ADVERSE DRUG REACTIONS REPORTING BY CONSUMERS IN THE STATE OF PENANG, MALAYSIA: PERSPECTIVES FROM HEALTHCARE PROFESSIONALS AND CONSUMERS

by

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LIST OF ABBREVIATIONS

ADRs.....Adverse Drug Reactions

ADRAC……... Australian Adverse Drug Reaction Advisory Committee

AME…….. Adverse Medical Event

CIOMS……. Council for International Organizations of Medical Science

CPs…….Community Pharmacists (MY)

DGV…… Dutch Institute for Rational Use of Medicine

DoH ……... Department of Health (UK)

EMEA……. European Medicines Evaluation Agency

FDA …….Federal Drugs Agency

GP…….. General Practitioner (MY)

HCP……... Healthcare Professional

ISMP…….. Institute for Safe Medication Practices

JCAHO…….. Joint Commission on Accreditation of Healthcare Organizations

MADRAC……. Malaysian Adverse Drug Reaction Advisory Committee

MHRA…… Medicines and Healthcare Products Regulatory Authority (UK)

MPA (LV)……... Medical Products Agency (Läkemedelverket) S

NSAIDS……... Non-steroidal Anti-inflammatory Drugs

OTC ……Over The Counter

RF……... Reporting Form

PSUR…….. Periodic Safety Update Report

WHO…… World Health Organization

WHO-UMC ……..WHO-Uppsala Monitoring Centre

PELAPORAN KESAN MUDARAT UBAT OLEH KONSUMER DALAM NEGERI PULAU PINANG, MALAYSIA: PERSPEKTIF PROFESIONAL KESIHATAN DAN KONSUMER

ABSTRAK

Pemonitoran kesan mudarat ubat adalah perlu untuk mengurangkan atau mencegah bahaya kepada pesakit yang berpunca daripada ubat-ubatan yang mereka ambil. Pertama, kajian ini membandingkan sistem ubat di Malaysia, Australia dan Sweden serta menilai beberapa aspek penting dalam kalangan profesional kesihatan terhadap kesan mudarat ubat dan farmakovigilans. Analisis perbandingan telah menggunakan Model *Leavitt's Diamond yang* telah disesuaikan oleh Scott dalam beberapa komponen. Struktur, proses dan hasil akhir sistem keselamatan ubat di ketiga-tiga negara digunakan sebagai pembolehubah dan ukuran hasil akhir. Kemudian kajian kes telah dijalankan di Pusat Sejahtera, Universiti Sains Malaysia melibatkan profesional kesihatan dan pesakit. Akhir sekali, kajian ini meneliti persepsi orang ramai tentang kesan mudarat ubat dan menilai persepsi doktor klinik swasta dan ahli farmasi komuniti di Pulau Pinang tentang pelaporan kesan mudarat ubat oleh konsumer. Kajian ini menggunakan kedua-dua kaedah kajian kualitatif dan kuantitatif. Penyelidik menggunakan soal selidik yang telah disahkan dalam kajiselidik dalam kalangan profesional kesihatan dan orang ramai. Data dan maklumat telah dikumpul secara bersemuka dengan responden dan mel. Kaedah statistik deskriptif dan inferensi bukan parametrik telah digunakan dalam analisis; paras alfa adalah 0.05. Keputusan kajian menunjukkan sistem di ketiga-tiga negara adalah berbeza dari segi keperluan laporan, pengurusan laporan, sumber yang dibelanjakan dan pertukaran maklumat. Australia dan Sweden mempunyai pelaporan oleh konsumer yang betul dalam sistem keselamatan ubat dan negara-negara ini mempunyai pelaporan kesan mudarat dan penglibatan konsumer yang

lebih berkesan berbanding Malaysia. Dapatan kajian kes di Pusat Sejahtera menyarankan kebolehlaksanaan untuk membangunkan program farmakovigilans di universiti bagi pelaporan kesan mudarat ubat oleh konsumer. Tahap pengetahuan yang lemah dalam kalangan profesional kesihatan dan konsumer menyarankan perlunya intervensi pendidikan dan strategi penambahbaikan bagi memudahkan mekanisme pelaporan. Daripada 500 orang awam yang disoalselidik, 230 (46%) adalah lelaki dan 270 (54%) perempuan. Lebih daripada satu pertiga (38.2%) tidak tahu definisi kesan mudarat ubat dan 52.6% tidak boleh membezakan antara kesan mudarat dan kesan sampingan ubat. Sebaliknya, ramai responden mampu mengaitkan kesan mudarat ubat dengan situasi seharian berdasarkan pengalaman mereka (54.2%), dan hanya 48.2% dakwa doktor dan ahli farmasi ada menyuruh mereka melaporkan kesan mudarat ubat. Responden bersetuju tentang dua perkara: iaitu setiap orang tidak kira umur boleh mengalami kesan mudarat ubat (60.8%) dan pengumpulan data kesan mudarat ubat (96.4%) adalah sangat penting. Doktor klinik swasta dan ahli farmasi komuniti sedar tentang kepentingan dan faedah laporan oleh konsumer; 88% merasakan pelaporan sebegitu akan membawa lebih faedah kepada program farmakovigilans sedia ada. Pelaporan ini akan menambah lebih faedah kepada program sedia ada di Malaysia, walaupun terdapat rintangan dalam kalangan responden yang sangsi bahawa pesakit boleh menulis laporan yang sah serupa dengan laporan ahli profesional kesihatan. Ringkasnya, laporan kesan mudarat ubat di Malaysia perlu ditambahbaik dengan meningkatkan tahap kesedaran kesemua pemegang taruh dalam sistem penjagaan kesihatan. Konsumer perlu lebih pendidikan tentang ubat-ubatan mereka, bagaimana untuk mengesahkan sebarang komplain tentang penggunaan ubat, bagaimana untuk melaporkan dengan betul dan menyalurkan ia kepada individu atau badan yang betul.

