Quality Assurance System and Pharmacovigilance in Taiwan

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Quality Assurance Systems in Pharmaceutical Regulation

- **Pharmaceutical Manufacture – GMP/cGMP; Inspection;**
- **Monitoring the Products on the Market – Sampling and Examination;**
- **Medical Product Defects Reporting System**
- **Product Recalls**

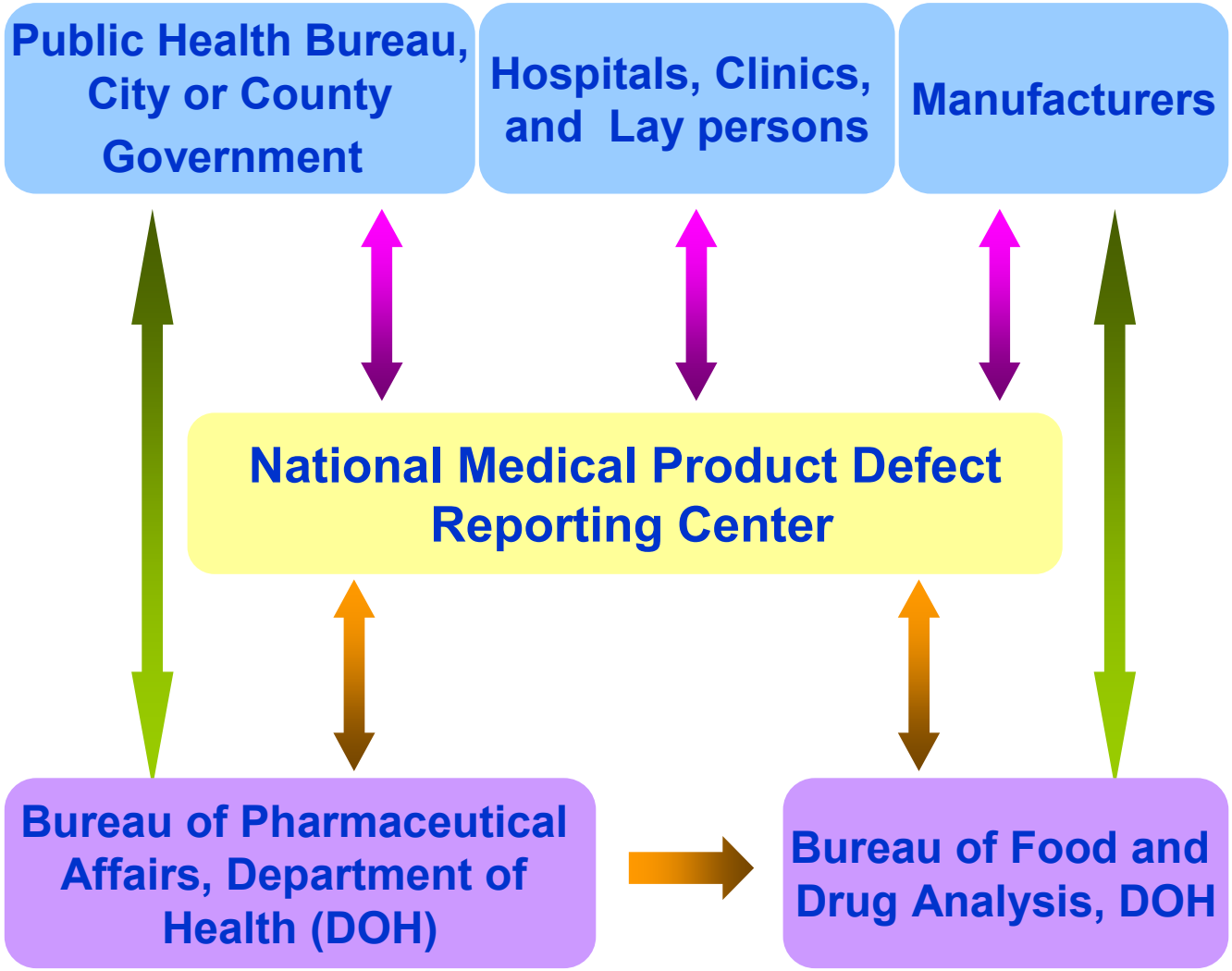
GMP

1982 ⇩ 1987	GMP was announced 5 yr program to implement the GMP 211 GMP pharmaceutical manufacturers by Dec. 1988.
1987	Started GMP Inspection
1991 ⇩ 1995	GMP applied to traditional herbal medicine manufacturer 67 GMP traditional herbal medicine manufacturers by Dec. 1995
1995 ⇩ 1999	Implementation the validation requirements: started with the validation of sterilization, then to the validation of backup system, equipment, assay method, process, etc.

