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Overview of Pharmacovigilance and Good Distribution Practices: Program and Activities in Indonesia

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In Collaboration with GP FARMASI Indonesia
Jakarta, 13 Februari 2013

RAJA AMPAT, PAPUA - INDONESIA

Outlines:

- Vision & Missions
- Organizational Structures
- Regulatory Framework to Ensure S, E, & Q
- Linked between Pre-Market and Post-Market Control
- Overview of Pharmacovigilance in Indonesia
- Overview of GPD in Indonesia
- Key messages

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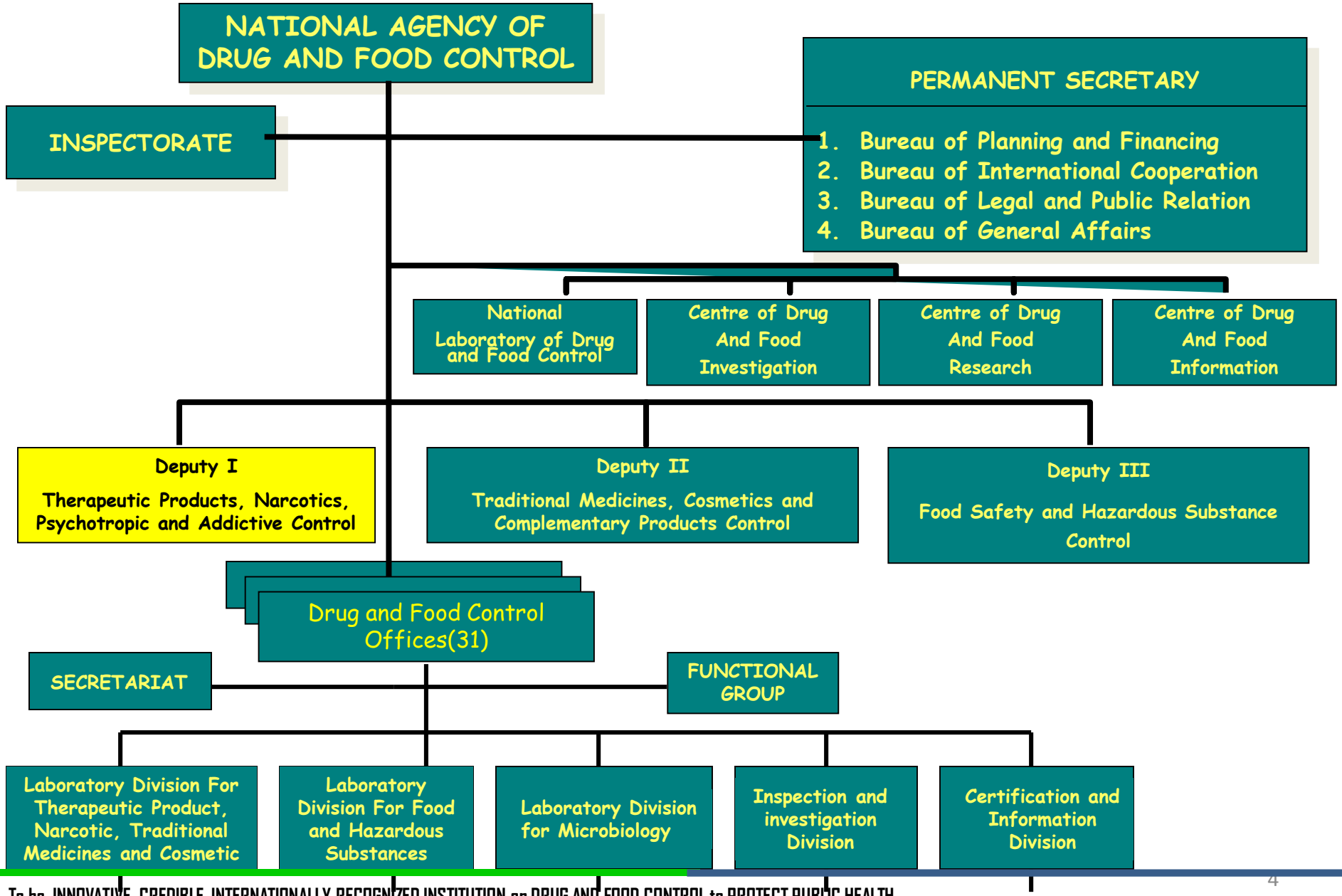
VISION

