Medicine	Adverse Reaction	Resulting Action
2007	Rimonabant.	Neurotoxicity	Banned
2008	Mepacrine Hydrochlorid	Hepatotoxicity	Warning
2009	Practolol	CVS Disorder	Banned
2010	Nialamide	Hepatotoxicity	Warning
2011	➢ Phenacetin.	Nephrotoicity	Revised dosing instruction and improved warning
2012	➢ Amidopyrine	Hepatic Disorder	Warning
2013	➢ Linezolid(Zymox)	Optic neuropathy	Monitoring Recommended
2014	➢ Mephenteramine	Cardiac arrest	prohibiited
2015	➢ Mesterolone	Nephrotoxicity	Prohibited

➢ **(Triangle)**: Drug at the time the major safety issuse was identified.

++**(**Sertindole) is reinstated in 2002 with increased warning.

+++**(**Cisapride) License have been cancelled.

Evaluating and Monitoring of ADRs

- UK – ”Yellow Card” , Since 1964
- Australia- “Blue Card”, Since 1964
- India- ”Suspected Adverse Drug Reaction Reporting Form
- US - “Med Watch” Form FDA 3500- Voluntary reporting

  Form FDA 3500 A – Mandatory reporting.

SUSPECTED ADVERSE DRUG REACTION REPORTING FORM

For VOLUNTARY reporting of Adverse Drug Reactions by healthcare professionals

INDIAN PHARMACOPOEIA COMMISSION
(National Coordination Centre-Pharmacovigilance Programme of India)
Ministry of Health & Family Welfare
Government of India
Sector-23, Raj Nagar, Ghaziabad-201002
www.ipc.nic.in

(AMC/ NCC Use only)
AMC Report No.
Worldwide Unique

A. PATIENT INFORMATION

1. Patient Initials _____
2. Age at time of Event or date of birth _____
3. Sex ☐ M ☐ F
4. Weight ____Kgs

12. Relevant tests / laboratory data with dates

B. SUSPECTED ADVERSE REACTION

5. Date of reaction started (dd/mm/yyyy)
6. Date of recovery (dd/mm/yyyy)
7. Describe reaction or problem

13. Other relevant history including pre-existing medical conditions (e.g. allergies, race, pregnancy, smoking, alcohol use, hepatic/ renal dysfunction etc)

14. Seriousness of the reaction

- ☐ Death (dd/mm/yyyy)
- ☐ Life threatening
- ☐ Hospitalization/prolonged
- ☐ Disability
- ☐ Congenital-anomaly
- ☐ Required intervention to prevent permanent impairment / damage
- ☐ Other (specify)

15. Outcomes

- ☐ Fatal
- ☐ Continuing
- ☐ Recovering
- ☐ Recovered
- ☐ Unknown
- ☐ Other (specify)

C. SUSPECTED MEDICATION(S)

S.No	8. Name (brand and /or generic name)	Manufacturer (if known)	Batch No./ Lot No. (if known)	Exp. Date (if known))	Dose used	Route used	Frequency	Therapy dates (if known, give duration)		Reason for use of prescribed for
								Date started	Date stopped	
i.										
ii.										
iii.										
iv.										

S.No As per C	9. Reaction abated after drug stopped or dose reduced					10. Reaction reappeared after reintroduction				
	Yes	No	Unknown	NA	Reduced dose	Yes	No	Unknown	NA	If reintroduced dose
i.										
ii.										
iii.										
iv.										

