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SULTANATE OF OMAN
MINISTRY OF HEALTH
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DIRECTORATE GENERAL OF PHARMACEUTICAL AFFAIRS & DRUG CONTROL (DGPA&DC)

PHARMACEUTICAL NEWSLETTER

vigiGrade - Completeness score Oman (2012 – 2017)

Uppsala Monitoring Centre (UMC), located in Uppsala, Sweden, the WHO Collaborating Centre for International Drug Monitoring, issued the document containing the Completeness scores for Individual Case Safety Reports (ICSRs) for Oman covering the past 5 years. The UMC works by collecting, assessing and communicating information from member countries' national pharmacovigilance centres about the benefits, harm, effectiveness and risks of drugs.

The vigiGrade is a scoring system by the UMC to grade the completeness the ICSRs sent by different stakeholders. The ICSRs sent by the National centres are graded for quality by the UMC, and assigned scores so that necessary refinements can be sought from reporters, for making the reports more meaningful and assuring quality reports. The reports are sent to the UMC using VigiFlow, which is a web-based ICSR (Individual Case Safety Report) or an ADR report, management system that is available for use by national pharmacovigilance centres of the WHO Programme for International Drug Monitoring. VigiFlow supports the collection, processing and sharing of data of ICSRs to facilitate effective data analysis.

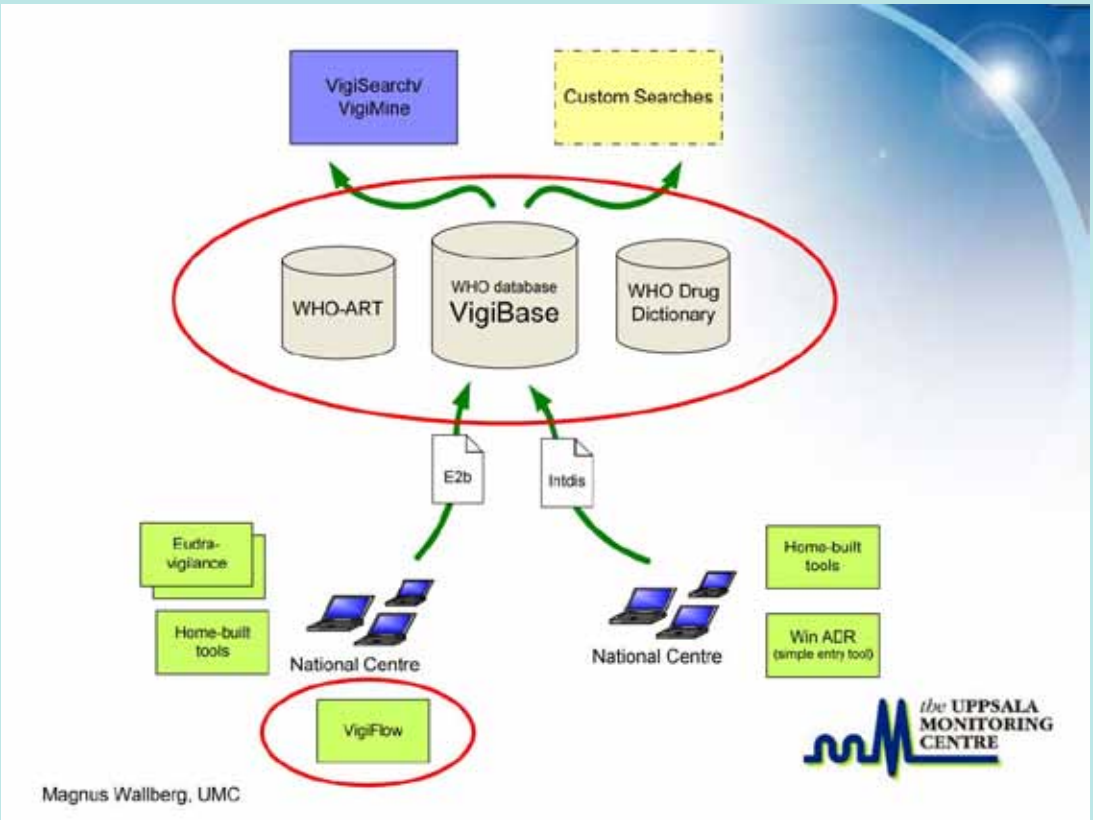
The Oman PV centre started using the Vigiflow in 2015, prior to that a simple format was used which could not apply the integrated international terminologies to make reports of good quality as expected. The use of vigiflow enabled such applications which is reflected on the score.

