Drug News
藥 物 情 報

Issue No. 20 : June 2011

This is a monthly digest of local and overseas drug safety news and information released in the previous month. For the latest news and information, please refer to public announcements or the website of the Drug Office of the Department of Health (http://www.drugoffice.gov.hk).

Safety Update

US: New restrictions to the prescribing and use of rosiglitazone-containing medicines

19 May 2011 – Further to the restriction of use of rosiglitazone-containing medicines due to their risk to cardiovascular events, the US Food and Drug Administration (FDA) required a restricted and distribution program to be included in the Risk Evulation and Mitigation Strategies (REMS) of all three rosiglitazone products marketed in US, namely Avandia, Avandamet, and Avandaryl. Under the REMS, healthcare providers and patients must enroll in a special program in order to prescribe and receive these drugs.

In Hong Kong, Avandia, Avandamet and Avandaryl are registered by GlaxoSmithKline Ltd (GSK). There are currently 15 registered pharmaceutical products containing rosiglitazone and they are prescription medicines. Rosiglitazone is a thiazolidinedione used for the treatment of Type II diabetes. The safety concern of rosiglitazone in increasing cardiovascular risks had been reviewed worldwide in 2010 and has been reported in Issue No. 7, 10 &12 of Drug News. On 4 October 2010, the Registration Committee of the Pharmacy and Poisons Board decided to restrict the use of rosiglitazone and revise the product package insert accordingly. The Department of Health (DH) also issued a press statement and letters to healthcare professional on the same day regarding this recommendation. In response to the recent development, the Registration Committee decided at its meeting on 15 June 2011 to request the registration holder of Avandia, GSK, to provide the details of the restricted access and distribution program implemented in USA, namely Avandia-Rosiglitazone Medicines Access Program, and submit a proposal of a similar restricted access and distribution program to be used in Hong Kong for the Committee's consideration.

EU: European Medicines Agency recommended suspension of oral buflomedil-containing medicines

21 May 2011 - The Committee for Medicinal Products for Human Use (CHMP) of European Medicines Agency (EMA) recommended suspending the supply of oral buflomedil-containing medicines in all EU Member States where it was authorised at that time.

Buflomedil, a vasoactive agent supplied in oral and injectable forms, is used to treat the symptoms of peripheral arterial occlusive disease (PAOD). This is a condition where the body's large arteries become obstructed causing symptoms such as pain and weakness, particularly in the legs. Buflomedil is used in patients with stage II PAOD, who experience severe pain when walking even relatively short distances.

The CHMP concluded that the previous measures imposed by regulatory authorities could not prevent the occurring of serious and sometimes fatal neurological and cardiac side effects, especially related to accidental or intentional overdose. The CHMP also noted that the medicine had only been shown to have a limited benefit for patients, measured in terms of walking distance, and the studies assessed had a number of weaknesses. As a result, the CHMP considered that the benefits of buflomedil-containing medicines in the form of tablets or an oral solution did not outweigh their risks, and recommended that the supply of these medicines should be suspended throughout the EU. This was an interim recommendation and the CHMP would adopt an opinion when the review of the benefits and risks of injectable buflomedil solution was finalized.

In Hong Kong, there was only one pharmaceutical product containing buflomedil, namely Bumedin tablet 150mg, registered. The registration holder, Anderson International Company Limited, voluntarily cancelled the registration of the product concerned. In response to EMA's recommendation, DH issued letters to inform healthcare professionals about the updated safety information on 21 May 2011. At the meeting held on 15 June 2011, the Registration Committee of the Pharmacy and Poisons Board decided that future applications for registration of oral buflomedil-containing medicines should not be approved unless information is provided to substantiate its safety and efficacy.

EU : European Medicines Agency did not support the use of celecoxib in familial adenomatous polyposis

21 May 2011 - After completing a review of the use of the COX-2 inhibitor celecoxib in the reduction of the number of adenomatous intestinal polyps in familial adenomatous polyposis (FAP), the EMA's CHMP concluded that existing evidence of safety and efficacy did not support the use of celecoxib in FAP patients.

