Problems of Current Interest

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39th Annual Meeting of Representatives of National Pharmacovigilance Centres participating in the WHO Programme for International Drug Monitoring
Problems of Current Interest (PoCI): Content

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Oral Presentations
An issue with dispersible sublingual glyceryl trinitrate (GTN) tablets—used to treat acute cardiac ischaemic pain in emergency situations—taking longer than expected to dissolve. It was identified from spontaneous reports, and was subsequently determined to be a result of recent formulation changes. Extensive internal collaboration was required to arrange confirmatory testing and to consider whether a recall should be undertaken given there was no alternative product available in Australia (an alternative spray product was not suitable for single use in emergency and paramedic situations). Other complexities include negotiating with the sponsor to supply an alternate product until the issue is addressed and the development of a risk communication strategy while securing an alternative supply.
Brazil: The new bylaws on phytomedications and the role of pharmacovigilance in Brazil
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Brazil’s ecosystem has the planet’s largest depository and greatest diversity of biomes, an untapped source of natural medicines and health products. Consequently, Brazil has recently enacted laws that regulate the identification, analysis, marketing and export of fauna and flora. Brazil has three main manners of addressing herbal medicines:

1. Herbals used traditionally are unregulated once ascertained to be safe;
2. Phytomedicines are registered after a simplified regulatory process;
3. Phytomedicines already registered in another country.

The therapeutic use of herbals can range from 60-70% in the north and north-eastern regions to less than 20% in the south. They may be taken together with homeopathic and/or allopathic drugs. Since they are natural medicines, they are deemed safe and reporting of adverse reactions is rare. CEATOX is one of the few centres that receive reports of adverse drug reaction (ADR). Since 2002 it has received many hundreds of reports from all areas of the country. We will present the data as well as the bases of Brazil’s ecosystem and its characteristic biomes.
**Croatia: ADR reports from poison control centres**

*P. Mas*

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According to the new European Pharmacovigilance (PhV) legislation, definition of adverse drug reaction was broadened to include reports which arise from drug overdose, off-label use, misuse, abuse and medication errors. In 2016, HALMED started receiving information from Croatian Poison Control Centre (PCC) on intoxication with medicinal products. PCC is a public health service providing professional assistance in treatment of poisoning via a 24-hour telephone information service. They receive calls regarding exposure or intoxication with a variety of products, of which approximately one third is associated to medicinal products.

In this short overview, HALMED’s experiences with currently received reports from PCC are presented. Reports were compared to those received from “conventional” sources, stressing out differences such as seriousness, patient demographics, suspected drugs or therapeutic groups. Challenges faced with these reports, such as choosing appropriate MedDRA terms for coding reactions are also presented. Input is sought from other members on their experiences with PCCs and their opinion on what type of safety information could be expected to arise from these reports.
India: Active surveillance on bedaquiline: India initiatives

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Bedaquiline, a drug for the treatment of multidrug-resistant tuberculosis (MDR-TB), was approved by the Drugs Controller General of India under the conditional access program. This drug is made available in six identified tuberculosis treatment centres across India. Incidentally, they are adverse drug reactions monitoring centres (AMCs) of Pharmacovigilance Programme of India (PvPI). Since the PvPI, under the Indian Pharmacopoeia Commission, is integrating with Revised National TB Control Program (RNTCP); both the partners kick-started an active surveillance (cohort event monitoring) to ensure the safety of bedaquiline in technical collaboration with the WHO Country Office for India. The training was conducted to strengthen the capacity building of causality committee members of AMCs, and other key functionaries of Revised National Tuberculosis Control Program (RNTCP) (medical officers and statisticians) and PvPI (coordinators and Pharmacovigilance Associates of six AMCs) on data capturing in cohort event monitoring form, causality assessment etc. The PvPI, WHO and RNTCP jointly developed an IT tool (bridge application) to facilitate the adverse events data flow between NIKSHAY – software for managing TB patients, developed by RNTCP and VigiFlow. This becomes an important initiative to ensure seamless data flow and ease in managing the data at PvPI. This strategic move not only aims to strengthen the partnership between PvPI and RNTCP but also aims to provide data for global learning.
India: An outlook of ADR reporting by consumers
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All over the world, reporting of adverse drug reactions (ADRs) by consumers is being streamlined. Consumer reporting has several advantages like good quality reports with full medical information, increases the number of ADRs, early detection of ADRs and also as a strategy to prevent medication errors.

