



Bioanalytical Technique: A quality check for pharmaceutical dosage forms

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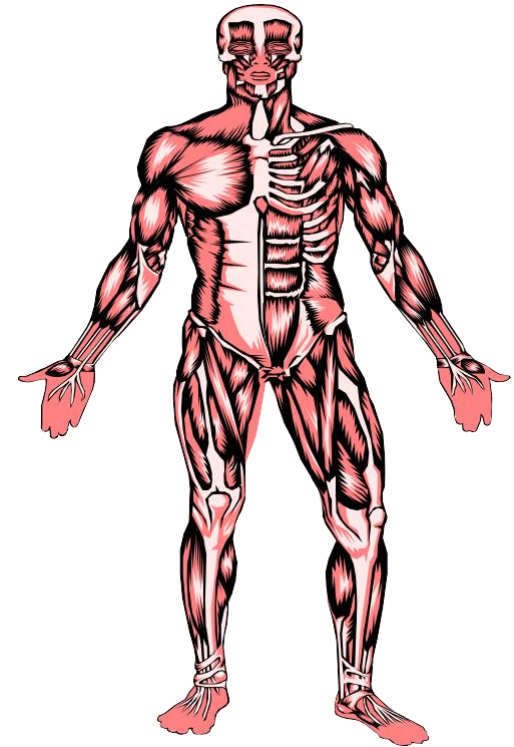
Malaysia



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Bioavailability?

Bioavailability refers to **rate (how fast)** and **extent (the amount)** to which the active substance is absorbed from a pharmaceutical dosage form and becomes available at the **site of action** (inside the body)



Bioequivalence

If two **pharmaceutically identical** medicines are also **bioequivalent**,

When **administered in the same molar dose**

- their bioavailability (rate and extent of absorption) are **sufficiently similar**.
- their effects should be **basically the same**.



It compares the **rate & extent** of absorption between **test & reference** product (to show that 2 drugs are bioequivalent to one another)



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BE REQUIREMENTS

BE is a requirement enforced by the NPRA, MOH (Ministry of health, Malaysia) for generics, to ensure quality, safety and efficacy of generics.



NPRA, Malaysia

After review the registration of generic products

- Received **complaints on efficacy** of the **generic products**.
- **Decided to include** BE studies as a **requirement for generics** (oral Immediate Release solid dosage form)
- To **ensure** that **generics are therapeutically equivalent** to the innovators → **clinically interchangeable**.



Generic Medicines



Reference	Definitions
DRGD (Malaysia)	A product that is essentially similar to a currently registered product in Malaysia
WHO <i>* Multisource product</i>	a pharmaceutical product, usually intended to be interchangeable with the innovator product , marketed after the expiry of patent or other exclusivity rights
USFDA	a medicine that is identical or bioequivalent to a brand name medicine in dosage form, safety, strength, route of administration, quality, performance, characteristic and intended use
EMA	a medicinal product which has the same qualitative and quantitative composition in active substances and the same pharmaceutical form as the reference medicinal product and whose bioequivalence with the reference medicinal product has been demonstrated by appropriate bioavailability studies



Comparator Drug

Innovator/comparator/reference products

A pharmaceutical product with which the multi-source product is intended to be interchangeable in clinical practice
- WHO