11. Concomitant medical product including self medication and herbal remedies with therapy dates (exclude those used to treat reaction)

D. REPORTER (see confidentiality section on first page)

16. Name and Professional Address :_____
Pin code: _____ E-mail _____
Tel. No. (with STD code): _____
Occupation _____ Signature _____

17. Causality Assessment

18. Date of this report (dd/mm/yyyy)

MEDWATCH

THE FDA MEDICAL PRODUCTS REPORTING PROGRAM

For use by user-facilities, distributors and manufacturers for MANDATORY reporting

Page ____ of ____

PLEASE TYPE OR USE BLACK INK

A. Patient information

1. Patient identifier (in confidence)
2. Age at time of event / Date of birth:
3. Sex ☐ female ☐ male
4. Weight ____ lbs or ____ kgs

B. Adverse event or product problem

1. ☐ Adverse event and/or ☐ Product problem (e.g., defect/malfunction)
2. Outcomes attributed to adverse event (check all that apply)
   - ☐ death (mm/dd/yyyy)
   - ☐ life-threatening
   - ☐ hospitalization – initial or prolonged
   - ☐ disability
   - ☐ congenital anomaly
   - ☐ required intervention to prevent permanent impairment/damage
   - ☐ other:
3. Date of event (mm/dd/yyyy)
4. Date of this report (mm/dd/yyyy)
5. Describe event or problem
6. Relevant tests/laboratory data, including dates
7. Other relevant history, including preexisting medical conditions (e.g., allergies, race, pregnancy, smoking and alcohol use, hepatic/renal dysfunction, etc.)

C. Suspect medication(s)

1. Name (give labeled strength & manufacturer, if known)
   #1
   #2
2. Dose, frequency & route used
   #1
   #2
3. Therapy dates (if unknown, give duration)
   #1
   #2
4. Diagnosis for use (indication)
   #1
   #2
5. Event abated after use stopped or dose reduced
   #1 ☐ yes ☐ no ☐ doesn't apply
   #2 ☐ yes ☐ no ☐ doesn't apply
6. Lot # (if known)
   #1
   #2
7. Exp. date (if known)
   #1
   #2
8. Event reappeared after reintroduction
   #1 ☐ yes ☐ no ☐ doesn't apply
   #2 ☐ yes ☐ no ☐ doesn't apply
9. NDC # – for product problems only (if known)
   – –
10. Concomitant medical products and therapy dates (exclude treatment of event)

D. Suspect medical device

1. Brand name
2. Type of device
3. Manufacturer name & address
4. Operator of device
   ☐ health professional
   ☐ lay user/patient
   ☐ other:
5. Expiration date (mm/dd/yyyy)
6. model # _____
   catalog # _____
   serial # _____
   lot # _____
   other # _____
7. If implanted, give date (mm/dd/yyyy)
8. If explanted, give date (mm/dd/yyyy)
9. Device available for evaluation? (Do not send to FDA)
   ☐ yes ☐ no ☐ returned to manufacturer on _____ (mm/dd/yyyy)
10. Concomitant medical products and therapy dates (exclude treatment of event)

E. Initial reporter

1. Name & address
   phone #
2. Health professional? ☐ yes ☐ no
3. Occupation
4. Initial reporter also sent report to FDA ☐ yes ☐ no ☐ unk

FDA Form 3500A

Submission of a report does not constitute an admission that medical personnel, user facility, distributor, manufacturer or product caused or contributed to the event.

Completeness Criteria of Suspected Adverse Drug Reaction Reporting Form

The **four sections** to validate the individual case report (ICSR) are as follow:

An identifiable patient

At least 1 of the following:

- Patient initials
- Sex
- Weight
- Age at time of reaction or date of birth

An identifiable reporter

- Name, initials
- Address
- Contact details
- Qualification (if healthcare professional)