Consumer reporting was started by the end of 2013 and several initiatives have been taken by National Coordination Centre (NCC)-Pharmacovigilance Programme of India (PvPI) to enhance consumer reporting across the country. Helpline (1800-180-3024), android app, availability of consumer ADR form in different regional languages and promotion through social media are the key measures available for the consumers to report ADR. These approaches are efficiently working still, sensitization and awareness programmes are organized to raise the outreach to every corner of the country to promote patient safety.
Adverse drug reaction (ADR) reporting and the quality of information required in term of completeness are two different aspects of pharmacovigilance. In the developing countries, the clinicians are overburden with patient loads, so they do not have much time to report ADRs with complete information. In India, the Pharmacovigilance Programme of India (PvPI) have a very unique and effective system of pharmacovigilance, in which the National Coordination Centre (NCC) under the aegis of Ministry of Health and Family Welfare; the government of India provides a trained pharmacovigilance staff to every ADR monitoring Centre. His duty is to capture complete information of ADRs and report the same to the NCC. Further, there are panels under the NCC-PvPI which further look into the technical matters for pharmacovigilance.
Adverse drug reaction (ADR) reports from health-care professionals (HCP) in Japan comprise 10% of the approximate 50,000 reports that the Pharmaceutical and Medical Devices Agency (PMDA) receives annually, while 90% of those are provided by the manufacturers. Manufacturer reporting in Japan has a limitation in the quality of the reports for various reasons. HCPs are obligated to report ADR via the designated format provided by PMDA with a clinical narrative.

In order to improve the quality of HCP reporting, an initiative has recently been started to have a medical advisory section in the selected regional core hospital, which receives and edits ADR drafts from the private, community and university-affiliated hospitals, and then sends the reports to PMDA. This unique HCP reporting system may increase the quality of the HCP reporting by utilizing the Japanese hospital networks without additional IT infrastructure.
**Oman: Change in reporting form format as a means of incorporating other medicine related problems**

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**Background:** Although adverse reaction reporting was made mandatory in Oman since 1994, the number of reports that were received was very minimal. Measures were devised to tackle this problem. Awareness about reporting was created through posters, workshops, training programs etc. As pharmacovigilance is not about adverse drug reactions (ADRs) alone, it was hard for reporters to be convinced about reporting other drug related problems like quality defects, medication errors despite the fact that quality defects were a concern among many health care professionals.

**Objectives:** To include other medicine related problems in the reports.

**Methods:** Conducted pilot study only in three tertiary care hospitals to do the piloting of the revised form. Total number of reports which were received at the centre, before and after the new reporting form was introduced, were compared.

**Results & conclusion:** The total number of other product related problems started increasing along with the reports related to ADR.
**Oman: Irrational use of proton pump inhibitor in secondary care**