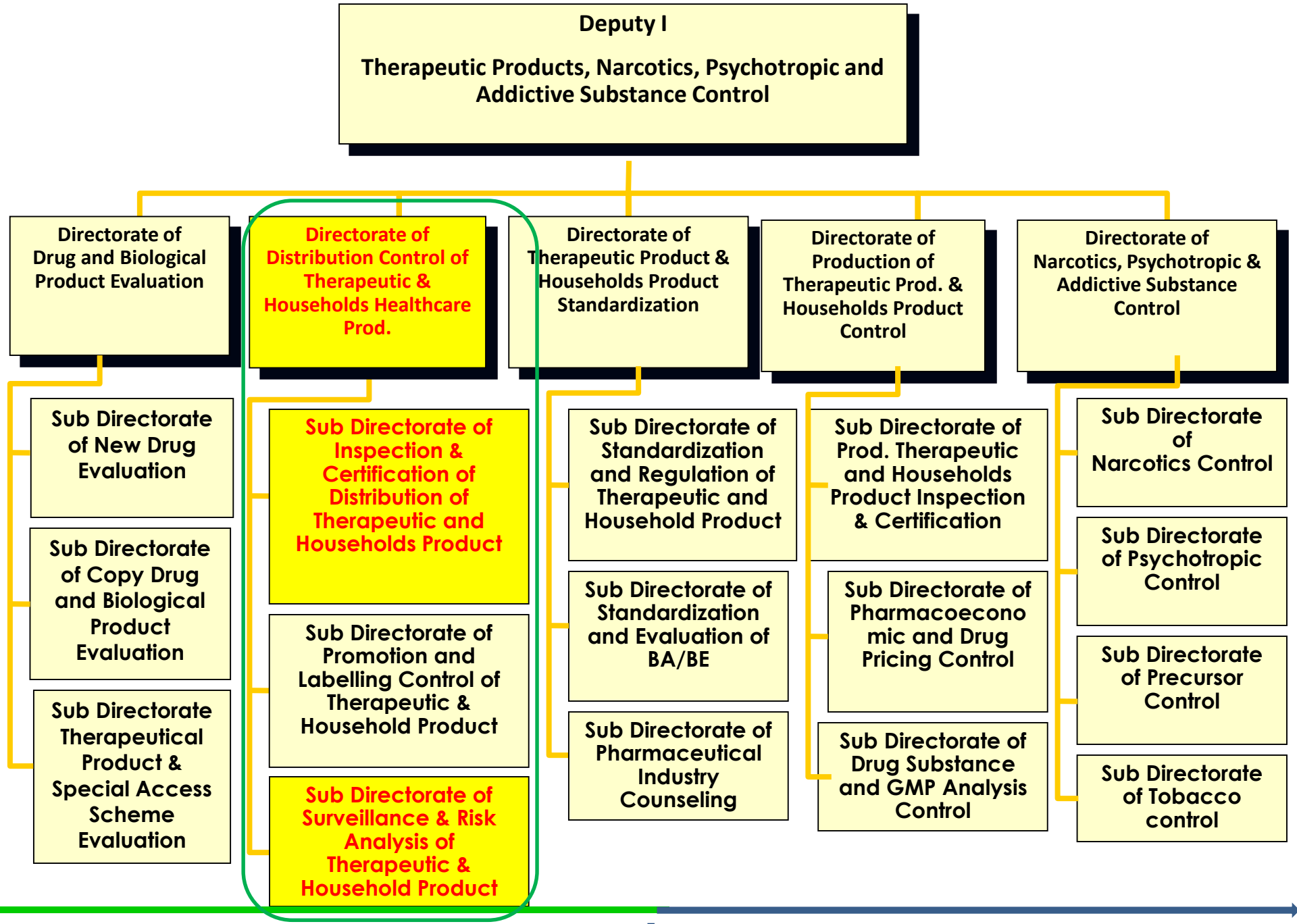
To be innovative, credible, and Internationally recognized institution on Drug and Food Control to protect public health

MISSIONS

1. Conducting pre- and post market control based on international standard
2. Implementing Quality Management System consistenly
3. Optimalizing networking/cooperation with all stake holders in all level.
4. Empowering public to have capability to protect themselves from drug and food which are risky to their health.
5. Establishing Learning Organization

ORGANIZATION CHART OF NA-DFC




Deputy I
Therapeutic Products, Narcotics, Psychotropic and Addictive Substance Control
Directorate of Drug and Biological Product Evaluation
Directorate of Distribution Control of Therapeutic & Households Healthcare Prod.
Directorate of Therapeutic Product & Households Product Standardization
Directorate of Production of Therapeutic Prod. & Households Product Control
Directorate of Narcotics, Psychotropic & Addictive Substance Control
Sub Directorate of New Drug Evaluation
Sub Directorate of Copy Drug and Biological Product Evaluation
Sub Directorate Therapeutical Product & Special Access Scheme Evaluation
Sub Directorate of Inspection & Certification of Distribution of Therapeutic and Households Product
Sub Directorate of Promotion and Labelling Control of Therapeutic & Household Product
Sub Directorate of Surveillance & Risk Analysis of Therapeutic & Household Product
Sub Directorate of Standardization and Regulation of Therapeutic and Household Product
Sub Directorate of Standardization and Evaluation of BA/BE
Sub Directorate of Pharmaceutical Industry Counseling
Sub Directorate of Prod. Therapeutic and Households Product Inspection & Certification
Sub Directorate of Pharmacoeconomic and Drug Pricing Control
Sub Directorate of Drug Substance and GMP Analysis Control
Sub Directorate of Narcotics Control
Sub Directorate of Psychotropic Control
Sub Directorate of Precursor Control
Sub Directorate of Tobacco control

