



# EPVC Newsletter

November 2014

Volume 5, Issue 11

## Egyptian Pharmaceutical Vigilance Center (EPVC)

## Pharmacovigilance Department

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## The 37th Annual Meeting of representatives of the National Centers participating in the WHO Programme for International drug Monitoring - Tianjin, China

Egypt Participated in the 37th Annual Meeting of representatives of the National Centers participating in the WHO Programme for International drug Monitoring that was held from 14 to 17 October 2014 in Tianjin, China.

This meeting was jointly organized by the World Health Organization (WHO), WHO's collaborative center for adverse reaction monitoring, Uppsala Monitoring Centre (UMC), Chinese Food and Drug Administration (CFDA). The meeting was attended by some 200 representatives of National centers from 54 countries worldwide participating in the programme.

### Discussions representatives of the National Centers included:

1. The necessity of **Pharmacovigilance (PV) Centers incorporation inside Drug Regulatory Authorities (DRAs)** in Countries where these Centers are Independent or Academic.
2. The necessity of the existence of these **PV Center locations at the top of DRA hierarchy** and to provide political and logistical



## World Health Organization

support in order to perform their Work without any obstacles.

3. The necessity of PV Centers work extension to support "**Drug Quality**" in addition to Detection of Adverse Drug reactions and take the necessary regulatory actions about it.
4. The necessity of "Substandard, spurious, fully-labeled, falsified, and counterfeit medical products (**SSFFC**)" **Monitoring incorporation in PV Centers Activities** in Different Countries.
5. Invitation and motivation of PV Centers participation in regular training courses held by (WHO) about (SSFFC).
6. The use of various means of Media to promote the idea of

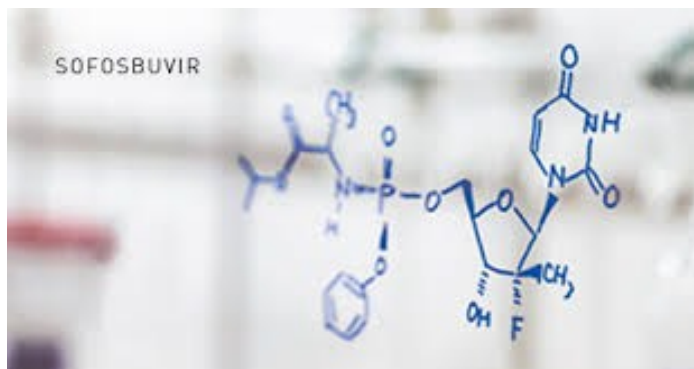
- pharmacovigilance in different communities and to motivate healthcare professionals and patients for early reporting of drug adverse events.
7. Development (Vigimed) to support the communication between Different PV centers Worldwide and to facilitate information transport in regards to Drugs safety in different communities.
  8. Encouragement of PV centers to perform Awareness and training activities inside different communities to disseminate Pharmacovigilance culture at the level of Marketing Authorization Holders and healthcare professionals.
  9. The importance of Pharmacovigilance programs incorporation in Different Health Programs in different communities.
  10. Encouragement of national PV centers to establish regional center so as to ensure coverage of all community sectors.
  11. Encouragement of PV Centers effective communication especially in case of medicinal disasters and epidemics.
  12. To take into consideration “Drugs Benefit-Risk Balance” during relevant regulatory decision taking which will vary among different communities.
  13. The necessity that PV Centers lead Media and not the opposite in regards to Drugs News.
  14. Extension of PV Centers activities to include Systemic collection of Data and information related to medication usage during Pregnancy and lactation, because of the inadequacy of available data in this field.
  15. The encouragement of PV centers to provide data related to Drug risk and benefit to the public and community in order to help drugs rational utilization.
  16. The necessity of monitoring “Risk/Benefit Balance” in addition to “Signal detection” in low-&Middle income countries, and not only relay on developed countries.
  17. The necessity of coordination in regards to extended Vaccination programs and extension of PV centers work to include “Serums, and vaccines” vigilance.
  18. To enable patients and civil society organizations to report adverse drug events.



## Egyptian Pharmaceutical Vigilance Center (EPVC) - Pharmacovigilance Training to Hospital Pharmacists responsible for SOVALDI® (Sofosbuvir) dispensing in Egypt.