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Proton pump inhibitors (PPIs) are frequently prescribed medications. Their superior acid suppression led to its use for the treatment of gastroesophageal reflux disease, *Helicobacter* eradication, and other gastrointestinal problems. However, irrational use outside the approved indications is observed in some settings. In our setting it was noticed that the PPIs dispensing increased dramatically for unusual treatment periods without clear diagnosis. Staffs were assigned to monitor the prescribing pattern among doctors. It was found that most of the patients were prescribed with PPIs for symptoms management without further investigation of the pathology of the gastric symptoms regardless the international guideline of gastric disease treatment. As a secondary care institute, we are not equipped with suitable facilities for diagnosis of different gastrointestinal problems, therefore, most of our cases end up undiagnosed and on long-term PPIs treatment. The availability of expensive medication neglects the cost-effectiveness consideration by the doctor; as a result they prescribe PPIs in cases that can be treated with other antacids like H₂-antagonist or antacid syrup. To rationalize the use of PPIs, the patient should be counselled properly for differential diagnose, the patient then can be referred to a tertiary health care institute for further investigation or manage patient symptoms with antacid other than PPIs. Activate the cost-effectiveness and international gastric disease treatment guidelines awareness among doctors.
Patients receiving chemotherapy are at high risk of developing invasive fungal infections (IFIs) which is mainly managed by triazole drugs. Voriconazole, a triazole antifungal is widely used for prophylaxis and treatment of life-threatening IFIs. In clinical practice, the use of voriconazole has rapidly increased mainly due to its extended spectrum of activity and reduced resistance compared to other azoles. In addition, voriconazole, has an excellent safety and interactions profile and less restrictions with diet and administration times. Adverse effects (AEs) reported include hepatotoxicity and neurologic adverse effects (e.g., hallucinations, confusion) which may be caused by high voriconazole plasma concentrations or its potential for drug-drug interactions. In immunocompromised patients even transient AEs may result therapy interruption and may have an impact on the patient quality of life. In practice, clinical pharmacists play a major role in detection, reporting and managing AEs of voriconazole in immunocompromised patients.
Sri Lanka: Case study on DMPA
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Until 2011, depot medroxyprogesterone acetate (DMPA) was the most popular temporary method of contraception in Sri Lanka. A marked decrease in the use of DMPA occurred following a cluster of reported cases of allergic reactions to generic DMPA products. Most were classified as level 1 of diagnostic certainty according to the Brighton Collaboration case definition of anaphylaxis. Depo-gestin 1 was available for comparison. Depo-gestin 1 resulted in a higher rate of allergic reactions - 15 times greater than Depo-Provera. This high incidence of allergic reactions caused by Depo-gestin 1 may be attributable to the possibility of contamination with antibiotics, which were also being produced concomitantly by the same manufacturing facility or the Sri Lankan female population having an increased sensitivity to one of the excipients contained exclusively in Depo-gestin 1.
**Thailand: From alert to action: case study of LASA**

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The Health Product Vigilance Center (HPVC) is the national center for adverse events (AEs) collection for risk management. Most of AE reports are adverse drug reactions (ADRs), which are sent to HPVC by hospitals, about 40 000 reports/year. Since 2015, HPVC has expanded scope of work beyond ADRs to others such as medication errors, look-alike/sound-alike (LASA), etc. Recently, HPVC received several reports of medicines which had the LASA name, then we evaluated the cases to see what could be done for risk management. In these cases, the medicines’ trade names were A-120 (sulfamethoxazole + trimethoprim) and A-250 (tetracyclin). The problems which occurred among physicians, pharmacists, patients or consumers were due to the confusion of names. We searched in HPVC database and found that there were serious ADRs from these two trade names, for example, Stevens-Johnson syndrome, fixed-drug eruption and angioedema, etc. After some meetings to solve this matter, we proposed 3 solutions as follows:

1. The companies have to file documents for changing trade name of the problem-medicines to ThaiFDA.
2. HPVC has to develop guidelines, AE program and promote them to networks.
3. ThaiFDA has to review the criteria and regulation for medicines’ names.

Finally, we are in the process of strengthening networks on effective detection, evaluation, better communication, sending reports to national HPVC, and management of risk minimization.
Uganda: Preliminary results from a baseline study to assess the effectiveness of community dialogues and sensitization in enhancing community participation in monitoring of drug safety

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Many countries have recently introduced direct patient spontaneous reporting of suspected adverse event reporting. This study was conducted to assess the effectiveness of the community dialogue and sensitization approach in enhancing the community's knowledge, perceptions and participation in reported suspected adverse drug reactions in Uganda.

We conducted a baseline survey using a structured questionnaire in 1034 random households in the two rural districts of Iganga and Mayuge in Eastern Uganda, in preparation for the implementation of community dialogues and sensitization about monitoring drug safety.

We found that despite limited knowledge of the possible harm that can result from medications, the community is willing to report adverse drug events. About one third of the community members admitted an experience of such events and reporting them to their healthcare providers. The reasons for not reporting included failure to tell if the reaction was due to the drug or not (38%), no need to report (33%) or it would disappear (12%), fear of being victimized (11%) or health workers had no time (6%). We also found that the healthcare workers tend not to report the adverse effects.