ADVERSE DRUG REACTIONS REPORTING BY CONSUMERS IN THE STATE OF PENANG, MALAYSIA: PERSPECTIVES FROM HEALTHCARE PROFESSIONALS AND CONSUMERS

ABSTRACT

It is essential to monitor adverse drug reactions (ADRs) in order to minimize or prevent harm to patients arising from their medicines. This study first compares the drug systems used in Malaysia, Australia and Sweden, and assessing several substantial aspects among the professionals in healthcare against ADR and pharmacovigilance. A comparative analysis that makes use of Leavitt's Diamond Model has been adapted by Scott in terms of several components. The structure, process and the outcome of the drugs' safety system in all three countries become the variables and outcome measure in this research. Then a case study was conducted involving healthcare professionals and patients at the University Wellness Center (UWC), Universiti Sains Malaysia. Finally, this study explores the perceptions of the public on ADRs and assessing the perceptions of the GPs (general practitioners) and the community pharmacists on consumers' ADR reporting in Penang. This study used both qualitative and quantitative research methods. The researcher utilized validated questionnaire in the survey among healthcare professionals and public. Both face-to-face and mail survey methods were used to gather data and information. Descriptive and non-parametric inferential statistics were utilized for analysis; alpha level used was 0.05. Findings show that the systems of the three countries are different with regards to reporting requirements, report handling, resources spent and the exchange of information in the environment. Australia and Sweden have proper consumer reporting in drug safety systems and these countries have more effective

ADR reporting and consumer involvement than in Malaysia. The findings of the case study in UWC suggest the feasibility for establishing a university based pharmacovigilance program for consumer reporting. Poor knowledge among the HCPs and consumers suggests the urgent need for educational interventions among HCPs in UWC and improvement of strategies to ease the reporting mechanisms. From 500 general public surveyed, 230 (46%) are male and 270 (54%) female. More than one-third (38.2%) do not know the definition of ADRs and 52.6% cannot differentiate between an ADR and side effects. In turn, a lot of the respondents have been able to link ADRs with real-life situations based on their experiences (54.2%), and only 48.2% claim that physicians and pharmacists did ask them to file ADR reports. They are in agreement about two things: that everyone, regardless of age, can suffer from ADRs (60.8%); and data collection on ADRs (96.4%) is very important. The GPs and CPs were aware about the importance and benefits of consumer reporting; 88% feel that such a reporting will bring more benefits to the existing pharmacovigilance programme. Such reporting will add more benefits to the existing programmes in Malaysia, although the barrier was the perception that respondents doubted if the patients can write valid reports similar to HCP reports. In summary, ADR reporting in Malaysia needs to be improved by increasing the level of awareness of all stakeholders in the healthcare system. The consumers need more education about their medications, how to validate any complaints they have about the drug consumption, how to file a proper report and channel it to the 'right' person or bodies.

CHAPTER 1

INTRODUCTION

1.1 Introduction

Every medication is potentially hazardous and can cause substantial harm to the recipient with varying degree of injury. One of the potential hazards that accompany the use of most types of medications is Adverse Drug Reactions (ADRs). ADRs can cause short- and long-term hospitalization, morbidity and even can lead to mortality (WHO, 1972).

The World Health Organization (1972) defines an ADR as 'any response to a drug that is noxious and unintended, and that occurs at doses used in humans for prophylaxis, diagnosis, or therapy, excluding failure to accomplish the intended purpose' (Lee and Thomas, 2003). The WHO reported that ADRs are responsible for a significant number of hospital admissions with reports ranging from 0.3% to 11% of overall hospitalizations (WHO Collaborating Centre for International Drug Monitoring, 2002). For instance, it has been estimated that over 770,000 people are injured or die each year from adverse drug events (Classen, et al., 1997). A commonly quoted meta-analysis performed in the United States (US) indicated that ADRs were between the fourth and sixth most common cause of death in 1997 (Lazarou et al., 1998), suggesting a major consideration for the entire healthcare system.

Hospital admissions due to ADRs have been reported as 300,000 admissions per year in the United States (Atkin et al., 1995), and accounted for 6.5% of total hospital admissions (Jha et al., 2001); in Canada 12% of hospital admissions were reported due to ADRs (Grymonpre et al., 1988); in the UK 6.5% of hospital

admissions were related to ADRs, with the ADR directly leading to admission in 80% of these cases (Pirmohamed, 2004); 13% of hospital admissions in France, (Pouyanne et al., 2000); in India 6.7% of hospital admissions (Malhota et al., 2001); and the worldwide reports range at an average between 0.2-21.7% of overall hospital admissions (Einarson, 1993).