Onsenal, a celecoxib-containing product that indicated for FAP, was withdrawn from EU market in April 2011 due to inability to provide the efficacy data to confirm the clinical benefit required by CHMP. Celecoxib-containing products were currently authorised in the EU only for treating symptoms of osteoarthritis, rheumatoid arthritis and ankylosing spondylitis. This review was initiated because of concerns that celecoxib might be used off -label in the FAP indication following the withdrawal of Onsenal. For details of the recall of Onsenal, please refer to Drug News issue No. 18.

The CHMP concluded that the benefit of celecoxib in FAP patients did not outweigh the increased risk of cardiovascular and gastrointestinal side effects, which would result from high dose and long-term treatment used in FAP patients.

In Hong Kong, there are 12 registered pharmaceutical products containing celecoxib and all are prescription medicines. In Hong Kong, celecoxib currently is not indicated for FAP. DH issued letters to inform healthcare professionals about the updated safety information on 21 May 2011.

China : Deregistration of Duxaril

21 May 2011 – The State Food and Drug Administration (SFDA) of China suspended the production, sale and use of products like Duxil (also known as Duxaril Tablets or Compound Almitrine Tablets) and cancelled their registration. The decision was made because the drug wholesaler, Servier (Tianjin) Pharmaceutical Co. Ltd., failed to demonstrate the efficacy of almitrine and raubasine in improving the cognitive function for patients suffering non-Alzheimer's vascular cognitive disorders according to the requirement of SFDA.

Duxaril Tablets, also known as Compound Almitrine Tablets, containing almitrine bismesylate 30mg and raubasine 10mg, is used for treatment of the symptoms of cognitive and chronic sensorineural impairment in elderly (excluding Alzheimer's disease and other forms of dementia); adjuvant treatment for visual impairment, visual field disorders, auditory impairment, vertigo and/or tinnitus presumed to be of vascular origin.

In Hong Kong, there are 2 registered pharmaceutical products containing almitrine and raubasine. Both are prescription medicines. DH issued letters to inform healthcare professionals about the updated safety information on 23 May 2011. At its meeting held on 15 June 2011, the Registration Committee of the Pharmacy and Poisons Board decided that the indication of almitrine/raubasine tablets for the treatment of "非痴呆性血管認知功能障礙" (non-Alzheimer's vascular cognitive disorders) should be removed. The registration certificate holders were requested to provide additional clinical data to substantiate the safety and efficacy of the other indications of the product within 6 months.

China : New restriction on the use of nimesulide

21 May 2011 – After reviewing relevant adverse reaction reports in China, clinical studies of different countries and expert advice, the SFDA of China decided to restrict the use of oral nimesulide-containing preparation. Its use would be limited to children 12 years of age or above, as a second line treatment in relieving pain and inflammation and after failed treatment with at least one non-steroidal anti inflammatory drug. Its indications would be restricted to chronic arthritic (e.g. osteoarthritic, etc)

pain, postoperative and acute post-traumatic pain and dysmenorrhoea. The maximum single dose should not exceed 100mg and its use should be limited to not more than 15 days.

In Hong Kong, there are 18 registered pharmaceutical products containing nimesulide and all are prescription medicines. The approved indications in Hong Kong are for treatment of acute pain, symptomatic treatment for osteoarthritis and primary dysmenorrhea which are the same as those approved in the EU. Safety information on nimesulide-containing medicines had been reported in Issue No. 17 of Drug News. The Registration Committee of the Pharmacy and Poisons Board discussed the use of nimesulide-containing medicines at its meeting held on 12 May 2011 and concluded that the products are contraindicated for children under 12 years of age. In view of the new restriction, DH issued letters to inform healthcare professionals about the updated safety information on 23 May 2011. The issue was also discussed in the meeting of the Registration Committee of the Pharmacy and Poisons Board held on 15 June 2011 and it was decided that the following information should be added on the sales packs or package insert of all oral nimesulide-containing pharmaceutical products

i) the product is used as a second line treatment in pain killing and inflammation, after failed treatment with at least one non-steroidal anti-inflammatory drug;

ii) the maximum single dose should not be more than 100mg; and

iii) In order to reduce undesirable effect, the minimum effective dose and the shortest duration of treatment should be used after taking consideration of the clinical condition of the patient.