Since VigiFlow is a web-based system no local installations, back-ups or maintenance are necessary, however it means that internet access is required and no off-line functionality is available. Internet access is encrypted and all data stored in VigiFlow is accessible only by authorised users.

A flow chart of the functioning of Vigiflow is depicted below.

In this issue:

vigiGrade - Completeness score

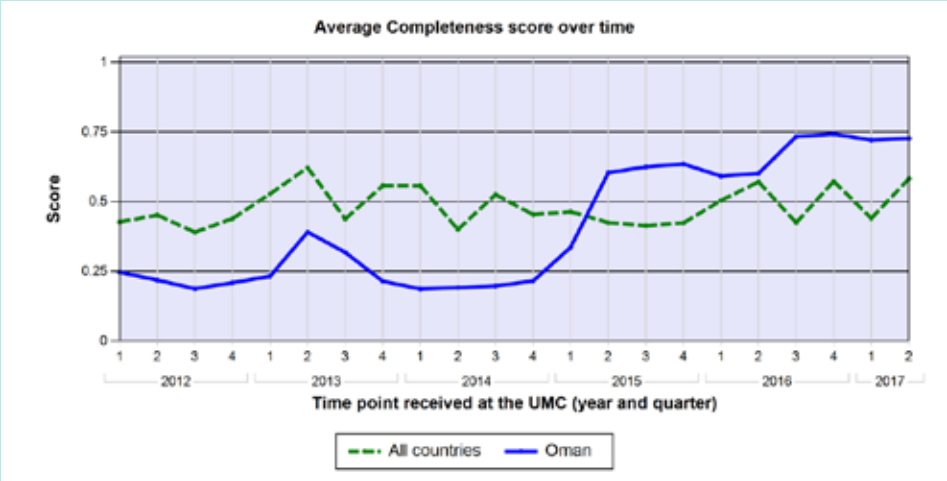


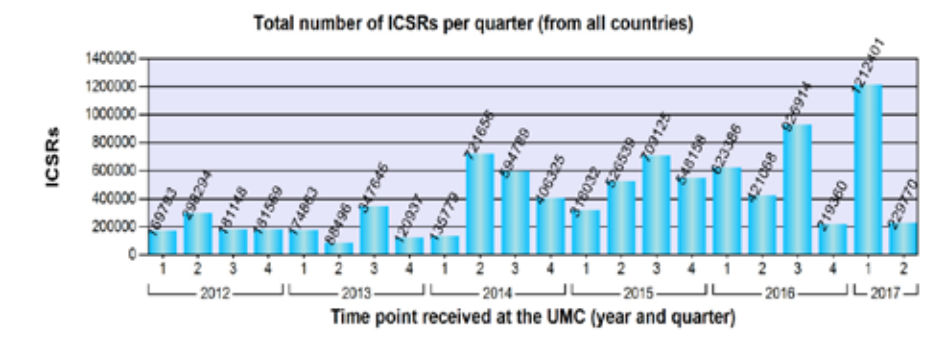
Other useful resources for WHO Programme members

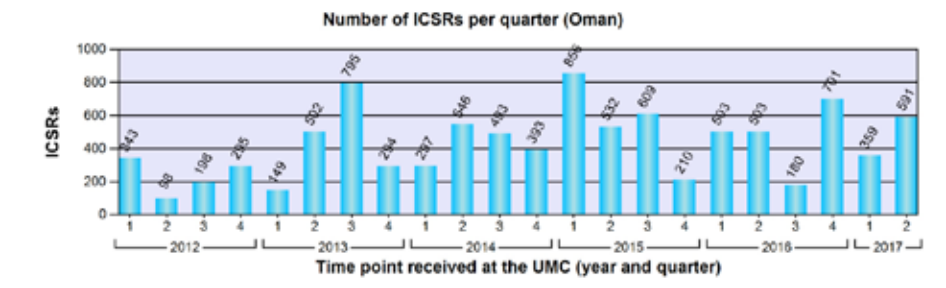
The recent updated VigiGrade scores over a period of time (2012 -2017) is copied below for reference. (The document as adapted and copied from the UMC).