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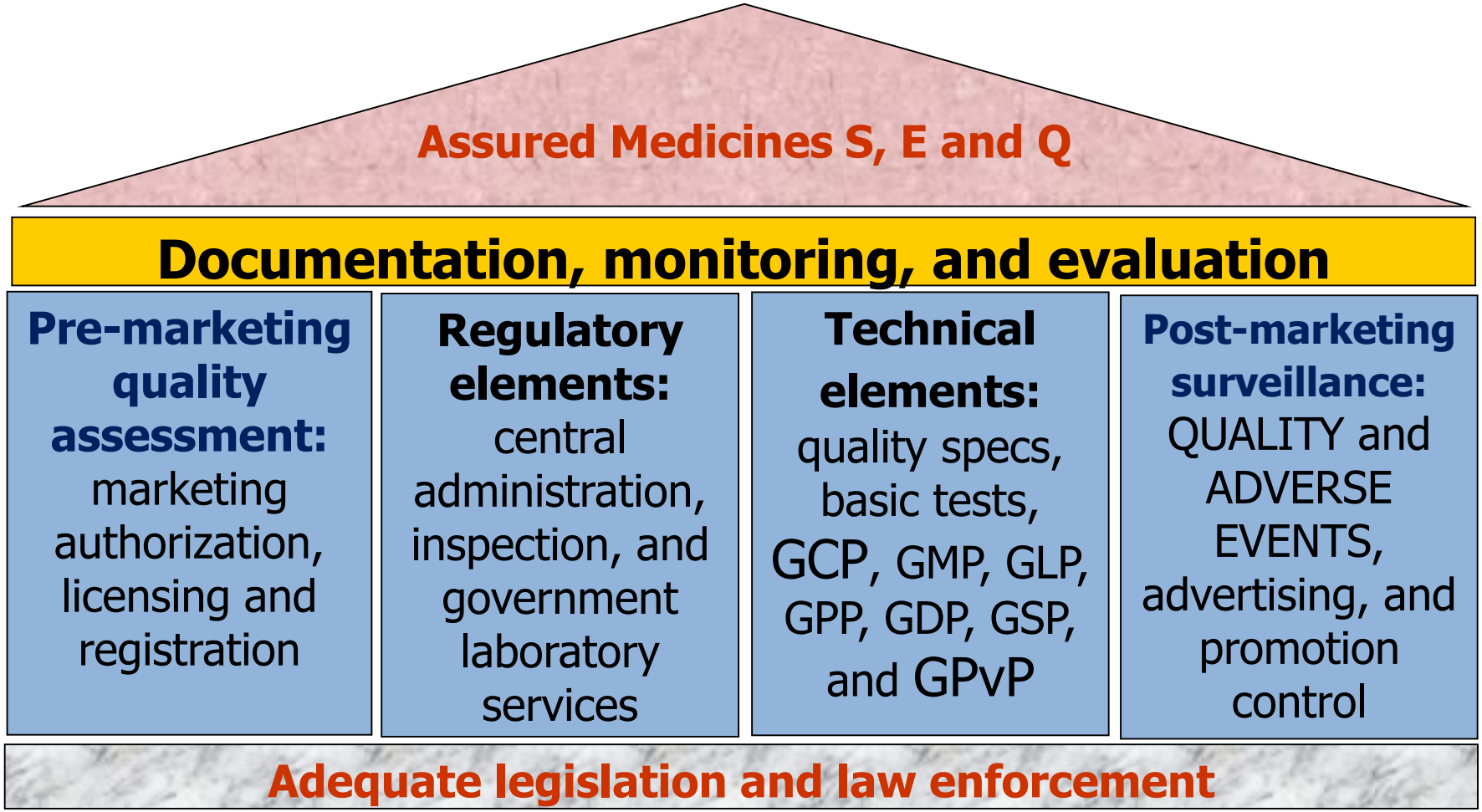
REGULATORY FRAME WORK TO ENSURE S, E AND Q



Explanatory notes: GCP=Good Clinical Practices; GMP=Good Manufacturing Practice; GLP=Good Laboratory Practice; GPP= Good Pharmacy Practice; GDP=Good Distribution Practice; GSP=Good Storage Practice; GPvP= Good Pharmacovigilance Practice

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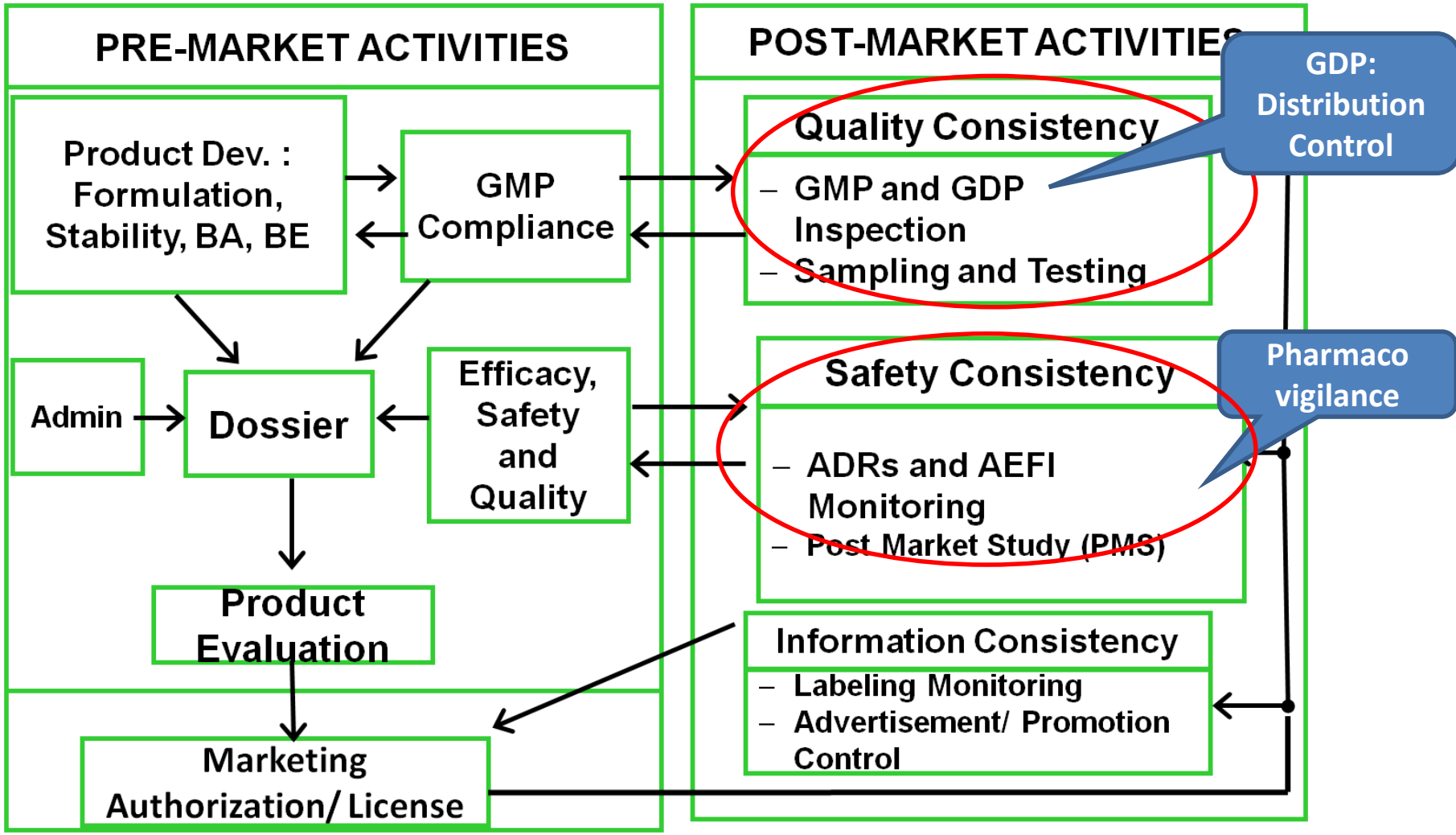
Linked between PRE - MARKET AND POST - MARKET CONTROL