UK and US: Safety review of risk of venous thromboembolism with the use of the combined oral contraceptive containing drospirenone

28 May 2011 –The Medicines and Healthcare products Regulatory Agency (MHRA) announced that an analysis of the available epidemiological data showed that the risk of venous thromboembolism (VTE) for combined oral contraceptives (COCs) that contain drospirenone, such as Yasmin, is higher than the risk for levonorgestrel-containing second generation COCs, and may be similar to the risk for desogestrel-containing or gestodene-containing third generation COCs. Nevertheless, the assessment has not changed the conclusion that the risk of VTE with any COCs is very small. Product information for Yasmin was being updated accordingly.

1 June 2011 - FDA announced that the agency was also aware of two newly published studies showing a greater risk of VTE in patients using birth control pills that contain drospirenone compared with those using levonorgestrel-containing pills. It would conduct a safety review of birth control pills containing drospirenone as the results from these studies were conflicting with those of the previous studies. FDA would continue to communicate any new safety information to the public as it became available.

In Hong Kong, there are 3 registered COCs containing drospirenone. They are Yasmin Tab (HK -48905), Angeliq Tab (HK-53676) and Yaz Tab (HK-56563) and all are registered by Bayer Healthcare Ltd. The risk of VTE has already been included in the current package insert of the above three products. At its meeting held on 15 June 2011, the Registration Committee of the Pharmacy and Poisons Board decided that the sales pack or package insert of these product should add information about the higher risk of VTE for COCs that contain drospirenone compared with levonorgestrel-containing second generation COCs, and the risk may be similar to that for desogestrel-containing or gestodene-containing third generation COCs.

US: No evidence to suggest an increased risk of cancer in patients taking angiotensin receptor blockers

3 June 2011 – After a safety review of angiotensin receptor blockers (ARBs), a group of medications used to control high blood pressure, FDA concluded that patients treated with these medications did not increase their risk of developing cancer. The review was initiated in July 2010 after a published study found a small increased risk of cancer in patients taking an ARB compared to those patients not taking an ARB. FDA evaluated controlled trial data on more than 155,000 patients randomized to ARBs or other treatments from 31 randomized clinical trials and found no evidence of an increased risk of cancer

in patients who took an ARB.

There are about 130 medicines containing angiotensin receptor blockers registered in Hong Kong. DH remains vigilant to any new findings about ARB.

UK: More exact paracetamol dosing for children to be introduced

7 June 2011 – MHRA announced that updated dosing for children's liquid medicines containing paracetamol had been developed to ensure children get the most effective amount, and to support giving it to them in the best way. The agency reassured that the change was not because of safety concerns. The current dosage system has a single age band 6 - 12 years. In the updated system, this will be divided into three separate age bands of 6 - 8 years, 8 - 10 years, and 10 - 12 years. The updated dosing advice clarified the doses, making it easier for parents and carers to know exactly how much paracetamol they should give their children. It was decided that paracetamol products for children currently on the market should have the updated dosage instructions by the end of 2011. In the meantime, parents and carers were advised to follow the current dosing and the advice on the packaging, making sure not to exceed the recommended dose.

In Hong Kong, there are 975 registered pharmaceutical products containing paracetamol and about 85 of them are liquid medicines. Paracetamol is used for treatment of pain and fever. DH remains vigilant to any new findings about the drug.

UK: Recall of Abilify 5mg, 10mg, 15mg and 30mg tablets parallel distributed by Chemilines Limited

7 June 2011 - Chemilines Limited recalled multiple batches of Abilify 5mg, 10mg, 15mg and 30mg tablets which were parallel distributed by them. The recall was commenced because the patient information leaflet did not include updated information on administration and safety warnings, including the mandatory warning on risk of venous thromboembolism in EU. The updated leaflet had been included in packs since February 2011.

In Hong Kong, Abilify (aripiprazole) tab is registered by Otsuka Pharmaceutical (HK) Ltd. and is a prescription medicine. Aripiprazole is used for treatment of schizophrenia, mania associated with bipolar disorder, and as adjunctive therapy in depression. Labeling requirement in United Kingdom is different from Hong Kong. In Hong Kong, the product label met the local registration requirement.