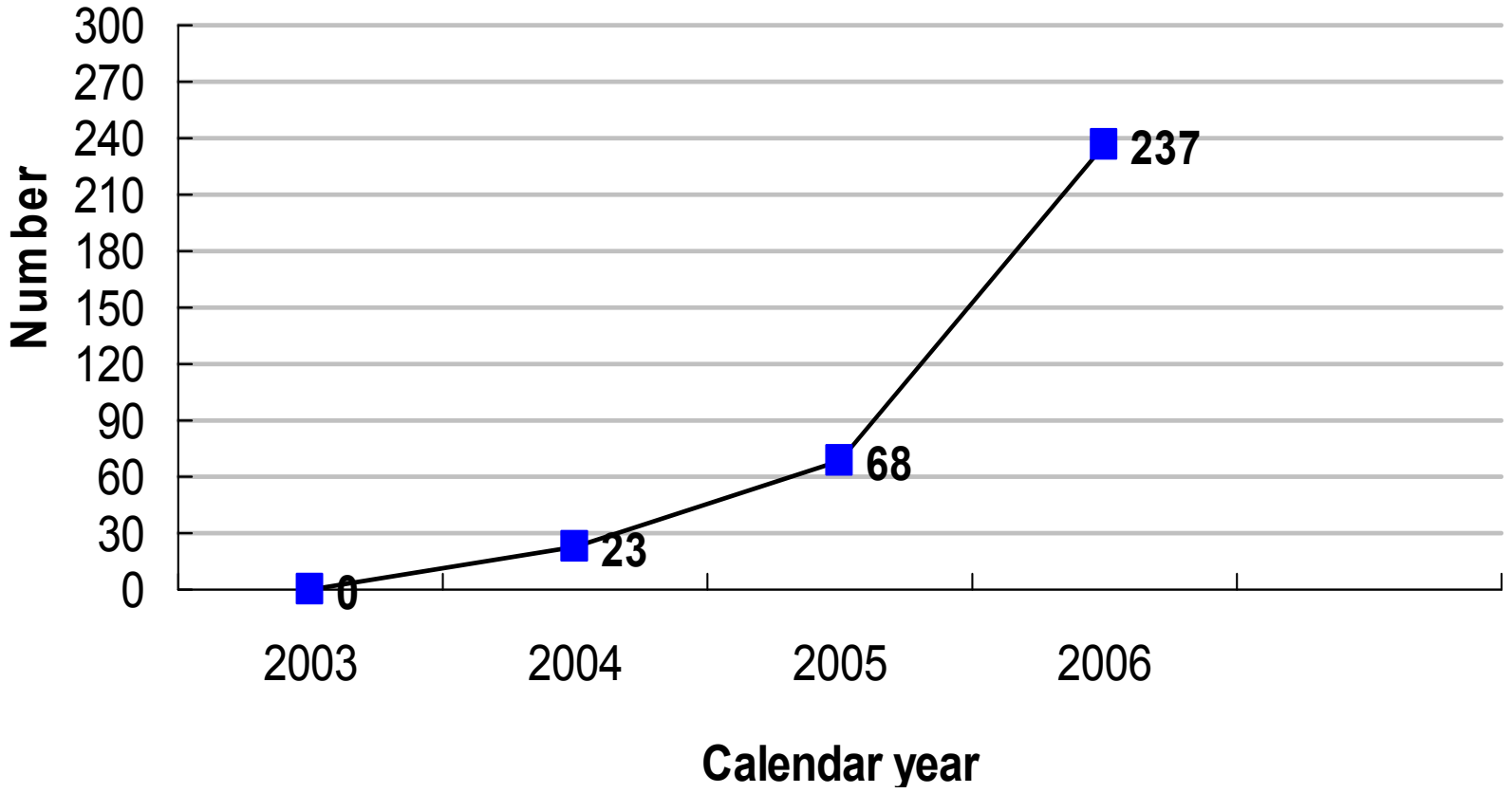
Reporting System of Medical Product Defects

- A pilot study in 2004, then started in 2005
- Objectives
  - An integrated quality enhancement program for medical products
  - A centralized reporting center
  - Reinforcement on the Recall Mechanism of Medical Products

National Medical Product Defect Reporting System



Medical Product Defect Reports



Up to April 2007, the number of report cases is 55.