There is therefore a need to engage the communities through dialogues and sensitization about monitoring drug safety and for more drug utilization studies to be done to inform them of the policy for direct patient reporting.
United Kingdom: Capturing harms associated with Novel Psychoactive Substances: launch of a new reporting system in the UK

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The MHRA is launching, in partnership with Public Health England (PHE), a pilot reporting system for adverse reactions to Novel Psychoactive Substances (NPS) in December 2016. NPS are widely available and have the potential to pose serious risks to public health. There has been rapidly increasing numbers of new substances identified in recent years with greater availability over the internet. Hospital admissions for poisoning by 'Psychostimulants with abuse potential' have increased 45% in England.

There is currently a lack of evidence relating to long term health harms associated with NPS use and more monitoring in this area is needed. This project will enable MHRA and PHE to collaborate more closely on safety issues impacting both licensed medicines and NPS. Modelling the 12 month pilot on the MHRA’s Yellow Card will simplify the process for healthcare professionals and increase engagement and reporting levels for this important public health concern.
**Zimbabwe: Individual Case Safety Reports (ICSRs) of pregnancy in HIV positive women on levonorgestrel implant taking efavirenz combination antiretroviral therapy- case series study.**

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**Background:** In most low and middle-income countries (LMICs), subdermal hormone-based birth control implants such as levonorgestrel (LNG) are the preferred contraceptives with an expected failure rate of less than 1% over five years\(^1,2\). However their use has been compromised in HIV positive women of childbearing age that are under efavirenz based antiretroviral therapy (ART) due to potential cytochrome P450 3A and uridine diphosphate-glucuronosyl transferases (UGTs)–mediated drug–drug interaction\(^2,3,4\). There is limited published data, examining the interactions of the hormonal contraceptives and ART\(^3\).

**Objective:** To understand and characterize individual case safety reports (ICSRs) of suspected pregnancy associated with levonorgestrel (Jadielle) implant in women on ART.

**Methods:** Retrospective analysis of ICSRs received from targeted spontaneous reporting (TSR) of antiretrovirals (ARVs) and anti-TBs pilot and main phase was done to understand and characterize ICSRs of suspected pregnancy associated with Jadielle implant and efavirenz based ART regimes. The ICSRs were evaluated and causality assessment done by PVCT Committee and uploaded onto the WHO Global ICSR database (VigiBase).

**Results:** MCAZ received 1240 ICSRs reports, of which 1202 were for ART and anti-TBs, with cumulative percentage of 41% for male and 59% for female. Of the reports received, 504 were from efavirenz based ART (42%), 0.5% of the reports were for pregnancy in women on efavirenz-based ART and levonorgestrel Jadielle implant.

**Conclusion:** Increased reporting of suspected pregnancy ICSRs due to use of Jadielle and efavirenz-based highly active antiretroviral therapy (HAART) from 2015 to 2016 was noted.
Alert notice was circulated to health-care facilities (HCFs) encouraging women on HAART and Jadielle to use other safer contraceptive methods. The limitation of the data is that it was from TSR methodology. Use of e-health and m-health including the recently introduced e-ADR form is recommended for active surveillance to generate real time pharmacovigilance data.

References

3. CDC. Technical Issue Brief: Drug Interactions between Hormonal Contraceptive methods and Anti-retroviral medications used to treat HIV. 2014 Oct
**Zimbabwe: Review of ICSRs of suspected gynaecomastia associated in patients on antiretroviral therapy and anti-tuberculosis medication**  
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**Background:** Gynaecomastia has been associated with the use of highly active antiretroviral therapy (HAART) and anti-tuberculosis medicines. A systematic review by Nuttall FQ et al 2015 reported that a large number of medications have been implicated in the genesis of gynaecomastia including efavirenz, indinavir, saquinavir and isoniazid although the mechanism of action is usually not understood, with highest number of cases reported in man.

**Objectives:** To understand and characterize suspected gynaecomastia associated with efavirenz antiretroviral therapy (ART) based regimens and/or Anti-TBs.

**Methods:** A descriptive, retrospective review of individual case safety reports (ICSRs) received through the targeted spontaneous reporting (TSR) system to the national pharmacovigilance centre over a four period.