Hong Kong and Canada: Fatal Infusion Related Reactions in Patients with Rheumatoid Arthritis treated with rituximab

26 May 2011 - DH of Hong Kong issued letter to alert healthcare professionals about the important new safety information on the use of rituximab in rheumatoid arthritis (RA). DH was informed by Roche Hong Kong Ltd. that there were 4 cases of spontaneous post marketing reports of fatal infusion related reactions. Rituximab is registered as Mabthera in 4 different strengths/ forms by Roche Hong Kong Limited (Roche) in Hong Kong. All are prescription medicines. The prescribing information for rituximab would be updated to reflect the new safety information.

8 June 2011 – Hoffmann-La Roche Limited, in consultation with Health Canada, alerted the healthcare professionals the same safety information of the drug which is marketed as Rituxan in Canada. The product monograph would be updated accordingly in Canada. Healthcare professionals were advised to provide premedication prior to infusion and to observe for signs of anaphylaxis or other hypersensitivity/infusion reactions, especially among patients with pre-existing cardiac conditions and with history of prior cardiopulmonary adverse reactions, and managed as appropriate when administering Rituxan.

US: New safety recommendations for high -dose simvastatin

9 June 2011 – FDA announced safety label changes for the cholesterol-lowering medication, simvastatin, because the highest approved dose--80 milligram (mg)--had been associated with an elevated risk of muscle injury or myopathy. This risk appeared to be higher during the first year of treatment, as a result of interactions with certain medicines or in patient with a genetic predisposition toward simvastatin-related myopathy. The agency recommended that simvastatin 80mg should be used only in patients who have been taking this dose for 12 months or more without any clinical features of

myopathy. It should not be prescribed to new patients. In addition, there were new contraindications and dose limitations of simvastatin when it is taken with certain other medications. The changes to the drug label for simvastatin-containing medications were based on the FDA's review of data from different sources, including a clinical trial data and reports submitted to the FDA's Adverse Event Reporting System. The relevant safety review by FDA had been reported in Issue No. 6 of Drug News.

In Hong Kong, there are currently 126 registered pharmaceutical products containing simvastatin and all of them are prescription medicines. Simvastatin is used for treatment of hyperlipidaemia. In light of the new information, the issue would be discussed in the next meeting of the Registration Committee of the Pharmacy and Poisons Board to be held in September 2011. DH issued letters to inform healthcare professional about this issue on 9 June 2011.

US: Increased risk of being diagnosed with a more serious form of prostate cancer in patients taking 5-alpha reductase inhibitors

10 June 2011 - FDA notified healthcare professionals that the labels for the 5-alpha reductase inhibitor (5-ARI) class of drugs had been revised to include new safety information about the increased risk of being diagnosed with a high-grade prostate cancer. The new safety information was based on FDA's review of two large, randomized controlled trials—the Prostate Cancer Prevention Trial (PCPT) and the Reduction by Dutasteride of Prostate Cancer Events (REDUCE) trial. Both studies showed an overall reduction in the risk of lower-grade prostate cancer but an increased risk of high-grade prostate cancer. 5-ARIs are a class of medicines primarily used to treat the symptoms of benign prostatic hyperplasia (BPH) in men. Drug in this class are finasteride [marketed as Proscar (finesteride 5mg) and Propecia (finesteride 1mg)] and dutasteride [marketed as Avodart (dutasteride) and Jalyn (dutasteride and tamsulosin HCl)]. Proscar, Avodart and Jalyn are approved to improve symptoms of BPH. Proscar and Avodart are also approved to reduce the risk of urinary retention or surgery related to an enlarged prostate. Propecia is approved to treat male pattern hair loss. FDA believed that 5-ARIs remained safe and effective for their approved indications. Healthcare professionals were advised to consider the risk and benefits of 5-ARIs when prescribing. They were also advised to perform appropriate evaluation to rule out other urological conditions, including prostate cancer, which might mimic benign prostatic hyperplasia (BPH), before initiating therapy with 5-ARIs.

In Hong Kong, there are 18 registered pharmaceutical products containing finasteride (including Proscar and Propecia) and Avodart is the only registered pharmaceutical product containing dutasteride. All these 5-alpha reductase inhibitor products are prescription medicines. DH issued letters to inform healthcare professionals about this issue on 10 June 2011. In light of the new information, the issue would be discussed in the next meeting of the Registration Committee of the Pharmacy and Poisons Board to be held in September 2011.