Cases Analyses

Content of the Complaint	Number (%)	
	2005	2006
Abnormal in appearance	26 (38)	135 (57)
Cannot be used properly	8 (12)	18 (8)
Observed abnormality after drug dilution	0 (0)	5 (2)
Label related problems	7 (10)	25 (10)
Insufficient in package	18 (27)	32 (14)
Others: impurities, et al	9 (13)	22 (9)
Total	68 (100)	237 (100)

Recalls of Medical Products

Item	2005		2006	
	Imported	Domestic	Imported	Domestic
Drugs	3	4	3	1
Devices	3	0	14	0
total	6	4	17	1

Pharmacovigilance System in Taiwan

Pharmacovigilance in Taiwan

Pharmacovigilance is the science and activities relating to the collection, detection, assessment, understanding and prevention of adverse effects or any other drug related problems

- **identifying new information about drug hazards**
- **preventing harm to patients**

WHO definition

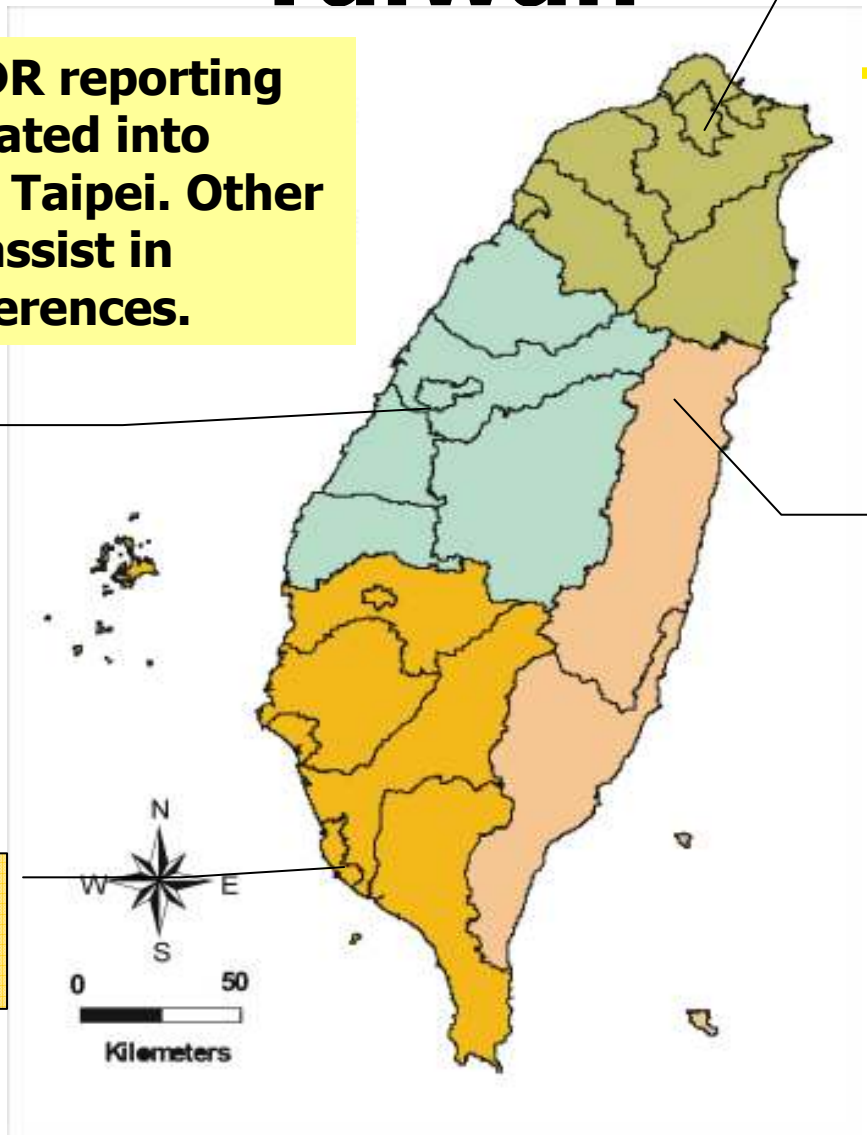
The Development of ADR Reporting System in Taiwan

Introduction

- Since 1998
- Include pharmaceutical products and medical devices
- The national ADR reporting center is operating inside the Taiwan Drug Relief Foundation (TDRF) (since 2002)
- TDRF was founded by government to assist the implementation of Drug Relief Act.