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OVERVIEW OF PHARMACOVIGILANCE PROGRAM AND ACTIVITIES IN INDONESIA

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EMERGING PHARMACOVIGILANCE FOR ENSURING DRUG SAFETY

WHY PHARMACOVIGILANCE IS NEEDED?

Pharmacovigilance (WHO Definition)

The science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other possible medicine-related problems

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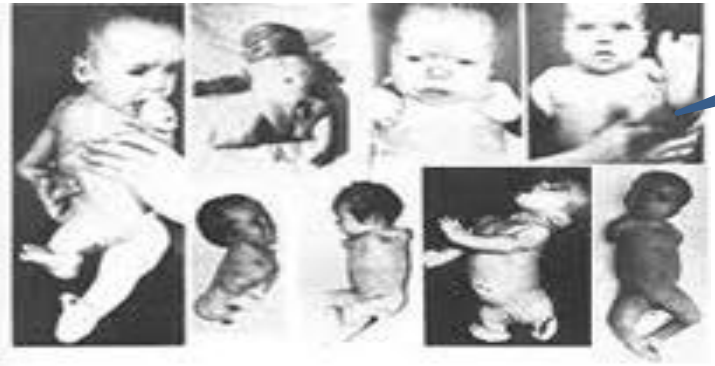
LESSON LEARNED FROM THALIDOMIDE

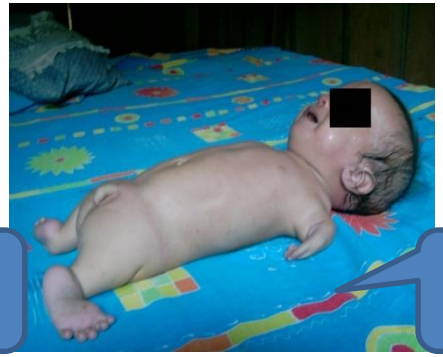
TRIGERRED AND STARTED...HERE!



1960's

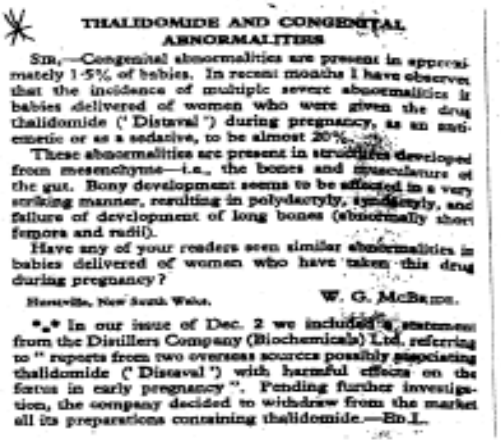
CONTINUED....

2004



2006

The Culprit



THALIDOMIDE AND CONGENITAL ABNORMALITIES

SIR,—Congenital abnormalities are present in approximately 1·5% of babies. In recent months I have observed that the incidence of multiple severe abnormalities in babies delivered of women who were given the drug thalidomide ('Distaval') during pregnancy, as an antiemetic or as a sedative, to be almost 20%.

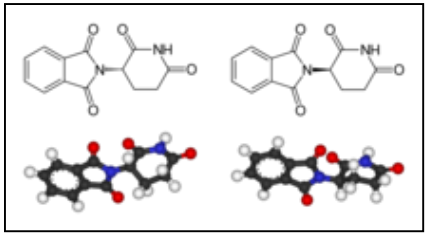
These abnormalities are present in structures developed from mesenchyme—i.e., the bones and musculature of the gut. Bony development seems to be affected in a very striking manner, resulting in polydactyly, syndactyly, and failure of development of long bones (abnormally short femora and radii).

Have any of your readers seen similar abnormalities in babies delivered of women who have taken this drug during pregnancy?

Hurstville, New South Wales. W. G. McBRIDE.

*** In our issue of Dec. 2 we included a statement from the Distillers Company (Biochemicals) Ltd. referring to "reports from two overseas sources possibly associating thalidomide ('Distaval') with harmful effects on the foetus in early pregnancy". Pending further investigation, the company decided to withdraw from the market all its preparations containing thalidomide.—ED. L.

The Lancet
December 16, 1961.



Thalidomide!