Looking at the scenario of ADRs in developing countries, only a few studies have examined the rate of ADRs in developing countries. A prospective observational study from Iran found 11.8% of patients had experienced at least one ADR (Pourseyed et al., 2009). In another study from Iran, approximately 16.8% of patients had at least one ADR and 2.9% of the ADRs were identified as 'lethal' (Gholami and Shalviri, 1999). A study from South India reported an overall incidence of 9.8%. This included 3.4% ADR-related admissions and 3.7% of ADRs that occurred during the hospital stay (Arulmani et al., 2008). In Nepal, the prevalence of ADRs was 0.86%, the male to female ratio was 0.85, and 10.81% of the ADRs were considered 'severe' (Jha et al., 2007).

The mortality due to ADRs is also a substantial problem. For instance, deaths due to ADRs in the US amount to 160,000 deaths annually (Shapiro et al., 1971); in the UK, the corresponding figure was 1044 deaths (Eaton, 2002). In France ADRs accounted for 0.12% of deaths (Pouyanne et al., 2000), and in Germany 1.6% deaths of hospital admissions (Riettling, 2000).

The above statistics on hospitalization and mortality due to ADRs highlight the fact that it is essential to monitor ADRs in order to minimize or prevent harm to patients arising from their medicines; to detect ADRs before they are clinically manifested, and to obtain more knowledge to ensure safe use of medicines, and to

assess the harms, benefits, and risks of available drugs (WHO Collaborating Centre for International Drug Monitoring, 2002).

During the past decade concerns over ADRs have widened to include herbal, traditional and complementary medicines, blood products, biological agents, medical devices, and vaccines (WHO Collaborating Centre for International Drug Monitoring, 2002). A few other areas are also of relevance to pharmacovigilance (which the study will be focusing on in later paragraphs), including substandard medicines, medication errors, lack of accurate reports, use of medicines for indications that are not approved and for which there is inadequate scientific basis, case reports of acute and chronic poisoning, assessment of drug-related mortality, abuse and misuse of medicines, and adverse interactions of medicines with chemicals, other medicines, and food. Thus, the science of safety monitoring should not be viewed only as a mere study on ADRs but rather should enclose the broad perspective of patient safety during the healthcare process.

On examining from the chronological perspective, this subject first appeared on the medical scene 50 years ago. Following the thalidomide disaster in the 1960s, which resulted in embryonic malformations in thousands of children whose mothers had used drugs during pregnancy, interest in the safety of medicine emerged.

In the 1960s, the WHO began the global monitoring of the safety of drugs and highlighted the need for pharmacovigilance because the information that was gathered before marketing any specific drug has always been incomplete (WHO Collaborating Centre for International Drug Monitoring, 2002) . In response to this, according to Olsson (2001), pharmacovigilance has been established in most countries, and it is 'the science relating to the detection, assessment, understanding and prevention of adverse effects or any other possible drug-related problems.'

Testing the effects of a medicine on animals cannot be used as evidence for toxicity in human beings, and any tests carried out on the latter during clinical trials involve only small numbers. Therefore, the effects of a medicine can only be assessed properly when the drug is widely used, and differences among countries may occur (WHO Collaborating Centre for International Drug Monitoring, 2002).

1.2 Pharmacovigilance and the human's rights

Pharmacovigilance may have stemmed from the awareness that the highest level of health standard is one of the basic human rights, as suggested in the declaration of Alma-Ata [Declaration of Alma-Ata,1978]. The term 'Health' does not only mean that the services of the health system must be available to all according to their needs, and does not depend only on the results of treatment, but also equally important, is the course of this process, for example, transparency, participation, equality, and fairness (Hunt and Beckman, 2008). Access to health services and information and the right to the highest attainable standards of health and health information enhance the health of both individuals and communities. A degree of transparency ensures that all key partners including the patients, the public and private sectors, international organizations and civil organizations will receive the correct treatment.

Similarly, the participation of everyone on issues that affect and have an impact on human health is a right for all, and includes participation in defining strategies, development, and policy-making, implementation and accountability, according to the declaration of Alma-Ata [Declaration of Alma-Ata, 1978]. Fairness and equality are among the most basic elements of international human rights (Hunt and Beckman, 2008).

1.3 Need for local pharmacovigilance programs in every country

Although there has been an International Drug Monitoring Program coordinated by WHO, still there is definite need for indigenous pharmacovigilance programs. It is because differences exist among countries (and even regions within countries) in the occurrence of ADRs and other drug-related problems. This may be due to the existence of differences in disease, prescribing practices, genetics, diet, traditions, drug manufacturing processes, which influence pharmaceutical quality and composition, and drug distribution and use, including indications, dose and availability of medicines (Olsson, 2001).

In addition, the use of traditional and complementary drugs may pose specific toxicological problems, when used alone or in combination with other drugs. Hence, data derived from within a country or region may have greater relevance and educational value and may encourage national regulatory decision making. Information obtained in one country (e.g., the country of origin of the drug) may not be relevant to other parts of the world, where circumstances may differ. Therefore, drug monitoring is of tremendous value as a tool for detecting ADRs and specifically in relation to counterfeit and substandard quality products. ADR monitoring helps ensure that patients obtain safe and efficacious products.