In accordance with Ministry of Health Announcement about “Launch of Sovaldi® (sofosbuvir), the new Hepatitis C treatment in Egypt”; Egyptian Pharmaceutical Vigilance Center (EPVC) organized a specialized Pharmacovigilance training Module for Hospital Pharmacists responsible for dispensing sofosbuvir in 8 hospital pharmacy centers on Friday, 24<sup>th</sup> October 2014.

Training Module composed of three parts; “Introduction to Pharmacovigilance and spontaneous ICSR reporting”, “Sofosbuvir Drug Profile” and “History of Sovaldi Registration in Egypt”.



It is worthy to note that, EPVC have published recommendations for HealthCare Professionals concerning Sofosbuvir in EPVC Newsletter (Issue: 55).<sup>[1]</sup>

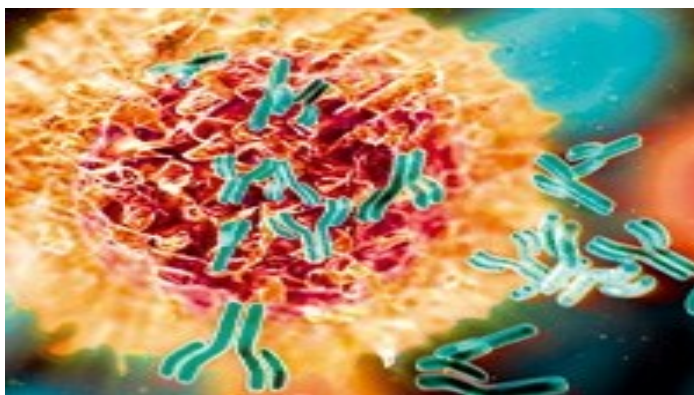
*Reference:*

[1] EPVC Newsletter “Issue:55” ([Click Here](#))

## Rituximab - Two Direct Healthcare Professional Communications (DHPCs) distribution Concerning “Risk of Hepatitis B reactivation” and “Usage in population known to bear a high potential risk of Hepatitis C Virus (HCV) infestation” in Egypt.

On 4<sup>th</sup> October 2014, Egyptian Pharmacovigilance Center Approved the Distribution of Two (DHPCs) Concerning “Risk of Hepatitis B reactivation” and “Usage in population known to bear a high potential risk of Hepatitis C Virus (HCV) infestation” with Rituximab to HCPs in Egypt.

**Rituximab** is a genetically engineered chimeric mouse/human monoclonal antibody representing a glycosylated immunoglobulin with human IgG1 constant regions and murine light-chain and heavy-chain variable region sequences. The antibody is produced by mammalian (Chinese hamster ovary) cell suspension culture and purified by



affinity chromatography and ion exchange, including specific viral inactivation and removal procedures<sup>[1]</sup>. It is used to treat diseases which are

characterized by excessive numbers of B cells, overactive B cells, or dysfunctional B cells.

### **Recommendations for Health Care Professionals Regarding Rituximab:**

1. Due to the High prevalence rate of HCV positive patients amongst the Egyptian population, it is per the Egyptian Pharmacovigilance Center recommendation to screen for serum (hepatitis C viral antibody) HCV Ab testing in addition to the previously known (hepatitis B virus surface antigen) HBV sAg testing, before the initiation of treatment.
2. Caution is required when Rituximab is prescribed for patients with a history of recurrent or chronic infection or an underlying disease that favors the occurrence of severe infections.

Patients who develop an infection after treatment with Rituximab should be promptly investigated and appropriately treated.

3. Based on the current data and following the updated new clinical guidelines, it is recommended that HBV screening performed in all patients before the initiation of treatment with Rituximab in all indications, and that patients with positive HBV serology should consult with a liver disease specialist before start of treatment. Those patients should be monitored and managed following local standards to prevent hepatitis B reactivation.

### **References:**

- [1] Rituximab : EMA Approved Summary of Product Characteristics ([Click Here](#))

## **Denosumab - Distribution of DHPC concerning “Risk of Osteonecrosis of the jaw and hypocalcaemia” in Egypt**

On 23<sup>th</sup> October 2014, Egyptian Pharmacovigilance Center Approved the distribution of (DHPC) Concerning “Risk of Osteonecrosis of the Jaw (ONJ) and hypocalcaemia” with Denosumab to HCPs in Egypt.