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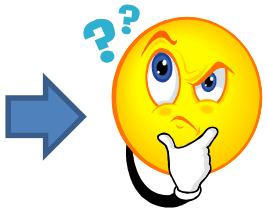
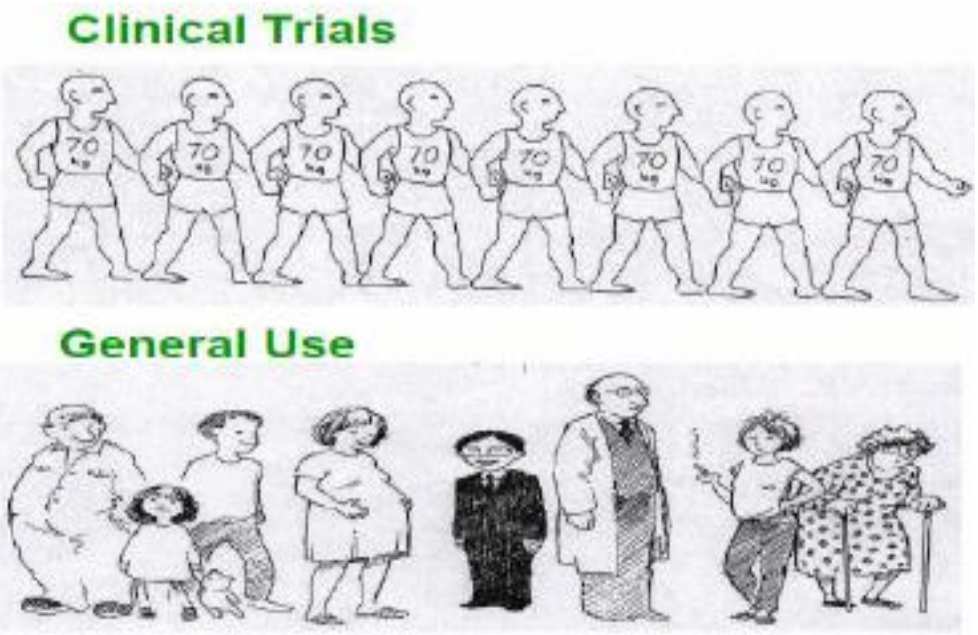
Facts on Clinical Development of Medicines (Pharmaceutical & Vaccine)

"Not all hazards of a drug can be known before it is marketed."

(UK Com on the Safety of drugs)



THAT'S WHY PHARMACOVIGILANCE IS NEEDED!



- Quite Homogenous
- Limited number of patients
- Rare side effects may not be seen

No drug is inherently safe
–unless it has no effect at all!
•Each patient is unique
•Each treatment situation is unique
–What is the right drug for me might be a bad choice for you

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Legal framework

POST-MARKET CONTROL ACTIVITIES ON DRUG SAFETY: Pharmacovigilance Program

MoH Regulation No. 1010/Menkes/Per/XI/2008 on Drug Registration , Article No. 22

Re – evaluation of marketed drug is done under following circumstances:

- Post-market surveillance reveals that the risk outweighs its benefit
- The effectiveness is not better than its placebo
- Not meet bioequivalence requirements
- Need to improve composition and reformulation

MoH Regulation No. 1799/Menkes/Per/XII/2010 on Pharmaceutical Industry, Article No. 9

Pharmaceutical Industry (Marketing Authorization Holder) must perform Pharmacovigilance

Head of NADFC Regulation No. HK.03.1.23.12.11.10690 of 2011 on Implementation of Pharmacovigilance for Pharmaceutical Industry

Technical Guidance of Pharmacovigilance for Pharmaceutical Industry

Ensuring Drug Safety: Risk Management Approaches

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REGULATOR and PI/MAH:

MANAGING RISK IN TERM OF RISK – BENEFIT RATIO FOR POPULATION

HCPs/HEALTHCARE FACILITIES:

MANAGING RISK IN TERM OF RISK – BENEFIT RATIO FOR PATIENTS

PATIENTS: MANAGING RISK IN TERM OF PERSONAL VALUES

Drug Safety Review Process with Risk Management Approaches done by NADFC

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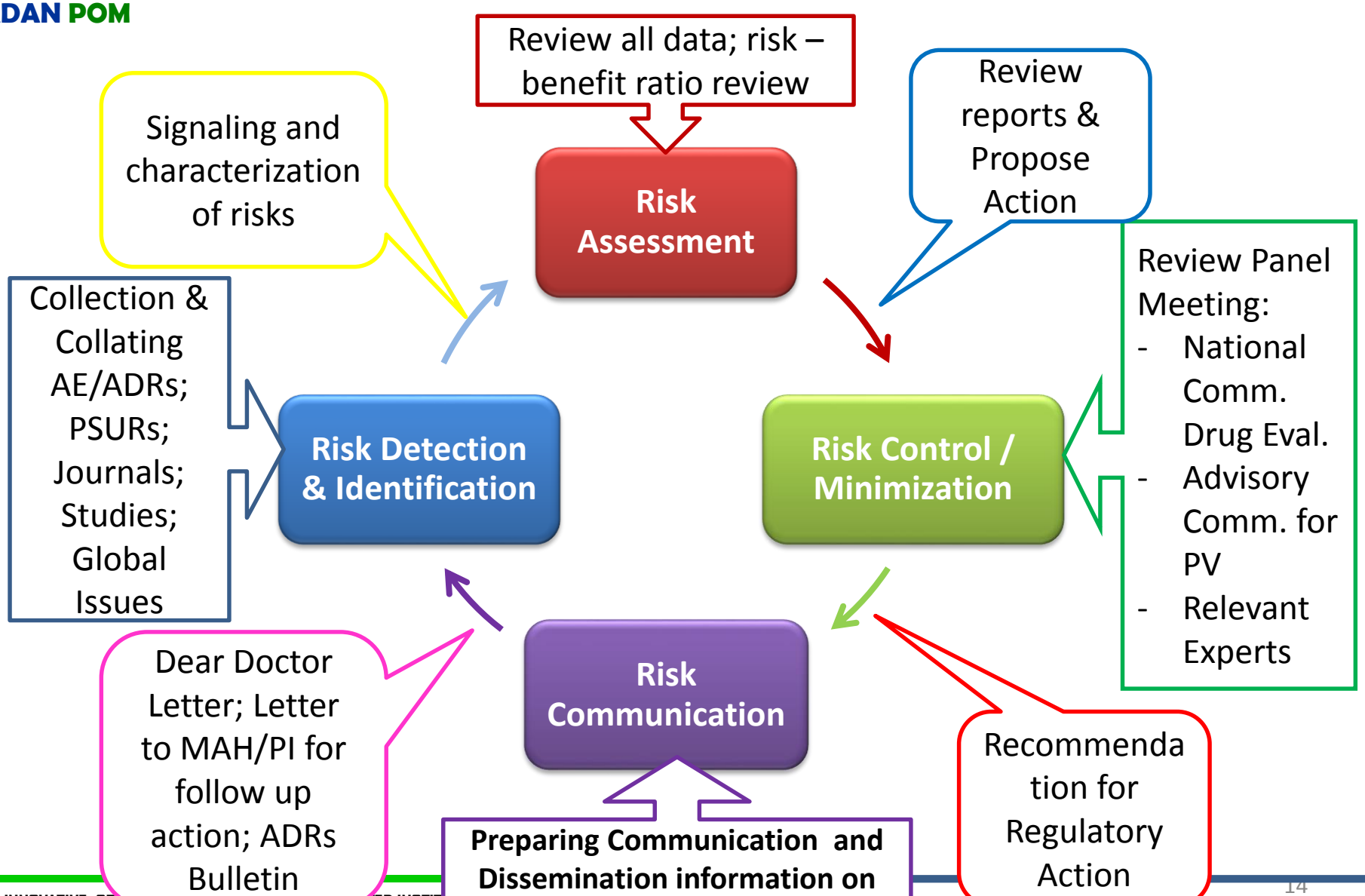