1.4 Drug regulation in Malaysia

In the Malaysian context, pharmaceuticals are regulated by the Drug Control Authority (DCA) under the control of the Drugs and Cosmetics Regulation Law passed in 1984. The DCA is managed by the Director General of Health, the Director of Pharmaceutical Services, the Director of the National Pharmaceutical Control

Laboratory and seven appointed members. It is the responsibility of the DCA to ensure the safety, quality, and efficacy of pharmaceuticals in Malaysia. Some of its duties include reviewing registration applications for drugs and cosmetics, licensing importers, manufacturers, and wholesalers, postmarketing safety surveillance of medicines, and ADR monitoring. (“BPFK”, 2013).

1.5 Existing pharmacovigilance program in Malaysia

Malaysia has a well established national centre of pharmacovigilance, namely the National Adverse Drug Reaction Monitoring Centre, which has a national coverage. Some major hospitals and pharmaceutical companies also operate ADR monitoring systems under it. One can report ADR either directly to the national center or through the hospitals and pharmaceutical companies that run pharmacovigilance programs which are then consolidated at the national center. Reports from doctors, pharmacists and dentists are made on a voluntary basis but reports from marketing authorization holders are mandatory. The centre monitors drugs for human use, vaccines, biological and herbal remedies, using prepaid postage report forms or report cards that are updated every month. It also records ADRs manually, and has a local database. The national centre has an advisory committee that assesses the causality of the reported ADRs (Lei et al., 2007). The Malaysian Adverse Drug Reaction Advisory Committee (MADRAC) was established under the Drug Control Authority (DCA) to monitor the safety profiles of drugs registered for use in Malaysia. The MADRAC provides the DCA with information pertaining to drug safety issues that occur locally and internationally. The National Drug Safety Monitoring Centre, which is the secretariat to MADRAC, was accepted as the 30th member of the WHO Safety Monitoring Program in 1990. Under this program, all ADR reports that have

been received and screened by MADRAC are submitted to the Uppsala Monitoring Centre in Sweden for inclusion in the WHO database.

MADRAC also promotes ADR reporting in Malaysia, and provides information and advice to the DCA so that regulatory action can be taken based on the ADRs received. It also provides information to doctors, pharmacists and other healthcare professionals on ADRs and participates in the WHO ADR monitoring program. A total of 7079 reports were received in the year 2010 which follows the ascending trend since year. This figure is a 21% increase from year 2009. Of the 7079 reports received, 5976 reports (84.4%) were sent in by healthcare professionals from the government sector. This is an increase from last year's 4698 reports from the government sector. The year 2010 also showed an increase (72.2%) in the number of ADR reports from private healthcare professionals (248 reports) compared to 2009 (144 reports). However, reports from Marketing Authorisation Holders (MAH) saw decreasing trend since year 2008. There was also an increase in the number of reports from the 'Others' category of reporters due to the higher number of reports submitted by nurses (338 reports) in accordance with the HPV national immunisation programme. Only 7 reports were submitted by consumers (MADRAC, 2011).

For all reports in year 2010, Selangor state contributed the highest number of ADR reports (1557; 22.0%), followed by Sabah (886; 12.52%) and Perak (845; 11.9%). All other states exhibited an encouraging increase in the number of ADR reports submitted compared to year 2009 except for Johor, Melaka, Penang and Sarawak. Classification of all reports according to SOC indicated that most adverse events reported were of the '*Skin and Appendages Disorders'* SOC (20.2%) followed by '*Body as a Whole – General Disorders'* SOC (16.7%) and '*Central and*

Peripheral Nervous System Disorder' SOC (15.4%). The reports involved 7753 suspected products, of which 7134 (92.0%) were prescription products while 443 (5.7%) were non-prescription products. The remaining 176 products (2.3%) involved were traditional products, cosmetic products, food products and unregistered products. Out of 5569 reports involving prescription products (excluding vaccines), more than half (56.9%) reported suspected drugs from the following 3 pharmacological groups i.e. *Cardiovascular* (26.1%), *Anti-infective* (21.0%) and *Analgesic* (9.8%). This follows the trend in year 2009 where the top 3 major pharmacological groups were also *Cardiovascular, Anti-infective* and *Analgesic.* In 2010, there was a surge in reports for vaccines (1565 reports) compared to the figure in 2009 (242 reports). This is due to the launching of the national Human Papillomavirus (HPV) immunisation programme as well as the usage of H1N1 vaccines in lieu of the H1N1 pandemic (MADRAC 2011).

The ADR monitoring center in Malaysia also makes recommendations to the drug control authority on labeling changes, restrictions on use and suspension or withdrawal of drugs from the market. The center also carries out assessment of the signals through manual screening for potential signals, maintains the local database and the WHO database, and examines the medical literature to analyze and understand ADRs to be brought up for discussion with the advisory committee which is a subcommittee to the drug control authority in Malaysia. This committee convenes six times a year (Olsson, 1999). Figure 1 depicts the existing Malaysian Pharmacovigilance Program.