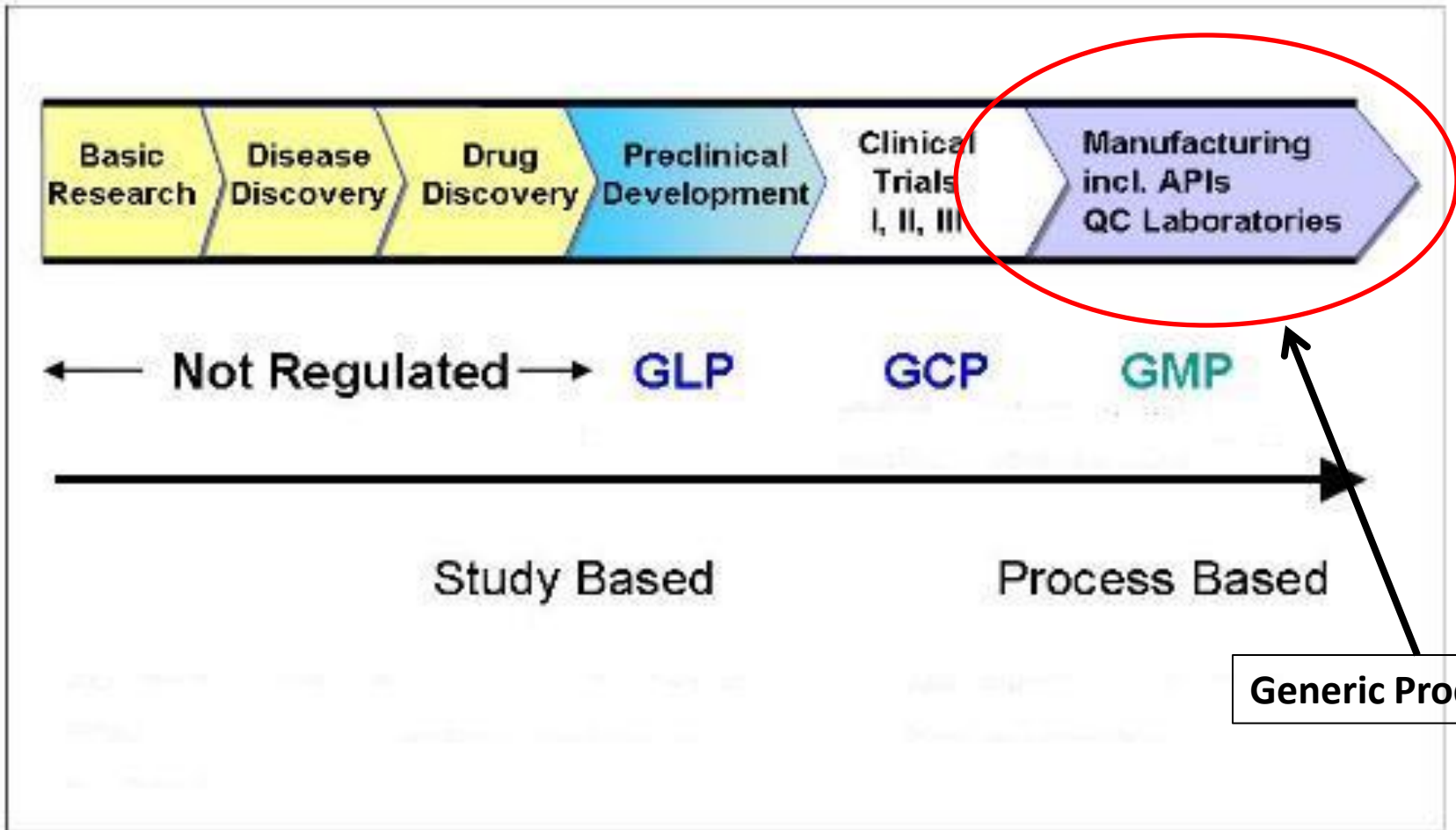
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BE requirements (Malaysia)

- Since Sept 2008
- > 229 products cancelled/suspended due to failure to fulfill BE requirements
- > 150 new applications rejected due to failure to submit adequate and satisfactory BE studies