The meritorious support and collaboration received from all health institutions and reporters across the country in this regard is recognized by the progress made by the Directorate in the field of Pharmacovigilance.

Average Completeness score, Oman

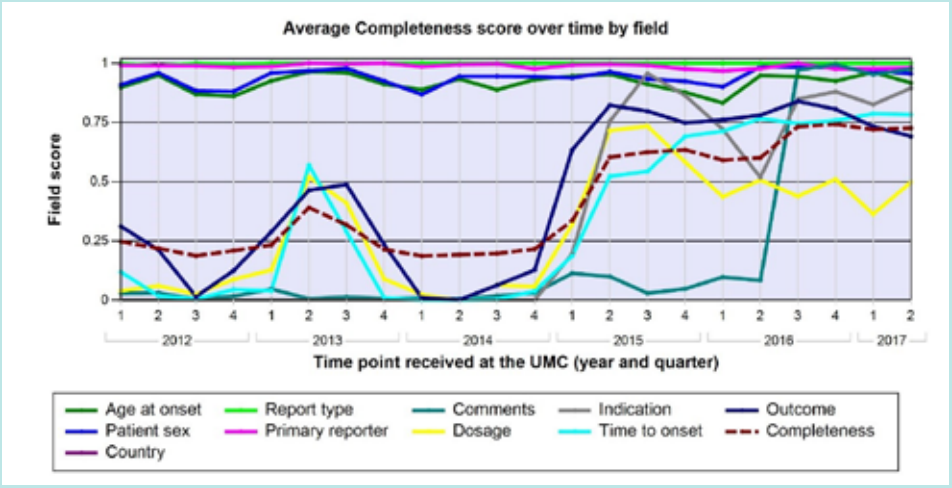






Completeness score by field, Oman

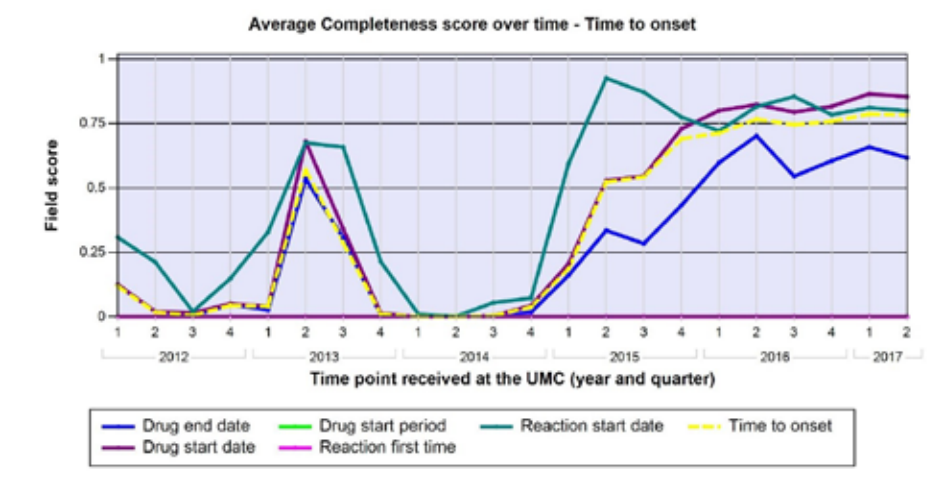
NC Name	Report format	E2B date	Member date
Directorate General Pharmaceutical Affairs and Drug Control	VigiFlow	2015-03-01	1995