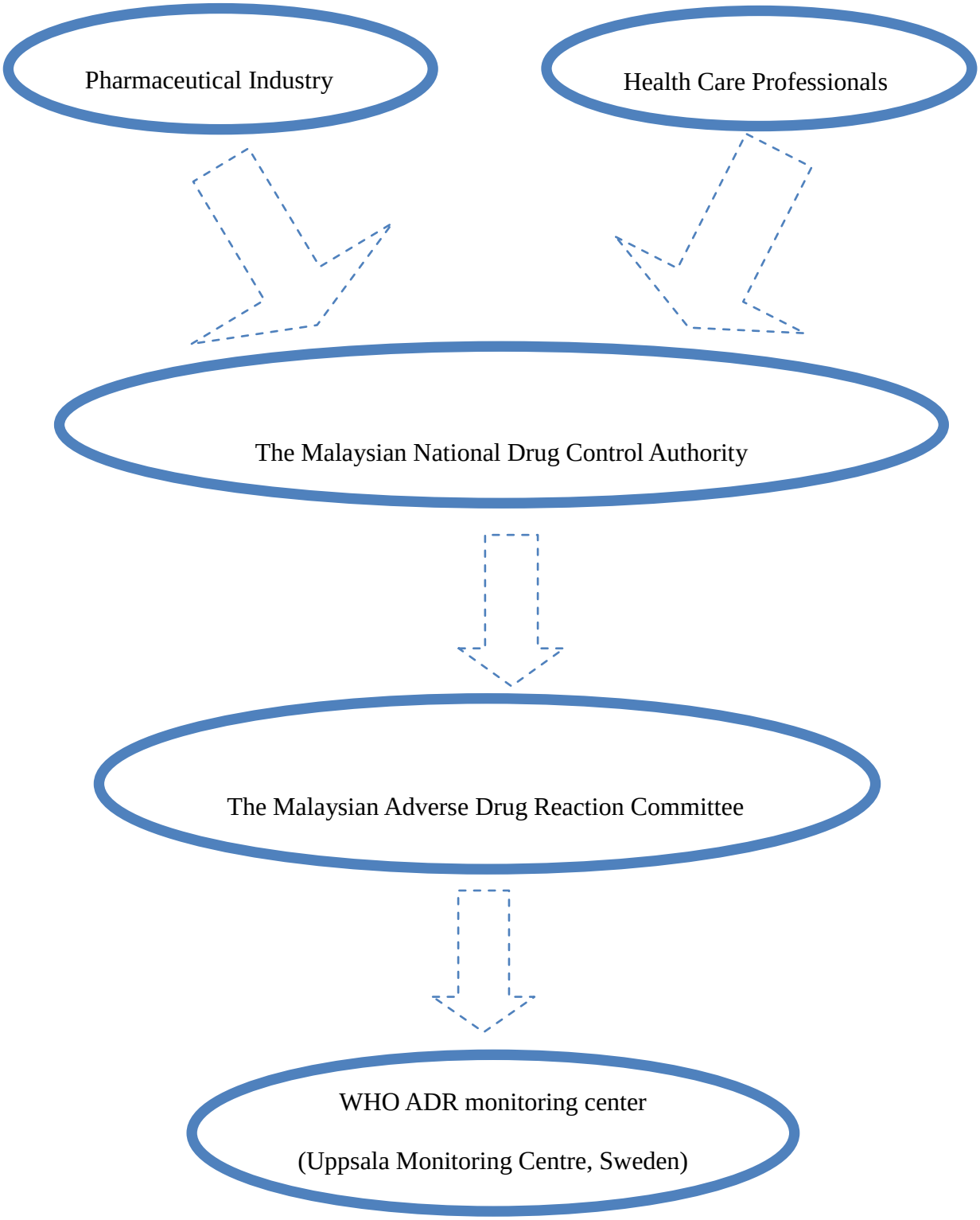

Figure 1.1: Malaysian Pharmacovigilance Program

1.5.1 Weaknesses of the existing national pharmacovigilance program in Malaysia

Although the existing pharmacovigilance program provided a strong base for drugs, drug safety and related activities it has few limitations. To name some, there is lack of awareness among health professionals regarding pharmacovigilance (Lei et al., 2007). Similarly, there is difficulty in signal generation, because there is no national computerized database on drug prescriptions available in the country. In addition, there is a lack of information generated on genetic effects, social practices and drug interactions associated with drug use and there is a scarcity of reports about traditional and herbal drugs which are widely used. The weaknesses seem to have originated from many angles; from the health professionals themselves, the government authority, and even the public.

Another major limitation of the program is underreporting of ADRs. A study by Aziz et al. (2007), reported a high proportion (81.4%) of the respondents to have suspected an ADR but not reported it, while about 40% of the respondents were not even aware of the existence of the national reporting system in Malaysia. Other reasons for underreporting include uncertainty regarding the types of reaction to report, and a lack of awareness about the existence, function, and purpose of the national ADR reporting scheme (Aziz et al., 2007). Thus the number of ADR reports received by the national centre is extremely low; although, this number has increased in recent years. Another limitation is the lack of availability of an official consumer reporting system, which limits reporting occurring at the consumer level; and there is a lack of involvement of nursing staff in the ADR monitoring program.

1.6 Consumer reporting of adverse drug reactions

In the global scenario , the existing ADR reporting system depends on spontaneous reports submitted by doctors, pharmacists, and pharmaceutical companies thus limiting the experiences from consumers. When consumers become involved in the process, they can reinforce their rights and ensure that they receive proper care in the future. Consumers' experiences and views can be used as a good tool to provide information about ADRs. Reporting by consumers about the possible harmful effects of drugs has been in place for almost 15 years in developed countries. Such reporting increases the amount of knowledge, and serves as significant indicators of the damage resulting from incorrect usage of medicines (WHO Newsletter, 2000).