Patented vs Generic



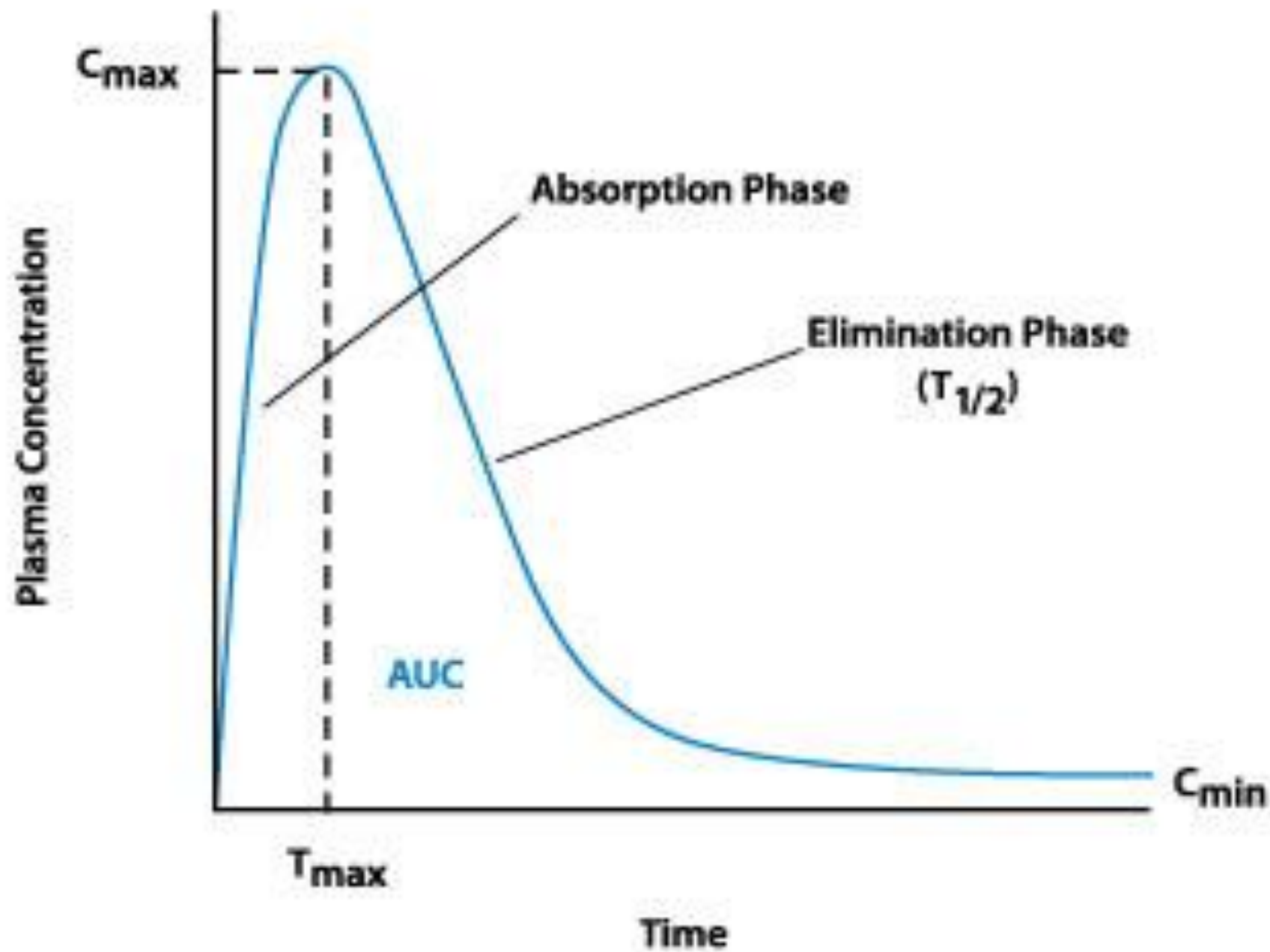
Generic Product



Bioanalysis

- Bioanalysis is defined as quantitative measurement of drugs in biological system (plasma, urine, and tissues).
- Bio analysis is very important in the field of drug development and generic formulation such as:
 - ❖ preclinical studies for new drugs
 - ❖ clinical studies in human plasma
 - ❖ therapeutic and toxicological concentrations.
 - ❖ pharmacokinetic studies for drugs
 - ❖ Bio equivalence of generic formulation





Choice of Drugs

RANK	ATC	THERAPEUTIC GROUP	PUBLIC	PRIVATE	TOTAL
1	A10	Drugs used in diabetes	42.0556	6.9074	48.9630
2	C08	Calcium channel blockers	20.4728	10.6096	31.0823
3	C09	Agents acting on the renin-angiotensin system	19.7722	4.4640	24.2362
4	C07	Beta blocking agents	17.6028	2.5778	20.1806
5	C03	Diuretics	14.6048	4.3189	18.9237
6	M01	Antiinflammatory and antirheumatic products	3.0869	11.9973	15.0843
7	C10	Lipid modifying agents	8.6305	4.6590	13.2895
8	J01	Antibacterials for systemic use	4.7513	7.9885	12.7398
9	R06	Antihistamines for systemic use	4.3263	7.9234	12.2497
10	H02	Corticosteroids for systemic use	3.6126	8.1238	11.7364



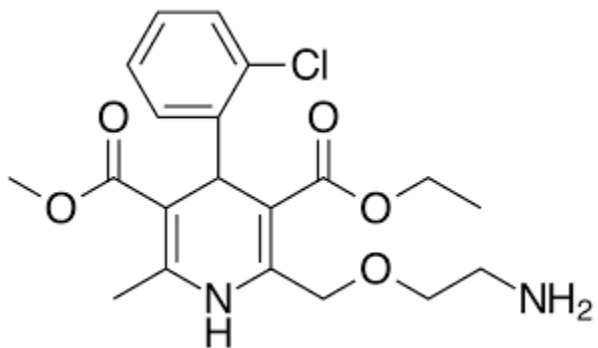
Contd..