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Safety Measures/Regulatory Actions on Safety

- CHANGE IN REGIMEN DOSE
- LIMITATION ON INDICATION
- LABELING CHANGES
- PRODUCT RECALL
- SUSPENSION OF MA
- CANCELLATION OF MA
- WITHDRAWAL

Regulatory Actions by NADFC for Marketed Drugs/Vaccines in 2009 -2012

Drug/Vaccine	Risk Identification & Assessment	Risk Control/Regulatory Acton
2009		
Acomplia	Risk of Cardiovascular	Suspension, recall/withdrawal
Floroquinolone	Risk of tendon rupture	Update of labeling: Box Warning
Mycophenolate mofetil	Risk of Pure Red Cell Aplasia (PRCA)	Update Labeling to include this risk on Warning and Precaution , and Undesireable effect.
Lovenox (LMWH)	Contamination of OSCS on certain bacthes	Recall/withdrawal of certain batches
2010		
Varenicline	Risk of psychiatric disorder, however the benefit remains outweigh the risk	Update of Labeling: Box warning
Rosiglitazone	Risk of cardivascular events	Suspension, recall/withdrawal
Sibutramine	Risk of Cardiovascular events	Registration cancellation, recall/withdrawal
Peg-Intron	Cartridge defect	Withdrawal of affected bacthes
2012		
Pioglitazone	Risk of bladder cancer	Update of Labeling
Albapure	Contamination of ethylene glycol	Recall /withdrawal of certain batches

Implementation of PV by PI/MAH

PI/MAH

MANDATORY TO PERFORM PVAND REPORT TO AUTHORITY

NEW REGULATION

- ✓ **MoH Regulation No. 1799/Menkes/Per/XII/2010 on Pharmaceutical Industry, Article No. 9**
- ✓ **Head of NADFC Regulation No. HK.03.1.23.12.11.10690 of 2011 on Implementation of Pharmacovigilance for Pharmaceutical Industry (Enacted in 5 January 2012)**

TO STRENGTHEN THE DIRECTION OF AND TO HAVE BETTER STRUCTURED PV SYSTEM IN INDONESIA, WITH OPTIMALIZATION OF THE ROLES AND RESPONSIBILITIES OF PI/MAH TO ENSURE DRUG SAFETY

PHARMACOVIGILANCE FRAME WORK: STEPWISE IMPLEMENTATION OF PHARMACOVIGILANCE BY INDUSTRY

2011-2012

- ✓ **Enacted and Launched Head of NADFC Regulation on PV Implementation for PI/MAH, incl. PV Technical GL**
- ✓ **Training PV**
- ✓ **Coordination and Communication Forum for PV**
- ✓ **Development of Tools for Monitoring PV Implementation**

2013

- ✓ **Dissemination and Workshop of PV Technical Guidelines and Tools for Monitoring PV Implementation**
- ✓ **Piloting for PV Inspection /Monitoring PV Implementation**
- ✓ **PV Symposium (Joint Symposium with Japan)**

2014

- ✓ **Piloting for PV Inspection /Monitoring PV Implementation**
- ✓ **Evaluate possibility of Changing Reporting Format into E2B (ICH standardized format)**
- ✓ **Development of Analysis system for Signaling/Upgrading Data Base System**

2015-….

- ✓ **PV Inspection /Monitoring PV Implementation**
- ✓ **Upgrading Reporting Format into E2B (ICH standardized format)**
- ✓ **PV Training**
- ✓ **Review PV Technical Guidelines**
- ✓ **Pilot Test for Analysis system for Signaling/Upgrading Data Base System**

PHARMACOVIGILANCE PROGRAM: STRATEGIC MEASURES AND THE WAY FORWARD

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- **ROLES AND RESPONSIBILITIES OF PHARMACEUTICAL INDUSTRIES**
  - **New MoH Regulation on Pharmaceutical Industry: PV is mandated and PV Guideline has been stipulated in 2012**
  - **Develop tools for PV Inspection/Monitoring of PV implementation**
  - **Workshops, Seminars, Disseminations**

- **LINK PV Activities with PUBLIC HEALTH PROGRAMS (PHP)**
  (AEFI for Vaccines used in EPI/Immunization Program; ATM Drugs (MDGs) and other PHP)

- **ENCOURAGEMENT OF HEALTHCARE PROFESSIONALS (HCPs)**
  (Workshops, Seminars and Trainings; development Electronic Reporting, feedback information: publish ADRs Bulletin)