**Results:** A total of 1 202 ICSRs received over a period of 4 years from TSR of ARVs and anti-TBs program were analysed, of which 504 (42%) were associated with efavirenz based regimens. Of these 162 (45%) were suspected gynaecomastia. 45% of the reported gynaecomastia cases had the disorder for one month to a year, 21% had gynaecomastia for more than one year, 8% for less than one month and the rest of the cases were of unknown duration. Of the total cases, most of the patients (54%) were between 21-45 years old, 15% were below 20% and the rest were above efavirenz and isoniazid.

**Conclusion:** The increase in the number of gynaecomastia reports might be attributed to efavirenz which was introduced as a first line medication in antiretroviral therapy since 2013 and/or isoniazid preventative therapy (IPT). Recent studies recommend the use of efavirenz 400mg instead of 600mg based ARV regimens so as to reduce the risk of ADRs in risk
population who are poor metabolisers of efavirenz, including men since they are the ones most commonly affected with gynaecomastia.
**Zimbabwe: Tenofovir and renal impairment ICSRs- case series study**

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**Background:** Tenofovir (TDF) based antiretroviral therapy (ART) regimen(s), have been widely used, as they are more effective and less toxic than some regimens and recommended as part of preferred first-line regimen for initiation and maintenance including second-line regimens. TDF may however be associated with acute kidney injury or chronic kidney disease and/or reduced bone mineral density in some few patients.

**Objectives:** To understand and characterize suspected TDF induced renal impairment individual case safety reports (ICSRs) received from 2012 to 2016 TSR program.

**Methods:** A descriptive, retrospective review of ICSR s received by the national pharmacovigilance drug through the targeted spontaneous reporting (TSR) pilot and main phase programme from 2012 to August 2016.

**Results:** A total of 1202 reports for ART and anti-TBs were received during the period. From this, 806 (67%) of the reports were from patients who had ART with TDF based combinations. 72 ADR reports (9%) were renal impairment cases, which had causality assessment that was classified as possible, due to TDF. The majority of these cases were reported between 2015 and 2016, with 65 (90%) been reported in this period. 50% of the cases were in the 20-45 year age group, followed by 36.11% in the 45-65 years age group. Causality assessment was done by the Pharmacovigilance and Clinical Trials Advisory Committee and ICSRs uploaded onto VigiFlow database for further analysis.

**Conclusion:** The results from the TSR programme indicate that there has been an increase in the number of reports of renal impairment that has been associated with TDF use. This could have been attributed to sensitization of reporters through the TSR programme and also the introduction of TDF based combinations as first line therapy on the national ART programme. Considering the thousands of patients on TDF ART regimens there is need for testing robust consumer driven e-health and m-health reporting tools linked to the recently introduced ADR form linked to VigiBase.
References:


Posters
Denmark: Major differences in report quality and indirectly reported ICSRs and no effect of follow-up information on report quality was found by using the VigiGrade completeness score algorithm

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Requests for further information (RFI), from marketing authorization holders (MAH) on individual case safety reports (ICSRs) reported directly to the Danish Medicines Agency (DKMA), has to go through the DKMA. Because of the increasing workload the DKMA decided to implement a risk-based procedure in order to decrease the number of RFIs and hence the workload. The immediate effect was a more than 50% reduction in the number of follow-up request from MAH. The VigiGrade Completeness Score algorithm was used to analyze the quality of reports before and after FU information was received. We found that the quality of reports received via MAH was much lower than if reported directly from health-care professionals or a member of public. Moreover, we found no increase in the quality of reports, if FU was initiated by MAH. High quality of the initial reports is of great importance, and DKMA will keep working to improve the ICSR quality.
France: French pharmacovigilance database and its evolution

M. Benkebil

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The French pharmacovigilance database is based on a network of 31 regional centres located in teaching hospitals and coordinated by the French Medicines Agency (‘Agence Nationale de Sécurité du Médicament et des Produits de Santé’ [ANSM]). Since 1985, they have shared a common database of cases of adverse drug reactions that are spontaneously reported by healthcare professionals and since 2011 by consumers.

The total number of reports between January 1985 and December 2015 is more than 572000, with a linear increase over time: 1149 cases were reported in 1985 and 38 823 in 2015.