Taiwan

Since 2004, all ADR reporting tasks were integrated into national center in Taipei. Other regional centers assist in holding ADR conferences.



The Development of ADR Reporting System in Taiwan

- **A web-based reporting system (adr.doh.gov.tw)**
  - ✓ ***Provide updated information of drug safety and related pharmaceutical regulation issues to the public***
  - ✓ ***On-line submission of ADR reports through the web system.***
- **National ADR Electronic Database**
  - ✓ ***SAE reports of clinical trials***
  - ✓ ***Postmarketing ADR reports***
  - ✓ ***MedDRA terminology is adopted***

Website of Pharmacovigilance in Taiwan

http://adr.doh.gov.tw/

http://adr.doh.gov.tw/ADR-eng/index.htm

- A Platform for Safety Information Exchange
- Provision of Information of Reporting Center and DOH
- Electronic On-line Reporting Mechanism

http://adr.doh.gov.tw/default.asp

ADR Reporting Database

- On-line reporting allows people to submit ADR reports directly through website and keep their own copy. Then the reports from website are electronically transferred to the database in the National Center.
- ATC code and MedDRA coding are adopted in 2005. All the cases in the database were retrospectively coded since then.

Amendments of Pharmaceutical Affair Act - April 2004

Article 45

The central health authority may set a specific period of time to monitor the safety of medicaments approved for manufacturing or import.

The central health authority shall establish measures for license holders to compliance to during the safety monitoring period.

Detail Regulations of Monitoring the Safety of Medicaments was announced on September 2004.

Amendments of Pharmaceutical Affair Act - April 2004

Article 45-1

Medical care institutions, pharmacies, and license holders shall report any serious adverse reactions of medicaments. Regulations regarding method, content, and matters to be complied with shall be established by the central health authority.

Regulations Governing the Reporting of Serious Adverse Reactions of Medicines

- **Announced on August 2004**
- **Article 3**

  When a suspected serious adverse drug reactions occurred, the medical care institutions, pharmacies, and pharmaceutical license holders shall, in accordance with this set of Regulations, fill out a report and submit it, along with any other relevant documents, to the central competent health authority or its commissioned agencies.

Article 4

The serious adverse reactions mentioned in this set of Regulations refer to one of the conditions of the following subparagraphs:

- **Death;**
- **Life threatening;**
- **Permanent disabilities;**
- **Congenital anomalies of fetus and infants;**
- **Resulting in hospitalization of patients or extension of patients' hospital stay;**
- **Other conditions that may result in permanent injuries requiring treatment.**

Article 5

- Medical care institutions and pharmacies shall, **within seven days** upon knowing of the serious adverse reactions of medicines mentioned in Subparagraph 1 and Subparagraph 2 of the preceding Paragraph, make report in accordance with regulations of Article 3, and make a copy to pharmaceutical license holders.
- If information of the report mentioned in the preceding Paragraph is not complete, it should be supplied **within fifteen days.**

Article 6

- Pharmaceutical license holders shall, **within fifteen days** upon knowing of the severe adverse reactions of medicines, make report in accordance with regulations of Article 3.

Reporting procedure

Domestic ADR cases
(hospitals, pharmacies, manufactures, publics)