EU: Update on ongoing review of pioglitazone–containing medicines

10 June 2011 - EMA had been informed by the French Medicines Agency (Afssaps) of its decision to suspend the use of pioglitazone-containing medicines in France (Actos, Competact), while awaiting the outcome of the ongoing European review on the benefits and risks of these antidiabetic medicines. This decision by the French authority followed the release of results of a retrospective cohort study carried out in France which suggested an increased risk of bladder cancer with pioglitazone. As reported previously in Issue No. 12 of Drug News, FDA also began to conduct a similar safety review on Actos in October 2010.

EMA's CHMP started a European review of pioglitazone-containing medicines in March 2011 to investigate the signal of a possible increased risk of bladder cancer with pioglitazone. The CHMP would discuss this issue at their next meeting on 20-23 June 2011 and recommend appropriate actions as necessary. While this review was ongoing, the CHMP would not recommend any changes to the use of pioglitazone-containing medicines at this juncture.

In Hong Kong, there are 24 registered pioglitazone-containing pharmaceutical products (including Actos). Pioglitazone is a prescription medicine. In light of the new information, the issue would be discussed in the next meeting of the Registration

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Committee of the Pharmacy and Poisons Board to be held in September 2011. DH remains vigilant to any new findings about pioglitazone.

US: Medication errors due to name confusion of risperidone (Risperdal) and ropinirole (Requip)

14 June 2011 - FDA notified healthcare professionals and the public of medication error reports in which patients were given risperidone (Risperdal) instead of ropinirole (Requip) and vice versa. In some cases, patients who took the wrong medication needed to be hospitalized. Healthcare professionals were reminded to clearly print or spell out the medication name on prescriptions and make certain their patients know the name of their prescribed medication and their reason for taking it.

In Hong Kong, Risperdal (risperidone) and Requip (ropinirole) are registered by Johnson and Johnson (HK) Ltd. and GlaxoSmithKline Ltd. respectively. Both are prescription medicines. Risperidone is an antipsychotic medication used to treat mental illnesses including schizophenia, bipolar disorder, and irritability associated with autistic disorder. Ropinirole is a dopamine agonist used in the treatment of Parkinson's disease and Restless Legs Syndrome. In view of FDA's action, DH issued letters to inform healthcare professionals about this issue on 14 June 2011.

Drug Recall

Recall of Potassium Chloride Injection 20mEq/100ml (HK-56421)

On 3 June 2011, DH instructed the Baxter Healthcare Ltd. (Baxter), a licensed drug wholesaler, to recall three batches of Potassium Chloride Injection 20mEq/100ml (HK-56421, Batch Nos: P259705, P259705A, P263673) as the endotoxin level exceeded the product specification limits. Potassium Chloride Injection is indicated for the treatment of potassium deficiency.

According to Baxter, the product was manufactured in the United States. So far, investigations by Baxter suggested that there was an error in test data interpretation when calculating the bacterial endotoxin test values on routine testing, resulting in lower than actual endotoxin values obtained. The raw materials met the requirements for endotoxin testing.

Nevertheless, as elevated endotoxins in the product might cause fever and in serious cases, cause septic shock, Baxter was instructed to recall the affected batches of the product as a precautionary measure. Press statement was issued on 3 June 2011. DH closely monitored the recall. Healthcare professionals were advised to stop using the affected batches of the product. So far, DH has not received any report of adverse event related to the product.

Recall of registered pharmaceutical products related to plasticizer contamination incident

In May 2011, it was reported that plasticizer agent was being used in flavouring agents by some food manufacturers in Taiwan. As responds to the plasticizers incident, the following pharmaceutical products were subsequently recalled in Hong Kong:

Date of recall initiated	Name of company	Name of the recalled product	Plasticizer found
a) 30 May 2011	Cerebos (Hong Kong) Ltd	Brand's Calcium Grow Chewable Tablets (HK-58001)	DEHP found in the product
b) 1 June 2011	Kai Yuen Pharmaceutical Company	Well Tab (HK-02886)	DEHP found in the product