RANK	ATC	THERAPEUTIC GROUP	PUBLIC	PRIVATE	TOTAL
1	C08C A01	Amlodipine	26.7411	2.9817	29.7228
2	A10B B09	Gliclazide	23.7710	1.9930	25.7640
3	C09A A04	Perindopril	13.7130	0.6026	14.3156
4	A10B A02	Metformin	13.1892	1.1200	14.3092
5	C08C A05	Nifedipine	10.0114	1.5413	11.5527
6	C03A A03	Hydrochlorothiazide	10.6896	0.2586	10.9482
7	G03C A57	Conjugated estrogens	3.6887	6.9684	10.6570
8	C07A B02	Metoprolol	9.8532	0.1297	9.9829
9	C07A B03	Atenolol	7.9423	1.2049	9.1472
10	A10B B01	Glibenclamide	7.6174	0.8190	8.4364

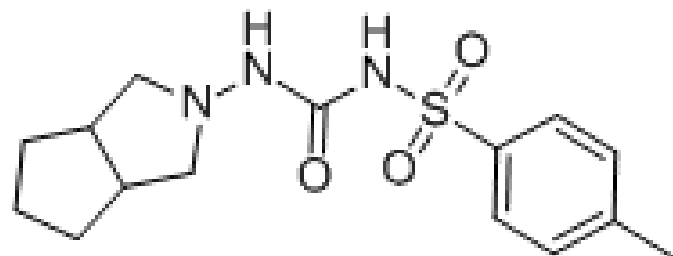


Generic Products: Dry Dosage Forms

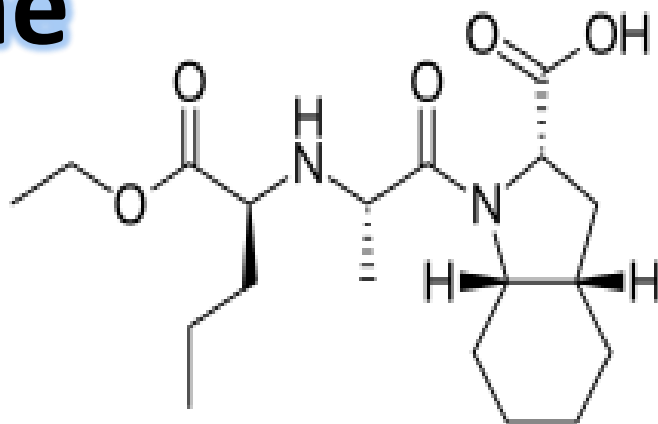
Pharmacological Groups	Dosage Forms
Antihypertensive (Amlodipine)	Tablets 5 mg Tablets 10 mg
Antidiabetic (Gliclazide)	Tablet 80 mg
Antihistamine (Cetirizine)	Tablet 10 mg
Analgesic (Mefenamic Acid)	Capsule 250 mg Tablet 500 mg