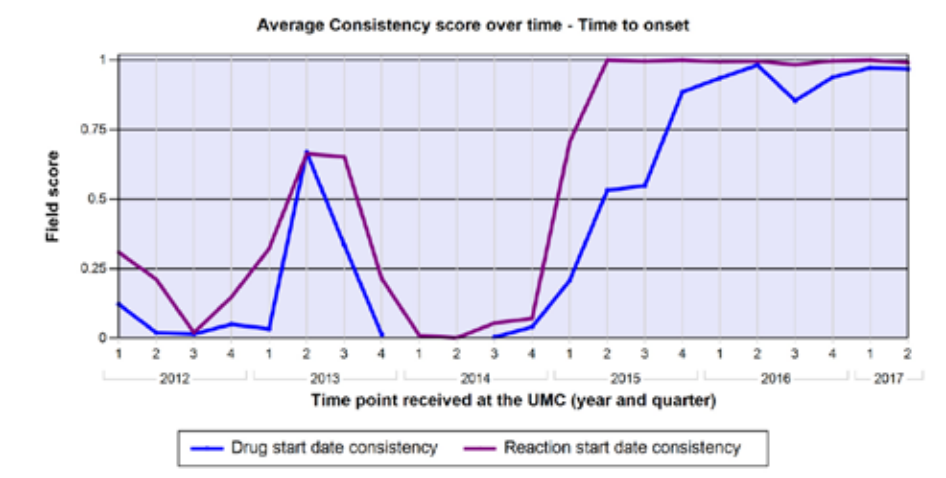
Age at onset	Age of the patient at the time the reaction started.
Patient sex	Sex of the patient.
Country	Country where the ICSR was originally reported, i e the country where the reporter documented the case.
Report type	Type of report, i e 'spontaneous report', 'report from study' or 'other'.
Primary reporter	Qualification of the primary reporter, e g physician or pharmacist.
Comments	Free text information, such as narrative text or reporter comments.

Dosage	Total daily dose for suspected and interacting drugs reported on the case. Concomitant drugs are not included within the score. A full score is given if the total daily dose is given or can be calculated.
Indication	Indication for use of the drug, i e the reason the patient was taking each of the suspected and interacting drugs. Concomitant drugs are not included within the score. A full score is given if the Indication can be mapped to a standard terminology (MedDRA, ICD8, ICD9 or ICD10).
Time to onset	Time elapsed from drug intake to the start of the reaction, for each drug-reaction combination reported on the case. Concomitant drugs are not included within the score. Imprecise information is penalized, for example incomplete dates for reaction start and drug start.
Outcome	Outcome of each reported reaction, e g 'recovered', 'not recovered' or 'death'.
Completeness	Average Completeness, which is calculated from all the pieces of information above.

Time to onset - completeness and consistency, Oman

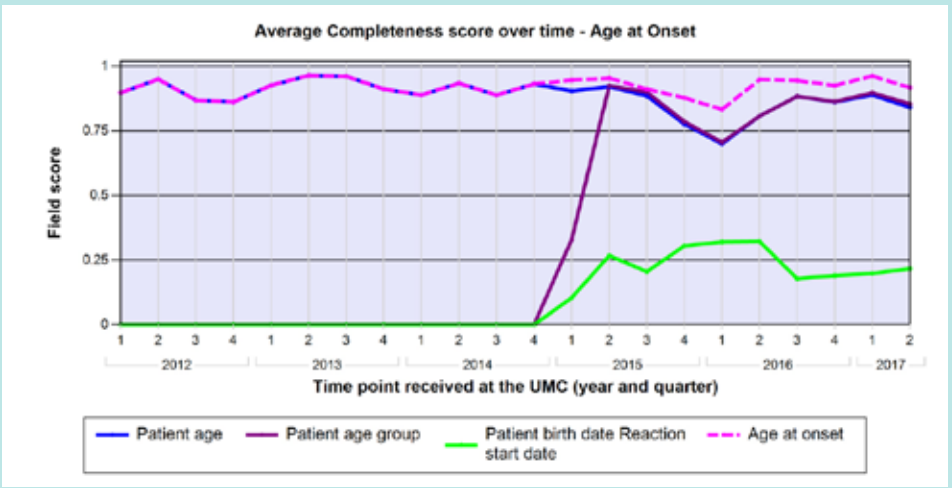


Drug end date	Date when the drug was stopped.
Drug start date	Date when the drug was started.
Drug start period	The interval between each drug start date and first reaction start date.
Reaction first time	The interval between first drug start date and each reaction start date.
Reaction start date	Date when the reaction started.
Time to onset	Time elapsed from drug intake to the start of the reaction, for each drug-reaction combination reported on the case. Concomitant drugs are not included within the score. Calculated for each drug-reaction combination from the fields above.