ADR Reporting Center

Follow up

Cases upload and evaluation

ADR Electronic Database

Reevaluation procedure

Death events related to suspected drugs

Drugs with high ADR reporting rate

Drugs pass surveillance period in the previous year

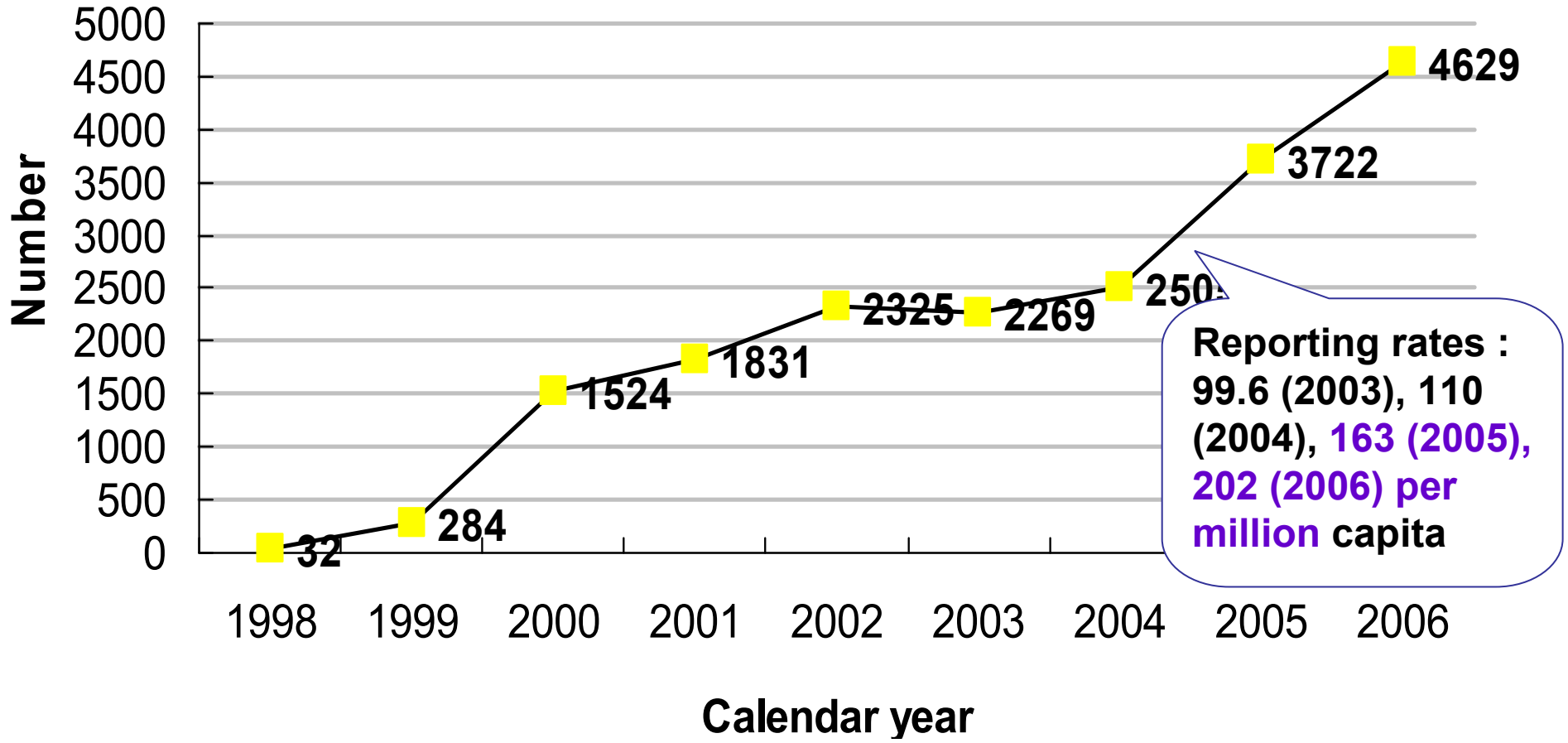
Preliminary evaluation and literature review by ADR Center staff