**Denosumab** is a human monoclonal IgG2 antibody produced in a mammalian cell line (CHO) by recombinant DNA technology. It is used for prevention of skeletal related events (pathological fracture, radiation to bone, spinal cord compression or surgery to bone) in adults with bone metastases from solid tumors <sup>[1]</sup>.

**ONJ** is a condition in which the jawbone becomes necrotic, exposed, and does not heal within 8 weeks. The etiology of ONJ is not clear, but may be associated with inhibition of bone remodeling.

Known risk factors for ONJ include invasive dental procedures (e.g., tooth extraction, dental im-



plants, oral surgery), poor oral hygiene, or other pre-existing dental disease.

Other risk factors for ONJ are advanced malignancies, infections, older age, concomitant therapies (e.g., chemotherapy, corticosteroids, angiogenesis inhibitors, radiotherapy to the head and neck), smoking, and previous treatment with

bisphosphonates. While on treatment, patients should avoid invasive dental procedures if possible.

### **Recommendations for Health Care Professionals:**

1. ONJ is a common side effect in patients treated with DENOSUMAB.
2. Before starting DENOSUMAB, a dental examination with appropriate preventive dentistry is recommended.
3. Do not start DENOSUMAB in patients with an active dental or jaw condition requiring surgery, or in patients who have not recovered following oral surgery.
4. Tell patients receiving DENOSUMAB to maintain good oral hygiene practices, receive routine dental check-ups, and immediately report any oral symptoms such as dental mobility, pain, or swelling during treatment with DENOSUMAB.
5. Hypocalcaemia  $\geq$  grade 3 is a common side effect of DENOSUMAB. The risk increases with the degree of renal impairment.
6. Pre-existing hypocalcaemia must be corrected prior to initiating therapy with DENOSUMAB.
7. Supplementation with calcium and vitamin D is required in all patients unless hypercalcaemia is present.
8. Monitoring of calcium levels should be conducted:
  - prior to the initial dose of DENOSUMAB
  - within two weeks after the initial dose
  - if suspected symptoms of hypocalcaemia occur
9. Consider monitoring calcium levels more frequently during therapy in patients with risk factors for hypocalcaemia (e.g. patients with severe renal impairment, creatinine clearance  $<30$  ml/min), or if otherwise indicated based on the clinical condition of the patient.

### **References:**

- [1] Denosumab : EMA approved Summary of Product Characteristics ([Click Here](#))

## **Clopidogrel - Distribution of DHPC Concerning “association of with acquired haemophilia” in Egypt.**

On 2<sup>th</sup> October 2014, EPVC approve distribution of DHPC Concerning “association of clopidogril with acquired hemophilia” to HCPs in Egypt.

**Clopidogrel** is an oral, thienopyridine class antiplatelet agent; it is indicated for the prevention of atherothrombotic events in myocardial infarction, ischaemic stroke, established peripheral arterial disease, acute coronary syndrome including Non-ST segment elevation myocardial



infarction and unstable angina, and ST segment elevation acute myocardial infarction with aspirin in medically treated patients eligible for thrombolytic therapy. Clopidogrel is also indicated in combination with aspirin for the prevention of atherothrombotic and thromboembolic events in atrial fibrillation in patients unsuitable for vitamin K antagonist treatment.

### **Recommendations for Health Care Professionals:**

1. small number of cases of acquired haemophilia associated with clopidogrel treatment in individuals with no previous history of abnormal haemostasis have been reported.
2. Acquired haemophilia must be promptly recognised to minimise the time the patient is at risk of bleeding and avoid major bleeding.
3. In case of confirmed isolated activated Partial Thromboplastin Time (aPTT) prolongation with or without bleeding, acquired haemophilia should be considered.
4. Patients with a confirmed diagnosis of acquired haemophilia should be managed and treated by specialists, clopidogrel should be discontinued and invasive procedures should be avoided.

## **Risk of Medication Errors Resulting From Mixing-Up Similar (Look-alike) Drugs - Cairo, Egypt.**

On 25/2/2014, Egyptian Pharmaceutical Vigilance regional Center in Cairo received three complaints from Children's Cancer Hospital in Egypt about potential for mixing-up of different drugs that are similar in their packaging design which may lead to many medication errors and consequently unexpected harm to the patient.