However, only a few countries currently accept patient reports: Sweden (1978), Denmark (2003), Netherlands (2004), USA (1993), Canada (2003), Australia (2003), and UK (2005), (the year in the bracket means the year the system started) (de Langen et al., 2008, Medawar and Herxheimer, 2003). Consumers in these countries can report directly to medical agencies or indirectly through consumer organizations. They can also submit electronic reports or paper based reports and even telephone reports.

Experience in the Netherlands obtained over a 3 year period showed that patient reporting can be a good source of information for drug safety monitoring and has qualitative and quantitative value. An evaluation of the first six months of patient reporting via the yellow card scheme in the United Kingdom showed that there were no differences in the proportion of serious ADRs reported, compared with reports made by health professionals (McLay et al., 2006).

1.6.1 Benefits of incorporating consumers in ADR reporting programs

As discussed previously in this chapter (Section 1.6), incorporation of consumers in ADR monitoring programs can provide immense strength to the programs. Some of the associated benefits are listed below (Blenkinsopp et al., 2007).

1.6.1 (a) A new source of information for the regulatory bodies of medicines

In many countries, consumer reporting has become an important source of new information on the harmful effects of drugs. Thus, it could benefit the regulatory authorities and is also an important source of information in clinical practice.

1.6.1 (b) Disclosure of effects that were previously unknown

When consumer reporting began in Denmark in 2003, the first year saw 149 reports from patients, which represented 7% of all reports. One-third of these consumer reports were about previously unknown adverse reactions, thus suggesting a vital role in identification of unknown ADRs.

1.6.1 (c) Earlier reporting than health professionals

In general, an ADR reported by health professional has to pass through various stages and finally reaches the regulatory authority. But consumer reports often reach the regulatory authority directly and hence make it an early source of documenting ADRs. A study from the Netherlands suggested that patients recognize and report adverse effects more quickly and earlier than health workers.

1.6.1 (d) Increase in the number of reports

Often under-reporting of ADRs is a problem associated with many ADR reporting programs. Hence efforts are being done worldwide to enhance the number of reports. In this view consumer reporting is suggested to improve the number of ADR reports. For instance, in the United States consumer reporting began in 1993 and by 2004, reports by patients accounted for 15% of the total 24,553 reports (Ahmed et. al., 2010).

1.6.1 (e) Information on quality of life

Often the ADR reports avail little information and do not mention the quality of life of the affected patient. Analysis of data in Sweden by the pharmacovigilance centre revealed that the style of reports made by patients differed from that of doctors, providing more information on the impact of medicine on the quality of life. Thus making consumer reporting important in understanding the 'real suffering' of the patients experiencing the ADR.

1.6.1 (f) The reporting of serious adverse effects

Data from the pharmacovigilance centre in the Netherlands noted that ADR reports by patients provide information on serious adverse effects (Blenkinsopp et al., 2007) which were often lacking during the health professional reporting. The patients reported 33 adverse reactions whereas only 12 out of these 33 reports were submitted by their healthcare providers. Upon analysis it was found that doctors reported serious adverse reactions, while the patients reported the reactions that made them stay in the hospital.

1.6.1 (g) Different style, but same quality

There has been a concern that patients do not use the expressions/terms used by doctors and pharmacists. Therefore, the authorities noted that it is difficult to assess their reports and that it requires more time. However, there is no information in the literature about the time taken for analysis of these data. In addition, some authors have reported concerns about the quality of the reports and their credibility. However, the Dutch pharmacovigilance centre pointed out that patient reports have the same amount of information as those provided by health workers (Blenkinsopp et al., 2007).

1.6.1 (h) Reports by elderly people

A group of Belgian authors compared reports made by 168 elderly patients and those made by their healthcare providers (Blenkinsopp et al., 2007). The authors asked the patients to explain the reason for their admission to hospital.

1.6.1 (i) Patients report effects that have a strong relationship with drugs

Researchers from the US interviewed 198 patients by telephone and the results of this study indicated that health workers reported only half of the complaints made by the patients (Blenkinsopp et al., 2007).

1.7 Problem statement and rationale

1.7.1 Problem statement

Malaysia, a developing country in South East Asia has established its own national pharmacovigilance program. The pharmacovigilance program in Malaysia, however,

has limited coverage and receives only a limited number of ADR reports. There is still room for improvement as regards the program. The problem statement of this study is derived considering the major weaknesses of the current program in the country. First, it is observed that there is a lack of awareness among health professionals with regard to the existence, function, and purpose of ADR reporting and pharmacovigilance. There is also no national computerized database on drugs prescribed, making signal generation difficult. There is less involvement of pharmaceutical industries on drug safety matters and the reason for this is not known. The next weakness is the lack of information on the genetic effects and social practices and drug interactions associated with drug use. ADRs to the widely-used traditional and herbal drugs have been less reported adding to the underreporting plaguing the country. Finally, and also perhaps most importantly, there has been no involvement of nursing staff and consumers in the ADR reporting program. These individuals are more directly involved with handling and consuming medicines.

1.7.2 Rationale for the study

Considering these complications and the limitations of the country's pharmacovigilance program, the rationale of this study was that the involvement of patients (consumers) in the process of drug safety monitoring in Malaysia will bring more benefits and advantages to the existing system. Also, knowledge about ADRs will be acquired by the persons involved, be it the patients themselves, the nurses, the healthcare practitioners, and even the authorities themselves. The findings of this study may also reduce underreporting, as the more knowledgeable the person is, the more he or she knows the importance of ADR reporting and how to report ADRs. The quality of life will be further improved, and consumer rights will be promoted.