- **IMPROVE CAPACITY BUILDING for PV UNITS**

- **STRENGTHEN NETWORKING on PV with ALL KEY PLAYERS (Both National and International)**

International net working: WHO-International Drug Monitoring Program, DCVRN, Global Vaccine Safety Initiative, ASEAN PMAs, Incl. Japan – Indonesia Symposium

- **PROMOTE PV PROGRAM**
  Collaboration with Academia to put PV on the curiculum

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OVERVIEW OF GOOD DISTRIBUTION PRACTICES IN INDONESIA

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GDP DEFINITION

That part of quality assurance that ensures that the quality of a pharmaceutical product is maintained by means of adequate control of numerous activities which occur during the distribution process as well as providing a tool to secure the distribution system from counterfeits, unapproved, illegally imported, stolen, substandard, adulterated, and/or misbranded pharmaceutical products

(Annex 5-WHO Technical Report Series, No. 957, 2010)

A practice of distributing medicinal products and/or starting materials to ensure that their qualities are maintained along the distribution chain in accordance with the requirement and their intended use.

Techinical Guidelines on GDP 2012

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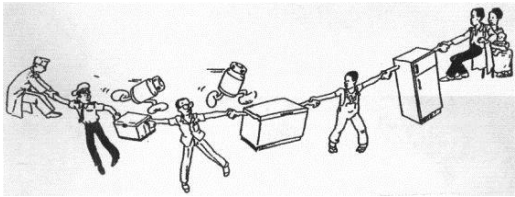
WHY IS GDP IMPORTANT ?

- Preservation of **product quality** down supply chain from manufacturer who implement GMP to distributor along the way down to retailers/consumers
- Prevention of the occurrence of **mix up & cross – contamination**
- Maintenance of **traceability** up to supply source (investigation)
- Facilitate prompt **product recall**



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GDP GENERAL PRINCIPLES

- The principles of Good Distribution Practices (GDP) are applicable to the aspects of procurement, storage, distribution and return of medicinal products and/or starting materials in the distribution chain.

- All parties involved in the distribution of medicinal products and/or starting materials responsible to ensure their quality and to maintain the integrity of the distribution chain throughout the distribution processes.

- The principles of GDP should also be applied to the donation of medicinal products, reference standards, and medicinal products for clinical trial.

- All parties involved in the distribution process should apply due diligence with adherence to the principles of GDP, for example, procedures relating to traceability and risk identification.

- There should be collaboration between all parties including governments, customs, law enforcement agencies, regulatory authorities, manufacturers, distributors and those responsible to the supply of medicinal products, ensuring the quality and safety of medicinal products and prevent the exposure of counterfeit medicinal products to the patients.

Source : Technical Guidelines on GDP, 2012

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LEGAL BASIS FOR IMPLEMENTING GDP

1. Drug Ordinance Stbl. 1949 No.419
2. Criminal Code (Kitab Undang-undang Hukum Pidana)
3. Law No. 5 of 1997 on Psychotropics
4. Law No. 35 of 2009 on Narcotics
5. Law No. 36 of 2009 on Health
6. Government Regulation No. 72 of 1998 on Controlling Pharmaceutical Preparations and Medical Devices
7. Government Regulation No. 51 of 2009 on Pharmaceuitical Practices
8. Ministry of Health Decree 1148/MENKES/PER/VI/2011on Pharmaceutical Wholesalers
9. Head of NADFC Decree No: HK .03.1.34.11.12.7542 of 2012 on the Technical Guidelines on Good Distribution Practices
10. Head of NADFC Decree No : HK.03.1.33.12.12.8195 of 2012 on the Technical Guidelines on Good Manufacturing Practices

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GDP ASPECTS

Quality Management

Organization, Management and Personnel

Premises and Equipment

Operations

Self Inspection

Complaints, Medicinal Products and/or Starting Material Return, Suspected Counterfeit and Recall

Transportation

Distributor By Contract

Documentation

Head of NADFC Decree No: HK .03.I.34.11.12.7542 of 2012 on the Technical Guidelines on Good Distribution Practices