### **1. Potential for mixing-up Potassium chloride ampoules (Egypt Otsuka Pharm. Co.) with Sterile water for injection ampoules:**

Potassium chloride ampoules are mistaken for ampoules of similar appearance, such as sterile water for injection when reconstituting a drug for injection (figure:1). Consequently, the patient is administered an accidental overdose/unintended dose of potassium.

### **Recommendations for Health Care Professionals:**

- Choose designated area for storage of potassium chloride only.

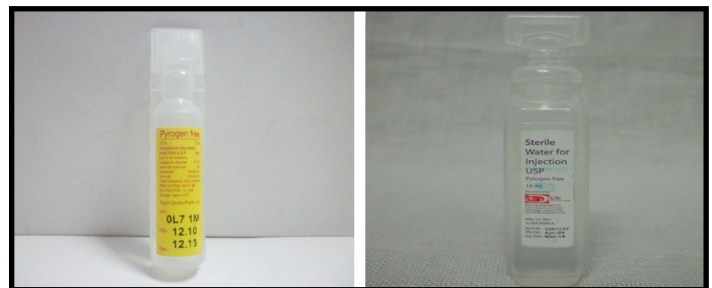


Figure: 1

- Due to risk associated with intravenous potassium chloride, Ampoules of potassium chloride should not be kept as stock item in wards.
- ### **2. Potential for mixing-up Tanakan® tablets with Oflam® 25mg tablets especially in Unit Dose Dispensing System:**

Tanakan® is manufactured by AMRIYA CO. under license of IPSEN CO; Oflam® is manufactured by MEDICAL UNION PHARMACEUTICALS-EGYPT CO. under license of MEPHA-SWITZERLAND CO. (figure:2)

### **3. Potential for mixing-up Morphine® ampoules -MISR CO. of different concentrations:**

Morphine® 20mg ampoules are mistaken for 10mg ampoules (or vice versa) of semi-typical appearance. Consequently, the patient is administered an accidental overdose/ subtherapeutic dose of Morphine®. Morphine® manufactured by MISR CO. (figure:3)



Figure: 2

### **4. Potential for mixing-up different products of some manufacturers due to packaging design similarity as following:**

- Orazone® syrup manufactured by ADCO; Hexitol® mouth wash manufactured by ADCO; Pirafene® syrup manufactured by MEMPHIS CO. (figure:4)
- Dompidone® tablet manufactured by ADCO. Deltasone® tablet manufactured by EL NILE. CO. (figure:5)
- Isopto-atropine® manufactured by Alcon CO; Mydriacyl® manufactured by Alcon CO. (figure:6)



Figure: 3

### **Recommendations for HealthCare Professionals:**

- ⇒ Product Label double checking in alignment with the written prescription together with intended indication.
- ⇒ Identify Different storage areas for Products with package design similarity.



Figure: 4



Figure: 6



Figure: 5



# NORCB Newsletter

October 2014

Volume 5, Issue 10

**National Organization for  
Research & Control of  
Biologicals**

**Post Marketing  
Surveillance and Adverse  
Event Following  
immunization Department**

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99 percent decrease in 10  
polio rates shows total  
eradication is near

## Are personalized approaches the solution for a troubled cancer vaccine field?

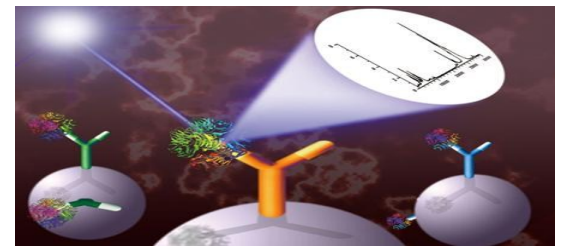
Cancer vaccine developers have seen their fair share of disappointments, and failures have spurred some companies to test their treatments in smaller patient subpopulations. Now, researchers at the University of Connecticut are narrowing their focus even further as they gear up to trial personalized cancer vaccines.

Using genome sequencing to identify the differences between protein sequences--called epitopes--in healthy versus cancerous tissue, they'll start up an initial clinical study for ovarian cancer

patients once they nab FDA approval. The team will sequence DNA from the tumors of 15 to 20 women with ovarian cancer, using that information to make a personalized vaccine for each woman.

**Reference**

*Fierce Vaccines:* [\(Click Here\)](#)



## Adult TB vaccine with low protection rate better than infant jab

Worldwide tuberculosis rates have been on a steady decline in recent years, but as resistance to commonly used antibiotics to treat the disease grows, most scientists and health advocates agree that a vaccine is the best route for prevention.