In addition, this study will help to increase the efficiency of Malaysia's healthcare system and medicines use process. Increasing the efficiency will allow healthcare professionals to focus on the detection of counterfeit medicines, which is another problem in the country.

Malaysia needs to involve consumers in drug safety issues due to the following reasons and the noticeable trends mentioned below that clearly make the justification of this study:

1. The numbers of reports given by doctors, pharmacists and dentists is still small.
2. Underreporting of ADRs is present.
3. There are substantial limitations on the existing reporting system.
4. Increased use of medicines without healthcare professionals' supervision.
5. Growth in use of unconventional products (herbal remedies), and
6. Promotion of consumer rights.

Patients and consumers as well as health professionals have the right to be involved and to report their experiences and sufferings as a result of these adverse effects which threaten their health and their lives. When consumers are involved in the process, their rights are subsequently reinforced thus achieving justice in the healthcare delivery.

1.8 Research objectives

The objectives of this study are as follows:

1. To compare the structure, process and outcome of existing drug safety systems between Malaysia and two other countries (Sweden and Australia) that have adopted consumer reporting of ADRs,
2. To evaluate the knowledge, attitudes and experiences of consumers towards and reporting of ADRs,
3. To evaluate the perceptions of health care professionals (general practitioners and community pharmacists in Penang) towards consumer reporting of ADRs, and
4. To evaluate the impact on pharmacovigilance, as well as analyze and assess consumer reports in the university-based pharmacovigilance centre during the operation of the Pilot Program in the USM's University Wellness Centre (UWC), with the following aims:
    a. To evaluate the knowledge, attitude and practice (KAP) among healthcare professionals in UWC towards pharmacovigilance and ADR reporting and the main reasons for underreporting, and
    b. To assess the reporting rate among healthcare professionals in the UWC by conducting educational interventions.

1.9 Research questions

Based on the literature survey and conceptual framework, this study aims to answer some relevant and significant research questions:

1. What are the differences in structures, process and outcome between drug safety monitoring systems in Malaysia, Sweden and Australia?
2. What are the level of knowledge, attitudes and practice among Malaysian consumers about adverse drug reactions in general and consumer reporting of adverse drug reactions?

3. What are the perceptions among Malaysian healthcare professionals regarding consumer reporting?
4. What is the impact of setting up a university-based pharmacovigilance center in the University Wellness Center at Universiti Sains Malaysia?

1.10 Contributions of the study findings

As consumer reporting is important for achieving better healthcare standards in Malaysia, this study seeks to highlight the importance of consumer reporting among different stakeholders as in the following:

1. Consumers are active players in drug safety and key stakeholders in relation to pharmacovigilance and can actively contribute through an integrated and efficient reporting system.
2. Direct consumer reporting is an essential tool to empower consumers and improve their involvement in the management of their own health.
3. With consumer reporting, ADRs will be detected earlier, and more ADRs would be reported especially those associated with over-the-counter medicines.
4. Consumer reporting can be a useful method to overcome underreporting of ADRs.
5. Consumer reporting can be a good solution for the limitations of the existing ADR monitoring system that is based on health professionals' reports.
6. Involvement of consumers in ADR reporting will promote consumer rights.
7. Consumer reporting cannot replace the existing system, but can complement and strengthen it.
8. It will help in detection of counterfeit and unsafe marketed drugs.

A significant message from the study is the importance of the healthcare professionals and need for a broader healthcare system in supporting patients (consumers) to be involved in enhancing drug safety. The professionals need to be receptive and open to patients' concerns and questions, and to facilitate patients' attempts to be involved in their care. The findings suggest that care providers should not take concerns voiced by patients lightly. These professionals also need to be properly educated about ADR reporting. A positive patient professional relationship is important for patients to be able to contribute to the improvements in healthcare safety. It also suggests the need for appropriate attitudes and good communication skills among professionals and patients.

This study also offers an interesting insight about the power of the consumers. In terms of ADR reporting, consumers are the most valid reporters of ADRs as they are the ones experiencing any ADRs that occur. This study also addressed some of the problems mentioned previously in the study (lack of belief that ADR reporting can help consumers in obtaining safer drugs and leading to better quality of life; customers not knowing how to write proper, valid reports; not being clear of the purpose of the reports, etc., to name a few), and justifies that consumers would be able to contribute to the ADR reporting system in a successful manner.

Overall, the study has also given a new meaning to the word pharmacovigilance. The public, the medical staff, MADRAC as well as the government, through various ministries, bodies and organizations must all work together to make sure that ADRs are responded to and channeled properly.

Having outlined some lessons learnt about consumer reporting, safe and effective drug therapy demands profound knowledge of every drug product being prescribed. Consumer reporting and pharmacovigilance should complement each

other to enhance the standard of healthcare and better the medical system in the country. If these essentials are observed, as well as practiced and supported, most drug-induced diseases and most drug-related malpractice litigations can perhaps be avoided, and human beings get to enjoy at least one basic human right to which they are entitled, that is *'the right to health'*.

CHAPTER 2

LITERATURE REVIEW

2.1 Adverse drug reactions

There has been a growing trend in recent years on reporting of the Adverse Drug Reactions (ADRs). The majority of the drug regulatory agencies around the world have developed reliance on the detection and reporting of suspected ADRs for improving medicine safety in the population.