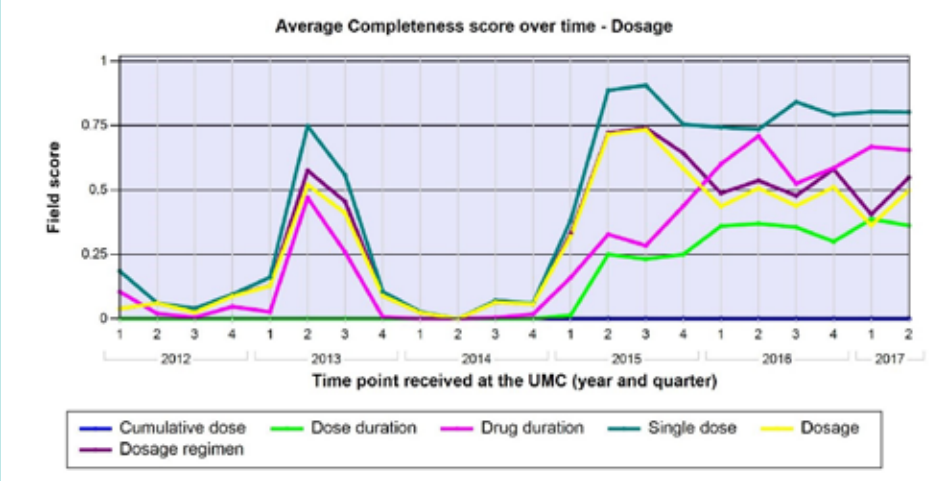
Reaction start date consistency	In order to receive a score of the reliability of the reaction start date, its consistency towards other fields, including other dates, is tested. For details, please see 'Technical description to vigiGrade Complenetess score'.
Drug start date consistency	In order to receive a score of the reliability of the Drug start date, its consistency towards other fields, including other dates, is tested. For details, please see 'Technical description to vigiGrade Complenetess score'.

Age at onset - completeness, Oman



Patient age	Age of the patient at the time the reaction started.
Patient age group	Age group the patient belonged to at the time the reaction started.
Patient birth date Reaction start date	Age calculated from the difference between the birth date of the patient and the reaction start date.
Age at onset	Age of the patient at the time the reaction started, taken from the most precise information in all the fields above. A full score is given if the exact age is given or can be calculated from a complete patient birth date and reaction start date.

Dosage - completeness, Oman



Cumulative dose	Total dose taken by the patient from drug start date to first reaction start date, as specified on the case.
Dosage regimen	Frequency of drug intake, e g once daily or three times/week.
Single dose	The dose taken each time the drug was administered to the patient (single dose), e g 3 mg.
Dose duration	Total time the drug was administered to the patient, as specificed on the case, e g 3 weeks.
Drug duration	Total time the drug was administered to the patient, as calculated from drug start and drug stop date.
Dosage	Total daily dose for suspected and interacting drugs reported on the case Calculated for each drug from the fields above. A full score is given if the total daily dose is given or can be calculated.

Reference:

https://who-umc.org/global-pharmacovigilance/vigiflow/about-vigiflow/

http://www.who.int/hiv/topics/pharmacovigilance/1_vigiflow_data_entry.pdf?ua=1

http://who-umc2010.phosdev.se/DynPage.aspx?id=97223&mn1=7347&mn2=7252&mn3=7254&mn4=7255

QUESTION & ANSWER

Question: What are the effects of statins on muscles, which biochemical parameters should be checked routinely for a patient presenting with statin-induced myopathy and how is it managed?