A new study suggests that a tuberculosis vaccine with low efficacy in adolescents and adults could be more successful at reducing rates of the disease than a vaccine intended for infants.

Using a model with data from 91 countries, researchers from the London School of Hygiene and Tropical Medicine and the World Health Or-

ganization found that vaccines targeted at adolescents and adults could prevent TB and be cost-effective, and even save money, before 2050 if the efficacy were as low as 20% with a 10-year duration.

**Reference**

*Fierce Vaccines:* [\(Click Here\)](#)





## Adaptimmune's novel cancer treatment posts promising early results

Adaptimmune's pioneering approach to cancer immunotherapy has charted some impressive results in a small study. And while the biotech is quick to point out that it's early days yet .

The treatment is based on a proprietary technology through which Adaptimmune can extract a patient's own T cells, which the immune system uses to fight infection, and rewire them to better detect cancer. Once scientists have equipped those T cells with tumor-philic receptors, they are re-injected into patients, ideally spurring a broad immune response against cancers that previously passed undetected.

And in preliminary results from a 10-patient

study on synovial sarcoma, Adaptimmune's treatment did just that. Among the 5 patients who have reached the 60-day assessment period, 80% charted a response to the treatment, with one patient's cancer completely gone at 9 months.

### Reference

*Fierce Vaccines:* ([Click Here](#))



## Flu vaccine may hold key to preventing heart disease

Flu vaccines are known to have a protective effect against heart disease, reducing the risk of a heart attack. For the first time, this research reveals the molecular mechanism that underpins this phenomenon. The scientists behind the study say it could be harnessed to prevent heart disease directly.

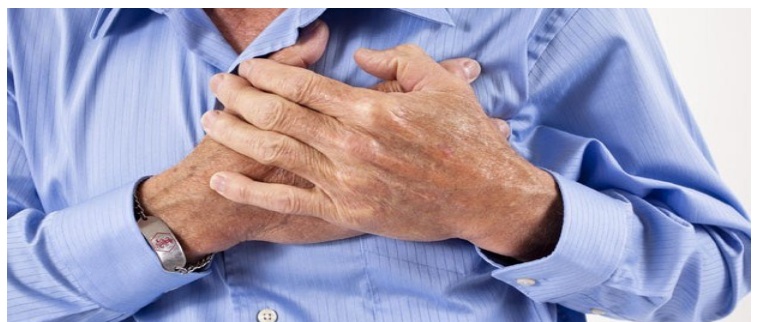
This new study for the first time reveals this mechanism, showing that the flu vaccine stimulates the immune system to produce antibodies that switch on certain processes in cells. These processes lead to the production of molecules that protect the heart. The researchers say that based on the results it may be possible to develop a new vaccine against heart disease.

The researchers identified a protein called

the bradykinin 2 receptor (BKB2R), which is involved in cellular processes that protect the heart. Some of the antibodies the body produces after flu vaccination switch this protein on, therefore protecting against heart disease. The researchers analysed 14 flu viruses used in vaccines, and identified four that could be investigated for use in potential heart disease vaccines.

### Reference

*Science daily:* ([Click Here](#))

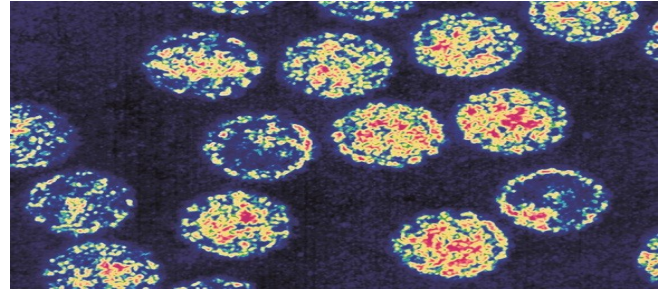


## Human papilloma virus vaccination provides long-term protection

Persistent infection with a high-risk human papillomavirus (HPV) type is a necessary prerequisite for the development of dysplasia and neoplasia of the cervix, precursors to cervical cancer. The HPV vaccination has been a subject of heated debate since it was launched. Now researchers have produced a systematic review that shows no decrease in protection over a period of five years following vaccination against HPV types 16 and 18.