An adverse event (AE) connotes 'any untoward medical occurrence that may arise during the treatment with a pharmaceutical product but which does not necessarily have a causal relationship with the treatment'. Perhaps, a better definition compared to WHO (2002) and the new Adverse Drug Reaction definition was given by Edward and Aronson as:

'An appreciable harmful or unpleasant reaction, resulting from an intervention related to the use of a medicinal product which predicts hazard from future administration and warrants prevention or specific treatment, or alteration of the dosage regime or withdrawal of the product'. (Edwards and Aronson, 2000)

ADRs are known to cause morbidity, mortality, increase duration of hospital stay and the cost of hospitalization. Lazarou et al. (1998) even pointed out that ADRs related to prescribed medicines are among the fourth to sixth most common causes of deaths in the US. Statistics show that 300,000 patients are hospitalized every year due to ADRs in the US (Atkin and Shenfiled, 1998). Shapiro (1971) has reported 160,000 deaths in the US annually due to ADRs and this figure may not be very different from what happens in other countries. Moving to the world at large,

Einarson (1993) draws attention to the fact that 0.2-21.7% of hospital admissions are due to ADRs.

ADRs are classified into four types, which are adapted from the original classification by Rawlins (1981): Type A is 'Augmented,' Type B 'Bizarre,' Type C 'Cumulative,' and Type D 'Delayed.' A deeper understanding on the nature of ADRs reveals them to be 'dose-related', 'time-related', and 'susceptibility-based'. As per the Dots classification system of ADRs, which is based on time course and susceptibility as well as dose responsiveness, ADRs that are dose-related contain some toxic effects, where the ADRs occur at doses higher than the normal therapeutic dose. Some ADRs may happen at standard therapeutic doses and the higher susceptibility reactions occur at subtherapeutic doses in susceptible patients. The time-related nature of ADRs is seen in the ADRs that occur at any time during the treatment given, causing various reactions.

Some ADRs are categorized as 'rapid reactions' that occur when a drug is administered too fast. Similarly, 'early reactions' occur early on in the treatment and then abate with continuing treatment. 'Intermediate reactions' occur after some delay, but if reaction does not occur after a certain time little or no risk exists. The 'late reaction', in turn, suggests that the risk of ADR increases with continued or repeated exposure, including withdrawal reactions. 'Delayed reactions' occur after a time period following exposure, even if the drug is withdrawn before the ADR occurs. Some individuals are known to possess a raised susceptibility towards occurrence of ADRs. The various factors that are associated with increased susceptibility of ADRs include genetic variation, age, sex, altered physiology, exogenous factors (interactions), and disease (Edwards and Aronson, 2000).

The American Food and Drug Administration defines a serious adverse event as one when the patient outcome is one of the following:

- Death
- Life-threatening
- Hospitalization (initial or prolonged)
- Disability - significant, persistent, or permanent change, impairment, damage or disruption in the patient's body function/structure, physical activities or quality of life.
- Congenital anomaly
- Requires intervention to prevent permanent impairment or damage.

2.2 Consumer reporting of ADRs

The renewal of interest in consumer ADR reporting is probably due to the decreasing number of ADR reports from healthcare professionals. Consumer self-monitoring of drugs has been used in the past, but only focusing on specific drugs of concern and has been argued to be essential to obtain trustworthy reports of effects from central nervous system drugs (Fisher, 1995). In general, consumer reporting is important to gain direct access to patients' views on the medicine prescribed, to grant people the opportunity to more actively contribute to medicine regulation, for the people to have more choice, and greater access to medicines. It is also important considering two growing trends - the increased use of medicines without supposed supervision from the professionals and the growing use of unconventional products (herbal remedies is one example). Patients' reports can capture personal experiences in a way that professional reports cannot. The 'richness' of such reports can serve as

a guide to relevant authorities and can focus attention towards ADRs normally dismissed as trivial by health professionals.

Blenkinsopp et al. (2007) published a systemic review on patient reporting of suspected ADRs. Authors provided more evidence on the importance of consumer reporting of ADRs and justified advantages, from international experience, regarding consumer reporting. They concluded that there is lack of publications about patients' reporting of ADRs in the literature, and if available, most published studies were very small in terms of duration and number of patients (Blenkinsopp, 2007). Qualitative examination of ADRs reported by patients has shown them to be rich in terms of their description of nature, severity and significance of reactions (Medawar and Herxheimer, 2003).

Underreporting of ADRs was recognized as a limitation of the ADR reporting program in Sri Lanka and authors from the same country suggested consumer reporting to be the best method for developing countries to overcome underreporting of ADRs. They also hypothesized that consumer reporting can complement the existing system of ADR reporting which is mainly physician and pharmacist centered (Fernandopulle and Weerasuriya, 2003).

Van Grootheest and his colleagues published a review on patients' roles in reporting ADRs. They discussed the involvement of patients in the reporting of ADRs. Authors concluded that people should positively value patients' involvement in drug therapy and their concern regarding possible ADRs (van Grootheest and de Jong-van den Berg, 2004). This review discusses the involvement of patients in the reporting of adverse drug reactions (ADRs). Patients benefit from drugs but also experience their adverse effects. Since concerns about the safety of drugs are also patients' concerns, the patient could also play a part in decreasing the risks of drug