Investigated by reviewers and further discuss in Drug Safety Committee meeting

Drug evaluation reports and recommendation

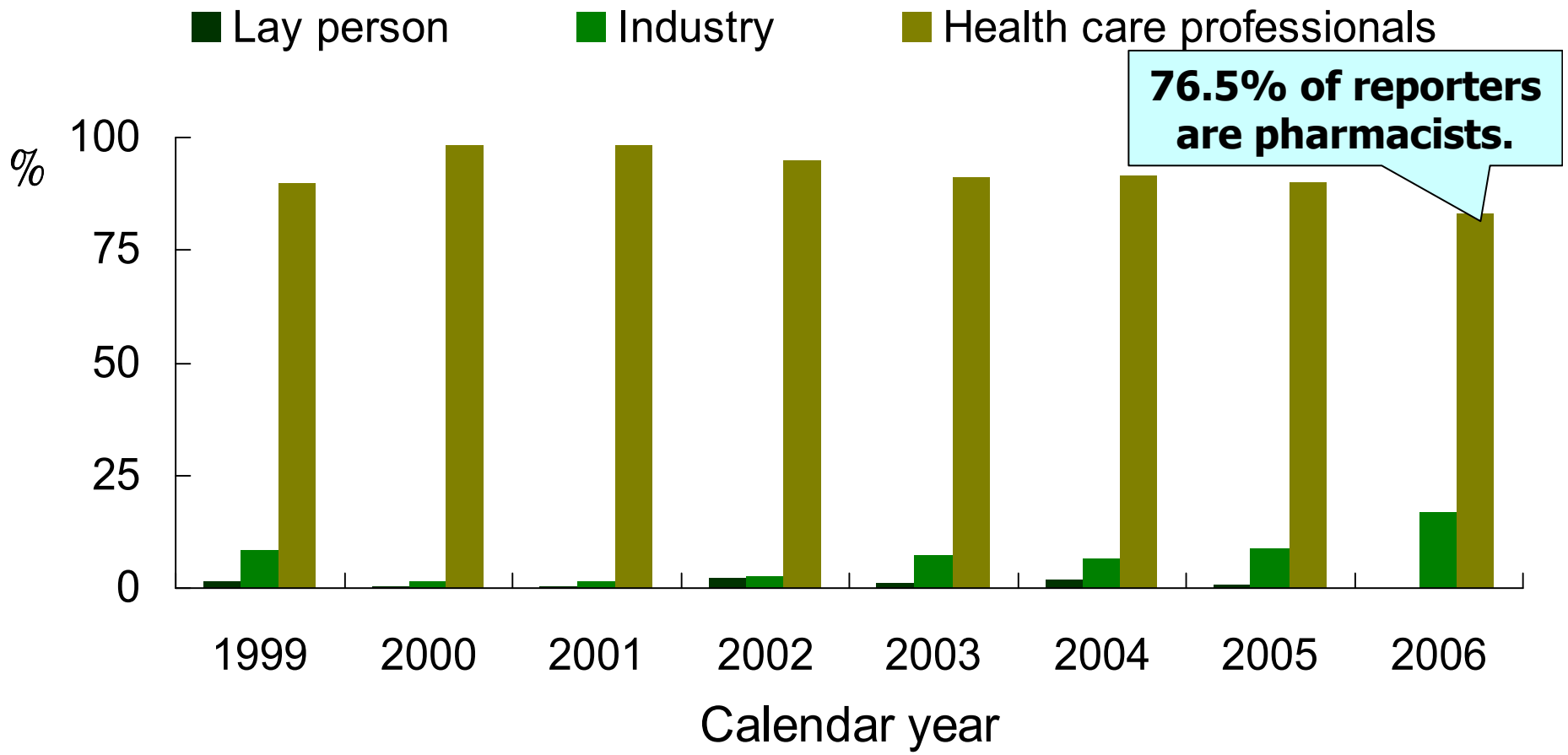
BPA final decision

Post-marketing ADR Reports



Up to April 2007, the number of report cases is 2271.

ADR Reports by Reporting Resource



Reevaluation for Drugs of Safety Concerns From 2003 to 2006

PPA	Benzbromarone	Carbamazepine	Acitretin
Cisapride	Diclofenac	Allopurinol	Basilimax
Indomethacin	Fenoverine	Ginkgo biloba extract	Benzonate
Thioridazine	Terfenadine	Coenzyme Q10	Enoxaparin
Amiodarone	Silymarin	Lamotrigine	Ofloxacin
Antacid containing aluminum		Phenytoin	
Antidepressants (bupropion, Citalopram, fluoxetine, fluvoxamine, mirtrazapine, paroxetine, sertraline, escitalopram, venlafaxine)			
Glocuronolactone & glucuronic acid			
Selective Cox-2 Inhibitors (celecoxib, etoricoxib, valdecoxib); preferential Cox-2 inhibitors (meloxicam, etodolac, nebumetone, nimesulide)			
Diane-35 (cyproterone acetate and ethinyloestradiol)			
NSAIDs (Diclofenac, ketoprofen, ketorolac, mefenamic acid, aspirin,ibuprofen, naproxen, sulidac, idomethacin, nabumeton, piroxicam, tenoxicam, surgem)			

Drug Safety Newsletter

- in Chinese version
- published quarterly since 2003
- drug safety information for new drugs
- review of collected ADR reports
- evaluation of cases applied for drug relief payment
- news of activities and others

Prospection in Pharmacovigilance

- **Signal detection and evaluation on the signal from postmarketing ADR reports**
- **Establishing the Good Pharmacovigilance Guidance**
- **Implementation of pharmacovigilance planning**
- **Better communication tools to reach out healthcare providers and patients**

財團法人醫藥品查驗中心
Center for Drug Evaluation

Regulation, for Life

Thank You for Your Attention

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