A new development of the French national application (ANPV) became a necessity by the evolving regulatory environment at European and International levels, and by the will of ANSM to improve the functionality of this database to allow more user-friendly navigation and to answer specifically to user’s requirement.
France: Feasibility study on application of change-point analysis in drug safety signal detection

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We aimed to evaluate the benefits of combining Change-Point Analysis (CPA) with disproportionality analysis in pharmacovigilance signal detection using spontaneous reporting systems.

The power of CPA technique in detecting a safety issue has been assessed. It was applied on test cases from drug safety reference data set as well as validated signals. We identified the outcome measure for CPA method and estimated how well this method can reduce false-positive signals and detect signals as early as possible.

CPA detected change points in both number of reports and the lower bound of proportional risk ratio (PRR). However, change points with PRR are more powerful for signal detection purpose compared to the original method. On the reference data set, the CPA method was used as a complementary tool to disproportionality analysis (DPA) methods. It was able to confirm positive controls and eliminate negative controls as false-positive signals.
India: Adverse drug reactions related to herbal products: status in India (Analysis of PvPI data)

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Looking towards the pervasive use of herbal products with the belief that herbal medicines are safe to use compared to other pharmaceutical products. Consumers must be aware to ensure the safe use of the herbal products. The monitoring of herbal products is vital in order to ensure the safe use of these products to safeguard public health. The Pharmacovigilance Programme of India (PvPI) also monitors and encourages reporting of the adverse events associated with the use of herbal products. An analysis of the data on suspected adverse reactions on herbal products reported to National coordination centre (NCC)-PvPI was done until September 2016. The data was segregated, categorized and analysed relating to reporters category, patients age, gender, seriousness, diagnosis, type of herbal products, system organ class (SOC) affected and outcome. More awareness and data information is required to signal and prevent the consequences of adverse reactions associated to herbal medicines.
Iraq: Poisoning and death due to Sagwa (CAM)

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Sagwa is traditionally used in rural areas to treat diarrhoea besides other indications. It consists of more than 60 items, most of the items are herbal, in addition to, animal skin and shed, arsenic, led and other constituents and it is given via different routes. Signs and symptoms of poisoning include dehydration, hypotension, hypokalemia, renal failure and septicaemia. The number of reported cases reached 40 during 2014-2016. The age of the affected children ranges from one month to twelve months. Treatments given were antibiotics, i.v. calcium and sodium bicarbonate, frusemide, albumin, anti-epileptic and antifungal. Treatment outcomes were positive in most of the cases, 3 cases ended with renal failure and 6 deaths and in response to report cases, the Iraqi pharmacovigilance center started an awareness campaign to both public and health-care professionals in collaboration with many parties.
Oman: Oman Pharmacovigilance Centre- The journey

M. J. Almaskari, S. Varughese

Oman Pharmacovigilance National Centre, Oman

- The mile stones:
  - 1993- The IC section was given responsibility of adverse drug reaction (ADR) reporting
  - 1994- Circular issued to health care professionals to report ADR
  - 1994- Associate Membership WHO Programme for International Drug Monitoring (PIDM)
  - 1996- Full membership
  - 2006- Trial of revised reporting form in selected tertiary care centres in Muscat/ Issued booklet for pharmacovigilance guidelines.
  - 2007 onwards: Introduced annual training workshops among health-care professionals (HCPs) to create awareness about reporting.
  - 2010- Designated focal points in the governorates.
  - 2015- The IC section transformed to department status under the Director General of Pharmaceutical Affairs and Drug Control (DGPA&DC).

- ICSR per million inhabitants and year, received in VigiBase 2010-2015 in EMRO regions.
- Reporting rate over the years
- Gender /Age distribution
- Anatomical Therapeutic Chemical (ATC) Classification drug category
- System organ classification of reactions
- Frequently reported drugs
- Frequently reported reactions
Russia: Problems of the interchangeability of the calcineurin inhibitors

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Federal State Budgetary Institution “Scientific Centre for Expert Evaluation of Medicinal Products”, Russian Federation

An analysis of 7224 spontaneous reports (SRs) about adverse reactions (ARs) admitted to the national pharmacovigilance data base for the period from 1 January to 30 June 2015 was done. Information about ARs occurring on the replacement of the original to a generic drug was detected in 135 cases. 11.8% of these SRs contained information about immunosuppressants: cyclosporine, tacrolimus and mycophenolate mofetil. As the development of this research work the analysis of 398 SRs for cyclosporine and 451 SRs for tacrolimus admitted to the national database during the 7 years was made. From these ARs 20.9% of SRs contained the information about the problems that occur when interchangeability of the cyclosporine was done. The same was true for 12.2% of SRs with tacrolimus. Ineffectiveness was detected in 40.7% and 23.5% of these cases accordingly.