### Reference

*Science daily:* ([Click Here](#))



## Just how big is the biosimilars business going to be in 5 years?

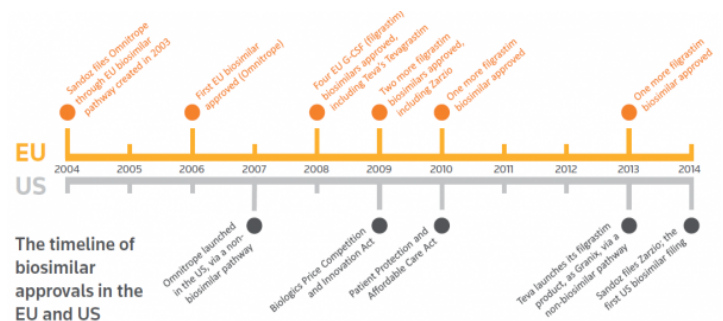
Thomson Reuters BioWorld took a deep dive into the subject and surfaced today with a detailed report outlining a bustling new global business with roughly 700 so-called follow-ons put in the clinic by 245 companies and institutions. Looking ahead to 2020, analysts say, you can anticipate that biosimilars will account for about \$25 billion out of \$100 billion in sales for off-patent biologics.

The EU was the first to outline a regulatory pathway for biosimilars, and it's been seeing the largest number of approvals. Drugmakers in India and Korea, meanwhile, have clearly outlined a big role for themselves in delivering less expensive biosimilars to the developing world, where people often find themselves unable to

afford biologics at branded prices. And while the U.S. is just now opening the door to biosimilars, Thomson Reuters BioWorld concludes that dozens of meetings have occurred at the FDA with developers racing to penetrate the world's biggest drug market.

### Reference

*Fierce Biotech:* ([Click Here](#))



## 99 percent decrease in polio rates shows total eradication is near

Polio has been reduced by 99 percent during the past 26 years thanks to polio eradication efforts reaching a global scale.

In 1988, polio was a leading cause of childhood disability cases. UNICEF now provides 500 million children with the polio vaccine each year.

Studies show that 10 million cases of polio have been prevented through eradication efforts. This means that approximately a thousand children each day are healthy instead of disabled by polio.

“The success of the eradication effort – reaching some of the most disadvantaged communities in some of the most dangerous circumstances – proves that it is possible to reach all children,” UNICEF Executive Director Anthony Lake said. The only remaining countries with high polio rates are Afghanistan, Nigeria and Pakistan. All other nations have eradicated polio from their populations.

### Reference

*Vaccine News Daily:* ([Click here](#))

## What is Pharmacovigilance

According to the WHO, Pharmacovigilance is the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other medicine-related problem.

## What is the Egyptian Pharmaceutical Vigilance Center

With the increasing demand for patient's safety which is becoming more stringent, the regulatory authorities are facing an increased demand for patient welfare and safety. Thus, The Egyptian Pharmaceutical Vigilance Center (EPVC) is constructed within The Central Administration of Pharmaceutical Affairs (CAPA) Ministry of Health to be responsible for the collection and evaluation of information on pharmaceutical products marketed in Egypt with particular reference to adverse reactions. Furthermore, EPVC is taking all appropriate measures to:

1. Encourage physicians and other healthcare professionals to report the suspected adverse reactions to EPVC.
2. Necessitate the pharmaceutical companies to systematically collect information on risks related to their medical products and to transmit them to EPVC.
3. Provide information to end-users through adverse drug reaction news bulletins, drug alerts and seminars.

## A call for reporting

Please remember that you can report suspected adverse reaction of medicines to EPVC, and adverse reaction following immunization to NORCB using the following communication information

## Communications information

### Central Administration of Pharmaceutical Affairs Egyptian Pharmaceutical Vigilance Center Pharmacovigilance Department

21 Abd El Aziz Al Soud Street. El-Manial, Cairo, Egypt, PO Box: 11451  
Phone: +202 - 23684288,  
Fax: +202 - 23610497  
Email: pv.center@eda.mohealth.gov.eg



[www.epvc.gov.eg](http://www.epvc.gov.eg)

### National Organization for Research & Control of Biologicals Post Marketing Surveillance and Adverse Event Following immunization Department

51 Wezaret El Zeraa Street, Agouza, Giza P.O. Box: 354 Dokki  
Phone: +202 - 37 480 478 ext. 118  
Fax: +202 - 37480472  
Email: pmsdep@yahoo.com