Answer: One of the most common complaints of people taking statins is muscle pain. One may feel this pain as a soreness, tiredness or weakness in the muscles. The pain can be a mild discomfort, or it can be severe enough to make your daily activities difficult. Interestingly most randomized controlled studies of statins indicate that people taking statins develop muscle pain at the same rate as people taking placebo. However, up to 29 percent of the people who start taking statins report muscle pain and many discontinue statins because of it. Many of these people do well when switched to a different variety of statin.

Very rarely, statins can cause life-threatening muscle damage called rhabdomyolysis (rab-doe-my-OL-ih-sis). Rhabdomyolysis can cause severe muscle pain, liver damage, kidney failure and death. The risk of very serious side effects is extremely low, and calculated in a few cases per million of patients taking statins. Commonly it can occur when you take statins in combination with certain drugs or if you take a high dose of statins.

The mechanism by which statins cause muscle toxicity is not well understood. They inhibit the conversion of HMG-CoA to mevalonic acid, which is an important early step in cholesterol synthesis

When a patient taking a statin reports muscle pain, a detailed history should be obtained. Other conditions that could be causing the problem, but are unrelated to statin therapy, should be ruled out including osteoarthritis, tendinitis, and radiculopathy with muscle strain. Initial assessment should include measurement of CK (creatine kinase) or otherwise termed CPK (Creatine phosphokinase), both refer to the same. The magnitude of elevation will impact on how the patient is managed. The normal levels of which is 22 to 198 U/L (units per liter). Higher amounts of serum CPK can indicate muscle damage from chronic disease or acute muscle injury. Authors of several large case series of rhabdomyolysis agree that CK elevation 5 times the upper limit of normal is the defining biochemical abnormality for this condition. Patients with abnormal elevation in levels should be considered as potential rhabdomyolysis cases and investigated for elevated urine myoglobin levels and deteriorating renal function, statin therapy should be stopped immediately. For such patients the continued use of lipid-lowering therapy must be carefully balanced against the risks of further myotoxicity. Alternative non-statin therapy could be used or, should the perceived benefits outweigh the risks; reintroduction of a statin at a low dose with careful monitoring is possible. For patients whose CK is not elevated, statin therapy can be continued at the same or a lower dose providing muscle symptoms are tolerable. These patients should be monitored to ensure that CK levels are not continuing to rise and that symptoms remain the same. In the case of worsening symptoms, progressively rising CK levels or initially intolerable muscle symptoms, the statin should be stopped and resolve and the CK level returns to normal.

It has been suggested that lipophilic statins (such as lovastatin, simvastatin and atorvastatin) are more likely to cause myotoxicity because

they cross the cell membrane of muscle cells more readily than the more hydrophilic ones (e.g., pravastatin and rosuvastatin). There is insufficient evidence to support this theory fully and reports of rhabdomyolysis have been made in connection with both Pravastatin and Rosuvastatin — demonstrating that hydrophilicity is not the only factor determining myotoxicity typically a patient will present with muscle pain, often described as cramps, or with diffuse discomfort in the legs. Focal pain is less suggestive of myopathy and more likely to be a strain or alternative diagnosis such as osteoarthritis. Increased nocturnal cramping is commonly reported. In other cases generalised weakness or fatigue, particularly following exercise, can occur. Such symptoms are reversible on stopping statin therapy and are unlikely to occur in patients who have been taking a statin for several years.

NEWS:

Science and innovation for better medicines

EMA leaflet shows how work of the Agency benefits patients

As authoritative regulator for medicines in Europe, the European Medicines Agency (EMA) ensures that medicines which are prescribed and used across the European Union (EU) are safe, effective and of good quality. The best scientific experts made available through the European regulatory network for medicines carefully evaluate each new medicine and only recommend its authorisation if the benefits for the patients outweigh the risks of possible side effects.

The leaflet, entitled 'Enabling science that works for patients', explains that the Agency promotes science and innovation to find better medicines. EMA collaborates closely with patients to understand their point of view and to make sure that new medicines address their needs. The Agency provides scientific advice and guidance to encourage the development of new and innovative medicines, especially in areas with limited treatment options such as rare diseases and illnesses in children.