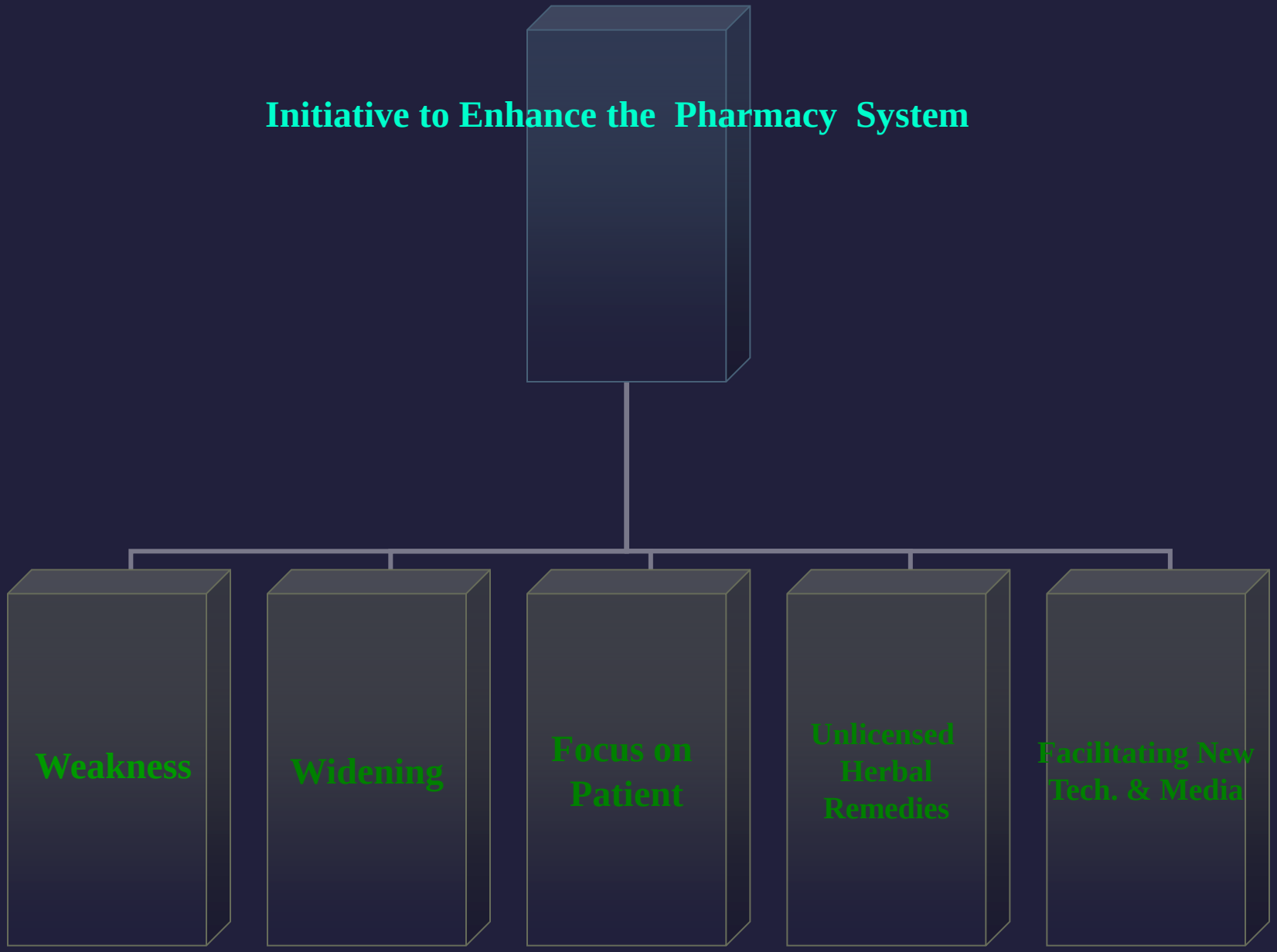
Suspected medicine

- Name (INN and brand name)
- Strength (concentration)
- Dose, Frequency
- Dosage form
- Route of administration
- Indication for use
- Duration of use, date started, date stopped
- Batch number (especially for vaccines)

Suspected adverse reaction

- Description of the reaction
- Expectedness of the reaction (in accordance with the approved product information)
- Seriousness of the reaction
- Date the reaction started, stopped
- Outcomes attributed to adverse reaction
- Relevant tests/laboratory data (if available)

Initiative to Enhance the Pharmacy System



Conclusion

- It is expected that 50 – 75 % of medical errors are preventable .
- Introduction of advanced medical information systems Electronic Health Record (EHR)
- Automatic check up for dose, interactions, allergies, should be done.

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THANK YOU