Amlodipine



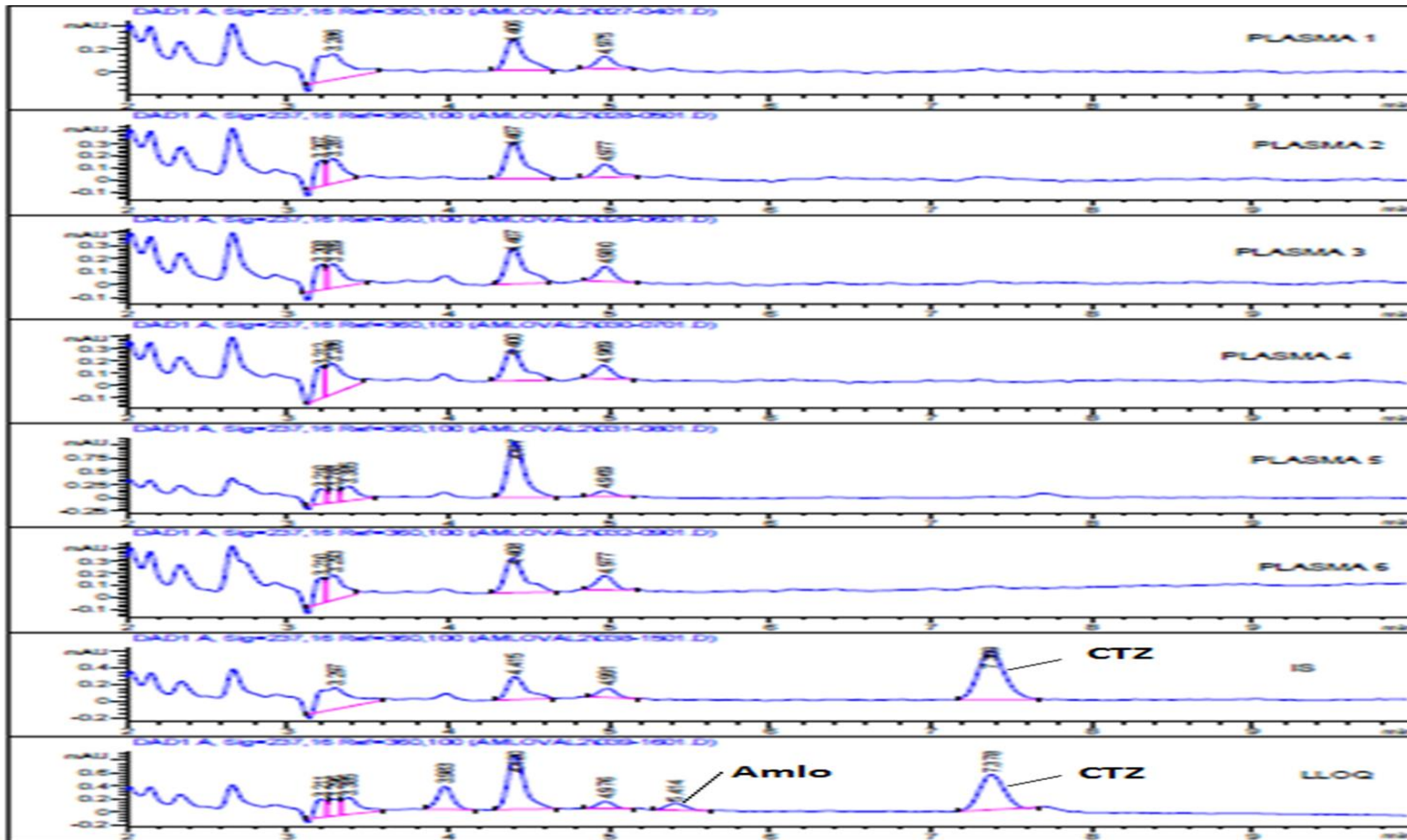
Gliclazide



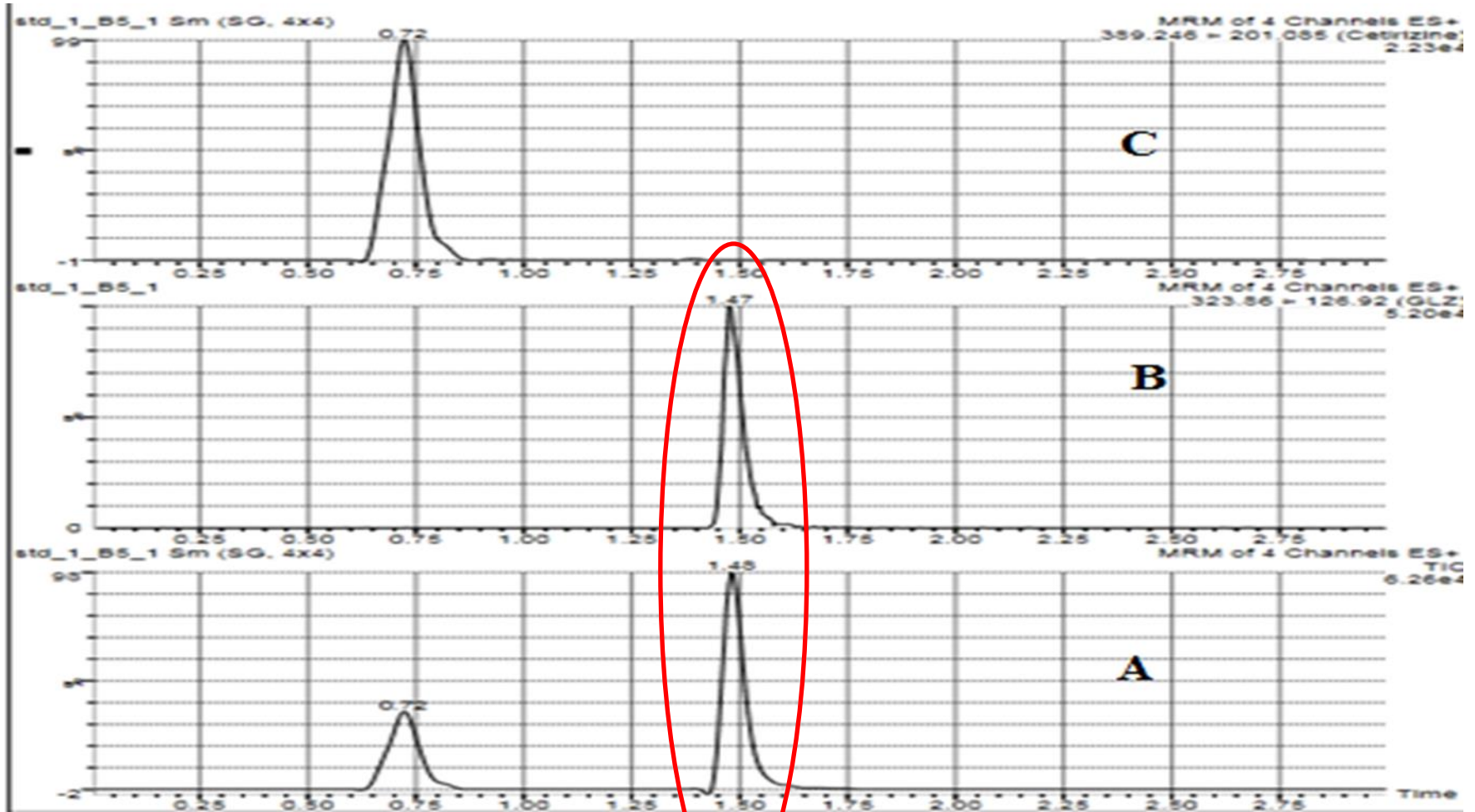
Perindopril



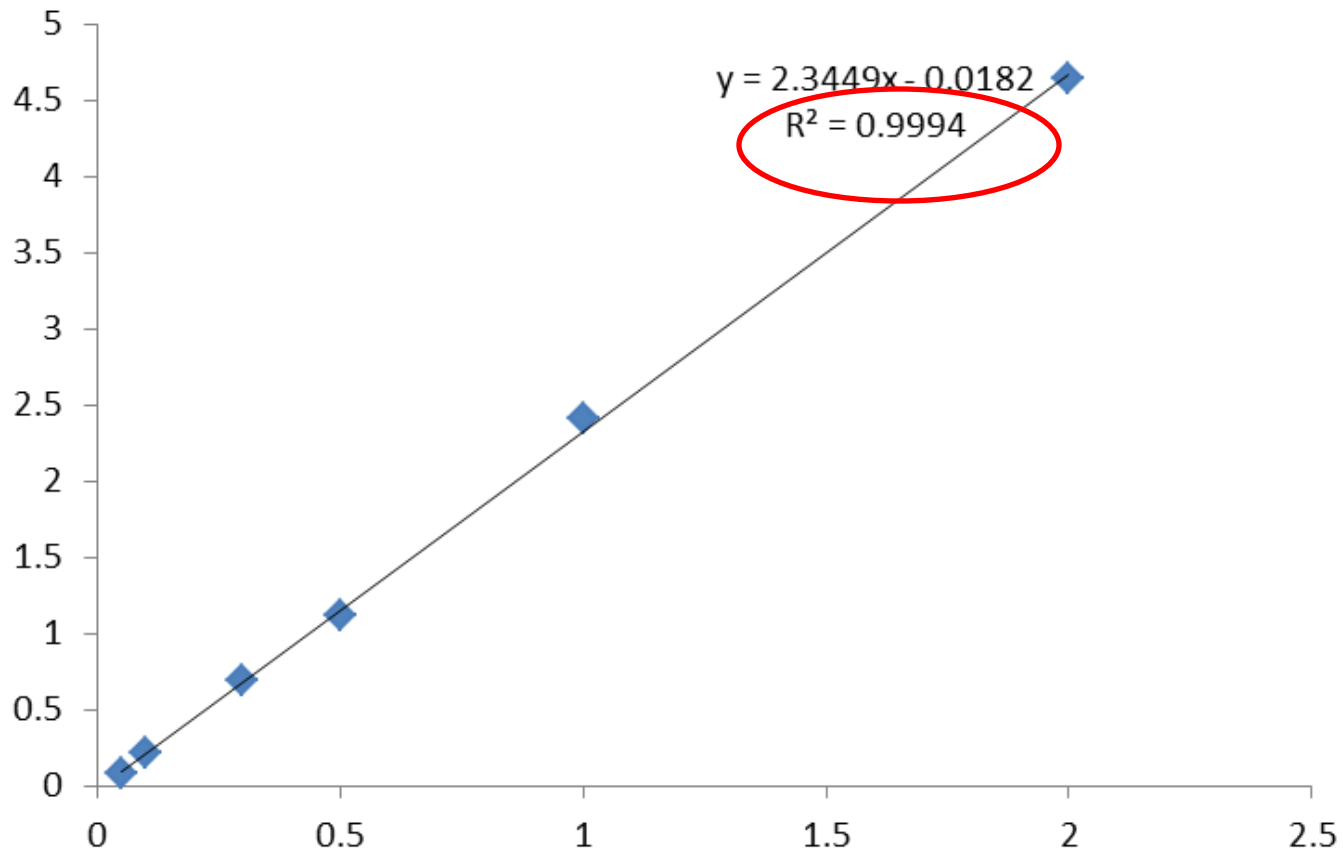
Specificity-Amlo



GLZ-Selectivity

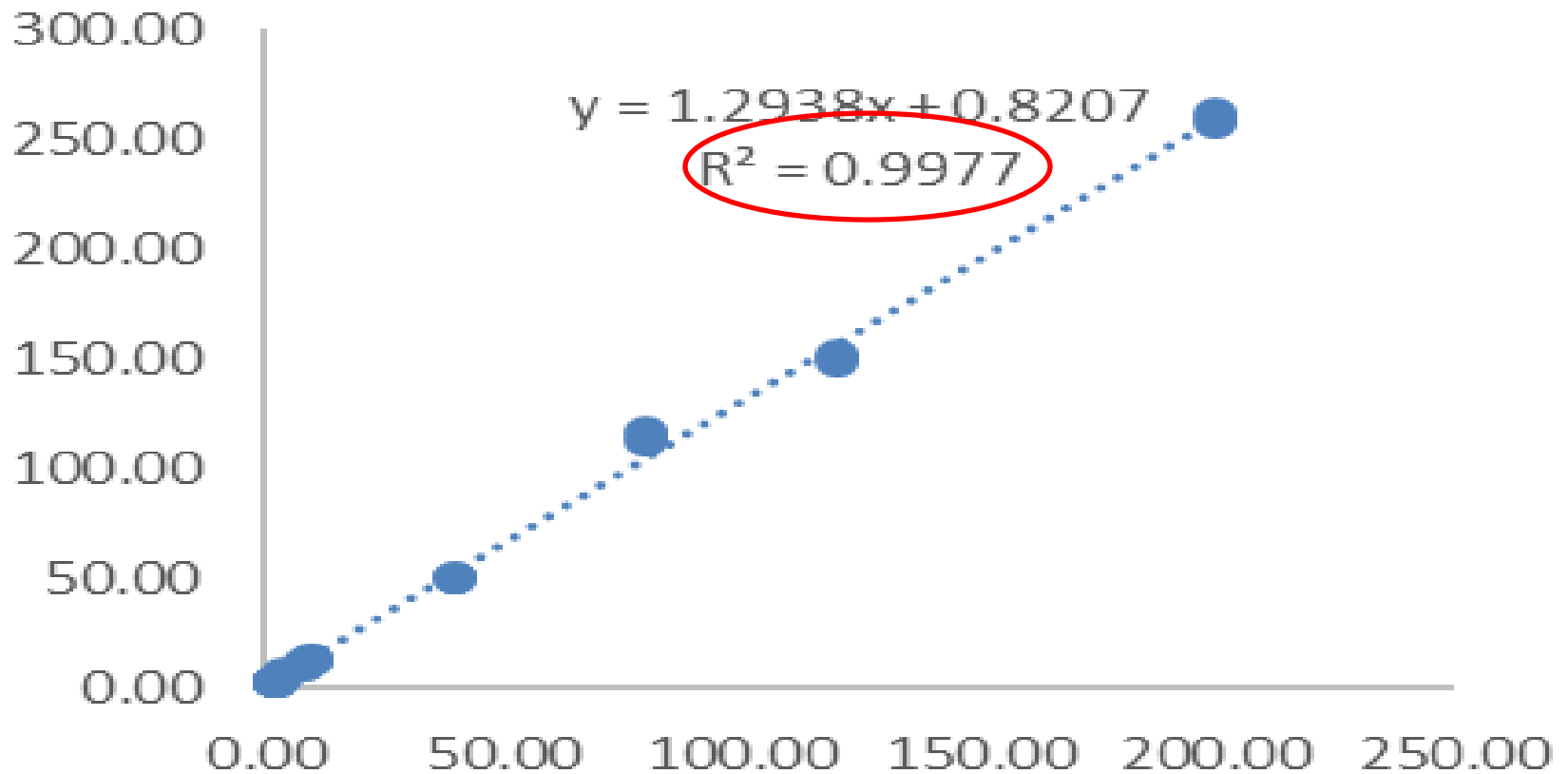


Linearity-Amlo



Linearity PER

Perindopril



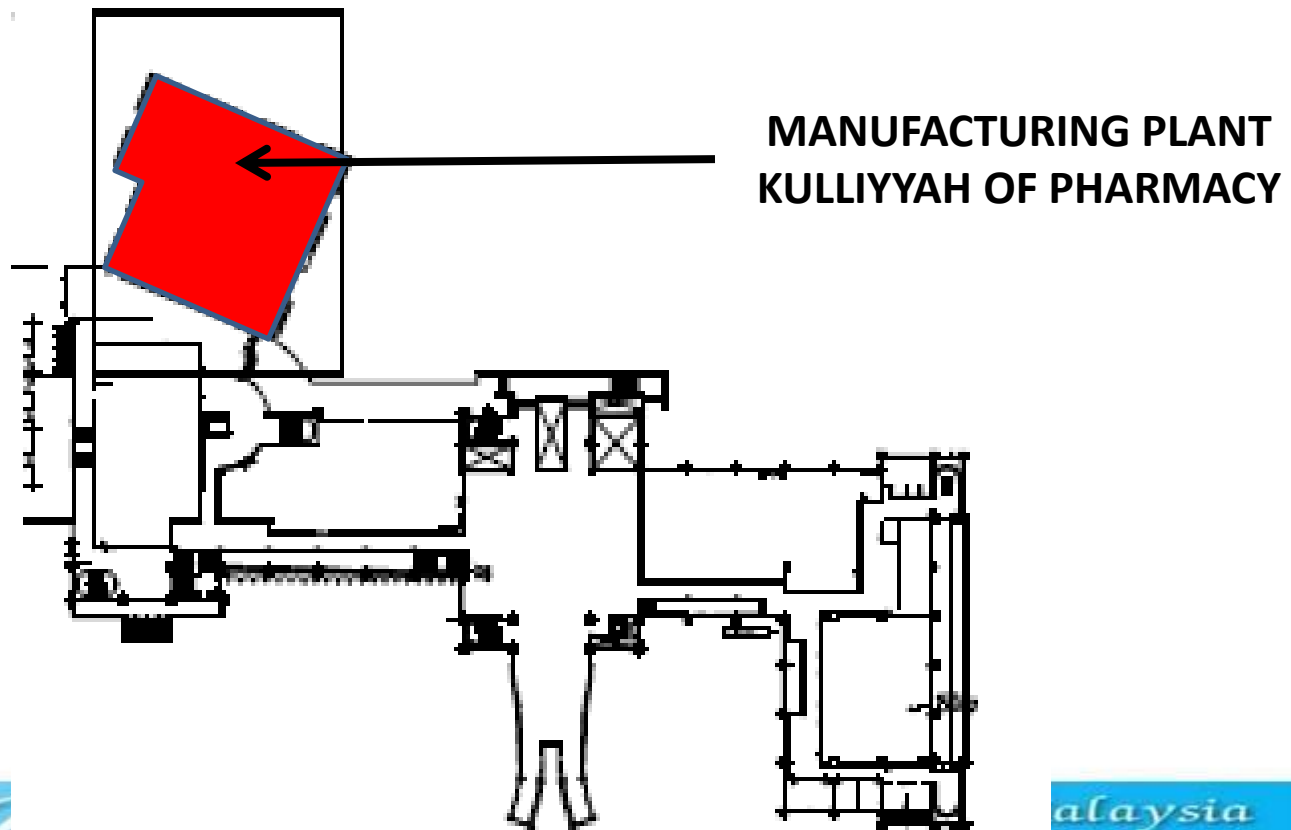
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Aims of setting up the Pharmaceutical Manufacturing Plant