Patients and their needs are at the centre of all activities of the Agency. EMA involves patients, consumers and their representative organisations in all decisions made during the lifecycle of a medicine - in the development of policies, regulatory guidance, and the evaluation and safety monitoring of medicines. Patients provide valuable 'real-life' insights on the impact of regulatory decisions as members of the Agency's management board, scientific committees and working parties.

Ref.: http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2017/08/news_detail_002796.jsp&mid=WC0b01ac058004d5c1

EMA encourages tailored development of medicines for older people

The European Medicines Agency (EMA) is inviting comments from the public on a reflection paper on how medicine developers can better address the needs of older people who take medicines.

In general, older people are the highest users of medicines. According to Eurostat, they are expected to make up almost a third of all Europeans by 2050, and they take more medicines than the rest of the population. Yet, medicines are rarely developed or packaged to take into account their specific needs.

For example, some older people can face challenges such as difficulty opening boxes or bottles, reading instructions, swallowing or breaking tablets and capsules, which can result in medicines not being taken as intended, medication errors and ultimately a reduced quality of life.

The reflection paper describes aspects that medicines developers may consider when designing medicines for older people, such as selecting appropriate routes of administration and dosage forms, dosing frequency, excipients, container closure systems, devices and technologies, and user instructions in the product information.

For example, when there is evidence that older people find it difficult to break a tablet by hand, companies may find ways to improve the breakability of the tablet or consider alternative administration approaches, such as small tablets in a dose dispenser. Similarly, companies may consider re-designing the containers so that older patients can open them easily without any assistance.

Comments are particularly invited on the accuracy of tablet breaking, the administration of medicines through feeding tubes, and on multiple compliance aids and multiple drug dispensing systems (containers that clearly state the name of the day or the moment when a medicine needs to be administrated).

Depending on the outcome of the public consultation, the content of the reflection paper might be further developed into regulatory or scientific guidance.

Ref.: http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2017/08/news_detail_002791.jsp&mid=WC0b01ac058004d5c1

DGPA&DC ACTIVITIES:

Implementation of the Pharmacy Law:

In line with the responsibility of DGPA&DC in implementing the Pharmacy Law issued in 2015 as per the Royal Decree No. 35/2015, the article stated that new pharmaceutical establishment shall be owned fully or partly by an Omani Pharmacist, the Director General of DGPA&DC and Director of Pharmaceutical Licensing Department visited some of the newly opened private pharmacies, owned by Omani pharmacist to discuss the challenges faced and how DGPA&DC can contribute in solving them. The visit was appreciated by the owner and stated that they are ready for more cooperation with DGPA&DC for the benefit of the pharmacy profession in Oman. Visits are expected to be continued for other pharmaceutical establishments including drug stores and pharmaceutical manufacturers.

In addition, DGPA&DC held a meeting with the directors of pharmacy and stores departments in the different regions. In the discussion the

Director General Dr. Mohamed Hamdan Al Rubaie, stated that the aim of the meeting is to enhance the coordination and collaboration. He also introduced the new organogram of DGPA&DC, the addition of two departments, i.e. the Pharmacovigilance and Drug Information Department and the Equipment's & Medical Devices Control department.

Continuous Pharmaceutical Development Programs.

DGPA&DC staff participated in different professional development programs in related fields to enhance their knowledge and experiences. The programs include:

1. The Second International Conference on Combating Counterfeiting in Medicinal Products; Dubai; 1-2 May 2017.

The conference emphasized, the importance of coordination among the countries in the region through an electronic portal and a shared database through which counterfeit medicines and products of low quality can be reported, as well as other topics related to medicinal products, including reporting of side effects and reporting of shortages of essential medicines. Another important agenda of discussion was promoting participation in global initiatives launched by the International Criminal Police Organization (Interpol) in the field of drug fraud. Ph. Nawal Al Alawi, Section head of Pharmacovigilance of Herbal Drugs & Health Products, represented the DGPA&DC in the conference.

2. Workshop on the Theory and Application of Bioavailability and Bioequivalence.

A one-day workshop was held on 8th May 2017 in City season hotel, Muscat, in collaboration with AlfaPharma company. The facilitator Dr. Suliman Al Fayoumi shared his long collaboration and experience with the US FDA. Members of the Bioequivalence committee in DGPA&DC attended the workshop and participated in the discussion on the topics presented, which include Review of key pharmacokinetic concepts and applications; The theory and application of Bioequivalence; Review of International Regulatory Guidelines on Bioequivalence; BA/BE Studies & Bio waivers – General Considerations.