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Drug Recall

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Date of recall initiated	Name of company	Name of the recalled product	Plasticizer found
b) 1 June 2011	Marching Pharmaceutical Limited	Deter-C 250mg Vitamin C Chewable Orange Flavoured tablets (HK-24067)	DEHP found in the flavouring agent
		Cebio Chewable Tablet Vitamin C 250mg (Orange Flavoured) (HK-24073)	
		Cevizo 250mg Vitamin C Chewable Orange Flavoured Tablets (HK-24074)	
		Super-C Chewable Tablets 250mg (Orange Flavoured) (HK-24075)	
		Arthritil Powder for Oral Solution 1.5G Sachet (HK-55430)	
c) 2 June 2011	Yat Seng Trading Co	Mebendazole Tab 100mg (Panbiotic) (HK-53603)	DEHP found in the product
	Yung Shin Co Ltd	Oxo Cap 100mg (HK-34702)	DEHP found in the product
	America Golden Rich Pharmaceuticals Ltd	Scoro Orabase 1mg/g Meider (HK-59097)	DEHP and DINP found in the product
d) 9 June 2011	GlaxoSmithKline Limited	Augmentin powder for syrup 156mg/5ml (HK-24658)	DIDP found in the product
10 June 2011		Augmentin powder for syrup 457mg/5ml (HK-42735)	DIDP and DINP found in the product
e) 20 June 2011	Mannings O/B The Dairy Farm Co. Ltd	Mannings Sore Throat Lozenges 0.25mg (HK-60010)	DEHP and DINP found in the products
		Mannings Folic Acid 5mg (HK-59704)	
f) 18 July 2011	GlaxoSmithKline Limited	Augmentin 375mg tablet (HK-47298)	DIDP, DEHP, DINP found in the product
2 August 2011		Augmentin 625mg tablet (HK-44027)	DIDP and DINP found in the products
		Augmentin 1g tablet (HK-42252)	

For further details, please refer to the website of the Drug Office of the Department of Health: www.drugoffice.gov.hk

Drug Incident

Woman arrested for selling slimming products containing banned drugs

On 16 May 2011, a joint operation was conducted by DH and the Police, resulting in the arrest of a 40-year -old woman for suspected sale of a slimming product known as "Slimming Capsules", which had been found earlier to contain undeclared banned drug ingredients.

DH first obtained samples of five slimming products, including the product connected to the above arrest, through purchase from Internet auction websites during the department's targeted surveillance. The other four products are "Super Fat Burning Bomb - Quick Result Slimming", "Super Fat Burning Bomb - Reduce Fat on Abdomen and Waist Type", "Super Fat Burning Bomb" and "Fat 2 and 1 Burners III Soft and Hard Gelatin Capsules Combination Pack".

Laboratory analysis by the Government Laboratory detected that all five products contained sibutramine and its analogues, and three of them also contained phenolphthalein.

Sibutramine was once a western medicine used as appetite suppressant. In November 2010, sibutramine-containing products have been banned because of the increased cardiovascular risk. Sibutramine analogues, being chemically similar to sibutramine, are expected to have the same side effects as sibutramine. Phenolphthalein was once used for treating constipation but has been banned for its cancer-causing effect.

DH appealed to members of the public not to buy or consume unknown or doubtful slimming products from the Internet as they may contain undeclared and banned drug ingredients that are dangerous to health. Weight control should be achieved through good diet and appropriate exercise. People should consult healthcare professionals before using any medication for weight control.

The products mentioned in the above drug incident were not registered pharmaceutical products under the Pharmacy and Poisons Ordinance in Hong Kong. A product containing any western drug ingredient must be registered under the Ordinance before it can be sold in Hong Kong. Under the Pharmacy and Poisons Ordinance, possession or sale of unregistered pharmaceutical product is an offence liable to the maximum penalties of a $100,000 fine and two year's imprisonment. Members of the public were exhorted not to sell products of unknown or doubtful composition. They should also stop using the aforementioned products that contained undeclared western drug ingredients and should see doctor if they feel unwell after using the products. Those still have the products in hand should destroy, dispose or submit them to the Department's Pharmaceutical Service during office hours.

Useful Contact

Drug Complaint:

Tel: 2572 2068

Fax: 2147 0457 & 2123 1996

E-mail: pharmgeneral@dh.gov.hk

Adverse Drug Reaction (ADR) Reporting:

You are encouraged to report any suspected or confirmed ADR cases to our office by:

Fax: 2147 0457

E-mail: adr@dh.gov.hk

Post: *ADR Monitoring Unit,*

Drug Office, Department of Health,

3/F, Public Health Laboratory Centre,

382 Nam Cheong Street, Kowloon