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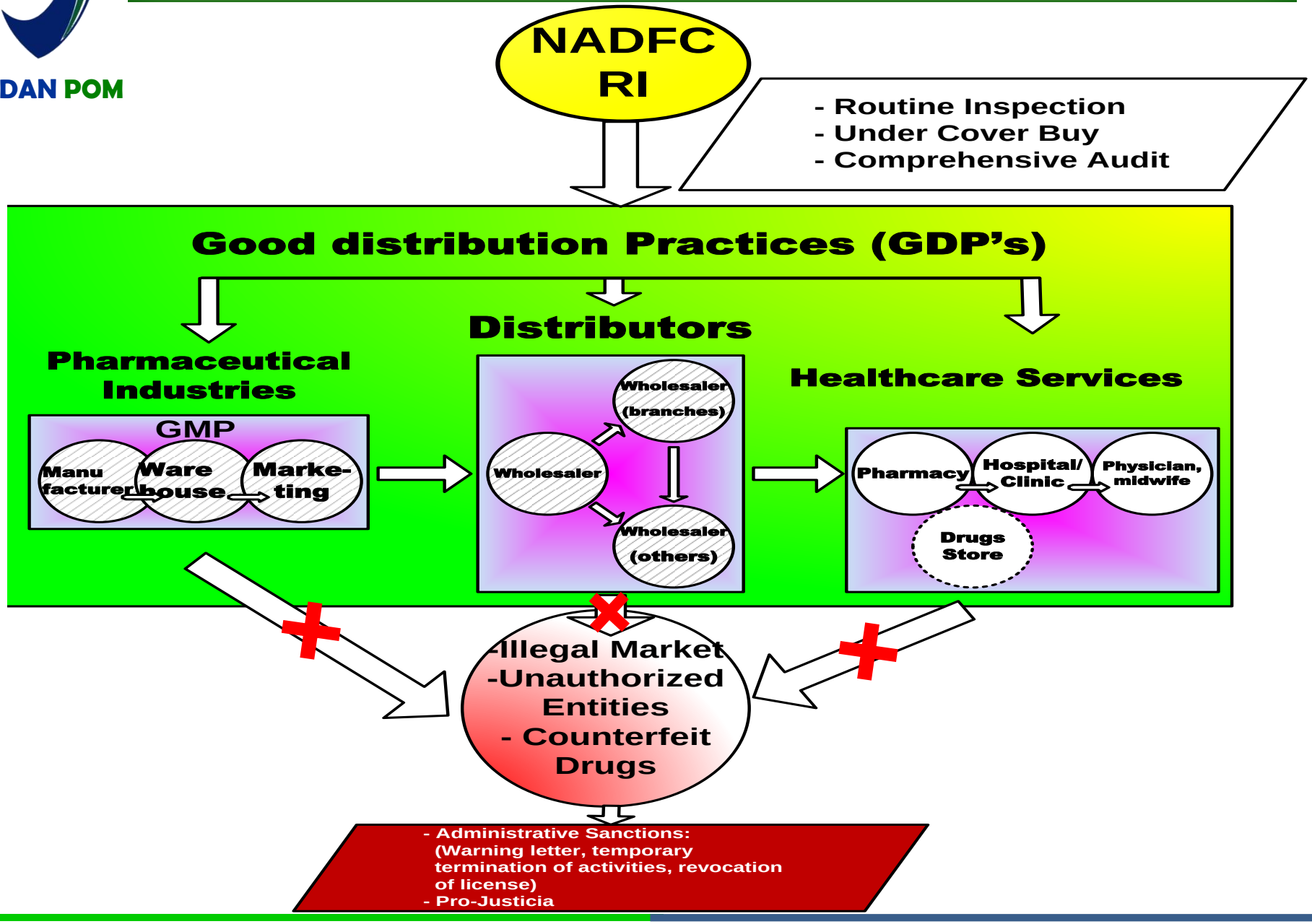
CONCEPT OF DRUG DISTRIBUTION CONTROL



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SPECIAL ATTENTION FOR INSPECTION BASED ON RISK

1. Documentation
2. Premises & Equipment
3. Operations
4. Transportation
5. Suspected Counterfeit/Illegal

Vaccines (CCP)	Narcotics and Psychotropics	Pharmaceutical Ingredients
✓ Need special storage requirements ✓ Sensitive to temperature fluctuation and extreme temperature	✓Addictive ✓Vulnerable to abuse	When the distribution chain is interrupted by manufacturing steps such as repackaging and relabelling, the principles of good manufacturing practices (GMP) should be applied to these processes.

COMMON GDP DEFICIENCES

Quality Management:

-Controlled documents e.g. SOPs were not subjected to periodic review

-SOPs do not reflect actual procedure performed

Premises and equipment:

◇Temperature monitoring device was not calibrated

◇Thermometer was not put in a place to monitor the highest daily temperature

◇Relative humidity (Rh) was not monitored

Operations:

-Batch number control was not adequately conducted

-No reliable system in place to ensure FEFO or FIFO

Self inspection:

◇Self inspection was not conducted

Distributor by contract:

-GDP aspects was not considered in a contract agreement with an expedition company.

GDP Roadmap

2003 - 2008

- GDP Guideline 2003 edition
- Technical Direction on GDP implementation
- GDP Inspection

2009

- Tools mapping Developed
- Training for GDP inspector
- GDP Inspection

2010 - 2012

- Training for GDP inspector
- Mapping dissemination
- Mapping on GDP implementation
  5% (2010), 15% (2011), 30% (2012)
- GDP Certification
  2% (2011), 10% (2012)
- **Technical Guidelines on GDP 2012 edition**
- GDP Inspection

2013 - 2014

- Training for GDP inspector
- Technical Guidelines on GDP dissemination
- Mapping on GDP implementation
  45% (2013), 60% (2014)
- GDP Certification
  25% (2013), 45% (2014)
- GDP Inspection

2015

- Training for GDP inspector (continue)
- Technical Guidelines on GDP dissemination (continue)
- Mapping on GDP implementation (continue)
- GDP Certification (continue)
- GDP Inspection

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IMPLEMENTATION STRATEGY

GDP MAPPING AND CERTIFICATION

General Objective

•Maintain the quality, validity and safety of the drug along the chain of distribution in accordance with the requirements and the intended use.

Special Objective

•Mapping

-Getting a picture of the real conditions of the GDP application on wholesaler in Indonesia

-Obtaining the data category wholesaler risk-based approach

•Certification

- Ensure the consistency of GDP implementation
- Ensure the consistency of medicines quality according to approved specifications.

918 wholesaler have been mapped from 2500 wholesaler (2010 – 2012)

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GDP CERTIFICATE FOR WHOLESALER (Voluntary)

Certification Application

Announced Inspection

- NADFC do inspection

Evaluation Inspection Report

CAPA

- Wholesaler do CAPA
- NADFC do evaluation

Certificate

- GDP Certificate for wholesaler that has implemented a GDP

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KEY MESSAGES

Improving PV Performance in Indonesia

- PV is one of strategic regulatory activity to ensure drug safety, with the goal is ensuring patient safety. NADFC will consistently promote PV Program in Indonesia.
- The roles and responsibilities shoud be shared amongst all key players, not only NADFC, but also PI/MAH, and HCPs
- Networking and cooperation with other stakeholders play important role in improving PV in Indonesia
- Safety measures based on Indonesia population need to be encouraged proactively. It can be done by Good PV Practices by all key players

Strengthening GDP Implementation in Indonesia

- Collaboration with academia to put GDP on the curiculum
- Dissemination
- Propose for mandatory GDP Certification

Terima kasih
THANK YOU
ARIGATO GOZAIMAS