3. Third WHO Global Forum on Medical Devices

The 3rd WHO Global Forum on Medical Devices took place in the Geneva International Conference Center (Switzerland) between 10th and 12th May 2017, 10 years after the Member States recognized in resolution WHA60.29 and WHA67.20 that medical devices are indispensable for health care delivery, but that their selection, regulation and use present enormous challenges. The Forum allowed discussing the achievements that have been made in the field and the enormous challenges in low and middle-income countries. This also served as an opportunity to share the WHO EMP strategy in the framework of Universal Health Coverage and the Sustainable Development Goals. The Director General Dr. Mohamed Hamdan Al Rubaie and Eng. Faiza Al Zadjali director of Equipment & Medical Devices Control Department and Eng. Hamed Al Rashdy from the same department represented DGPA&DC in the forum.

4. UMC International Pharmacovigilance Training Course 8 - 19 May 2017; – Sweden

The course, which is organized yearly by the Uppsala Monitoring Center, focuses on topics essential to effective pharmacovigilance, such as pharmacovigilance best practices, signal detection, reporting culture, and pharmacovigilance tools. The training, which is built around lectures, workshops, and hands-on exercises, takes place in an open and interactive environment with discussion. This year Ph. Nawal Al Alwai, was nominated by DGPA&DC to attend this course.

5. Common Pharmacovigilance (PV) Arab Guidelines Meeting: Kuwait, May 19th to 22, 2017

Ph. Hussain Al Ramimmi Director, DPV&DI with Ph. Madiha Al Maskari and Ph. Alia Al Salhi represented Oman, for the meeting where they discussed the 2017 Regulator's mission and vision with respect to Common Arab guidelines on Pharmacovigilance (PV). The event was co organized by the Ministry of Health Kuwait and Sanofi, Middle East. The deliberations focused on the status of PV in the Arab world, the recent

developments, concepts and practices. The discussions were extended to the adoption of "The new common Arab Guidelines in PV", and exhaustive applications of its modules.

Guidelines for Licensing Manufacturing Plants for Human Medicines, Herbal Medicines & Medical Devices:

In line with DGPA&DC efforts to encourage investment in the pharmaceutical sector and to develop a clear, unified procedure for licensing a local manufacturing plant for Human Medicines, Herbal Medicines and Medical devices, issued a booklet highlighting stepwise detailed procedure for the different stages, from the initial approval phase to the construction phase and the final approval phase. A hard copy of the guidelines is available at the Pharmaceutical Industry Section in DGPA&DC in addition a softcopy is available at the Minsitry of Health web page at the link: https://www.moh.gov.om/documents/16539/101124/Guidelines+for+Licensing+Manufacturing+Plant+for+Human+Medicines+Herbal+Medicines+and+Medical+Devices+-English.pdf/107c34dd-9694-4647-8c6c-0a4086e74418

Social Activity:

On the occasion of the Holy Ramadan Month, DGPA&DC organized an Iftar for its staff in City Season Hotel. The gathering, which brought together most of the staff, enhanced the social relationship among them, away from the routine working hours. The activity was hosted by the Director General Dr. Mohammed Hamadan Al Rubaie and it was also an occasion to meet and greet the ex-Director General Ph. Sawsan Ahmed Jaffer and other staff members who retired from the directorate.

13th Annual Workshop on Good Pharmacy Practice

As part of the pharmaceutical continuing education programme for the private sector pharmacists, the Directorate General of Pharmaceutical Affairs & Drug Control will be conducting the 13th Annual Workshop on Good Pharmacy Practice on ..... at ..... There is no registration fee for participation but those who wish to participate should send the confirmation. The maximum number of participants will be limited to 400 and the registration will be made on first come first basis. As usual, it is will be a one day event with two sessions.

DIRECTORATE GENERAL OF PHARMACEUTICAL AFFAIRS & DRUG CONTROL

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