Desmond Teo Chun Hwee, Ng Suet Leng Patricia, Tan Siew Har, Lim Theen Adena, Toh Su Lin Dorothy, Sui Yung Chan and Cheong Han Hu

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The use of complementary and alternative medicine (CAM) has been increasing over the years. A review of adverse events reports (AERs) associated with CAM in Singapore found a notable number of AERs submitted. This review focuses on AERs associated with CAM and hepatotoxicity submitted to Vigilance and Compliance Branch of HSA from 2009 to 2014.

Information extracted included demographic information, time to onset, hospitalization status, outcome, type of hepatotoxicity, ingredients of CAM, total daily doses (TDD), concurrent western medicines and health supplements and reporter details.

57 reports were eligible for analysis and 35 (61.4%) involved traditional Chinese medicine (TCM). The Roussel Uclaf Causality Assessment Method was applied in 29 (82.9%) of these cases and the median score was 4 (range: 1-8). Chai Hu (Radix bupleuri) was suspected in 11 (31.4%) cases.

Drug-induced liver injury is still poorly understood and more objective assessments are warranted. Reporting of adverse events should be strongly advocated to facilitate future analyses and the understanding of the risk-benefit profiles of CAM.
**The Netherlands: Insufficient pharmacovigilance awareness, skills and knowledge among future medical doctors in the Netherlands**

*L. Harmark*

*Lareb, The Netherlands*

**Introduction**

Pharmacovigilance centres play a vital role in the monitoring of drug safety after approval for marketing, and depend mainly on the quantity and quality of reported adverse drug reactions (ADRs). In the Netherlands not only health care professionals, but also patients and medical students can report ADRs. Although various efforts to stimulate reporting, underreporting of ADRs by healthcare professionals remains a major problem and a barrier to improve pharmacovigilance and medication safety. We aimed to assess pharmacovigilance awareness, skills and knowledge among future doctors in the Netherlands.

**Conclusions**

Although ADR reporting is considered relevant and important among future doctors, many don’t know where and what to report when they encountered an ADR. This is highly undesirable and would have important consequences for pharmacotherapy teaching. A national effort to improve pharmacovigilance awareness among medical students is warranted.
The Netherlands: The documentation of clinical information of adverse drug reaction reports: A paired comparison of duplicate reports of patients and health-care professionals

Lareb

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The value of patients reporting adverse drug reactions (ADRs) to pharmacovigilance centres has been widely acknowledged in recent years. However, little is known about differences in documenting clinical information, for example the description of the ADR and the course of the reaction, between reports of patients and health-care professionals (HCP). The aim of this study was to determine the differences in documenting clinical information between paired ADR reports of patients and HCPs. For the analysis all ADRs that were reported in duplicate, i.e. a report on the same case by the patient and the patient’s HCP were selected. This study shows that reports from both HCPs and patients are well documented with HCPs receiving a higher score than patients.
Venlafaxine is a serotonin and nor-adrenaline reuptake inhibitor used for the treatment of depression and anxiety disorders. The experience with venlafaxine use in pregnancy is still limited compared to selective serotonin reuptake inhibitors (SSRIs). The aim of this study is to assess the rate of major congenital malformation (MCMs). Secondary aims are pregnancy outcomes, spontaneous abortion, preterm delivery and birth-weight. The study was conducted using data from 9 centres of the European Network of Information Services (ENTIS). Venlafaxine exposure (n=732) is compared with a group of women not exposed to any known teratogen during pregnancy. Analysis was performed using logistic regression. In this study, venlafaxine was not associated with an increased rate of MCMs. The rate of spontaneous abortion and pre-term delivery was higher in the venlafaxine group. Further analysis of the data is necessary to investigate the role of potential confounding factors.