- Niche area of Faculty of Pharmacy
- **Real GMP-compliant teaching/training facility for students (undergraduate & postgraduate)**
- **Manufacture Permissible and Quality Pharmaceuticals (generic and in-house proprietary products)**



Location of Manufacturing Plant (Behind the Kulliyah of Pharmacy)





KULIYAH OF PHARMACY


IIUM Pharmaceutical Manufacturing Plant - IKOP



Main Office

Production Entrance

PICS/GMP Approval


Biro Pengawasan Farmaseutikal Kebangsaan
National Pharmaceutical Control Bureau
KEMENTERIAN KESIHATAN MALAYSIA
MINISTRY OF HEALTH MALAYSIA

LC No. 009/12 **Our Ref :** (16) dlm.BPFK/30/12/3250
Date : 13 February 2012

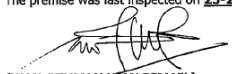
IIUM Pharmacy Sdn. Bhd.
Kulliyah of Pharmacy,
International Islamic University of Malaysia,
Jalan Sultan Ahmad Shah,
Bandar Indera Mahkota,
25200 Kuantan,
Pahang Darul Makmur.

Letter of Confirmation

This is to confirm that your manufacturing premises at **Kulliyah of Pharmacy, International Islamic University of Malaysia, Jalan Sultan Ahmad Shah, Bandar Indera Mahkota, 25200 Kuantan, Pahang Darul Makmur** have been inspected and conforms to the requirement of Good Manufacturing Practices (GMP) in accordance to the current Pharmaceutical Inspection Co-operation Scheme (PIC/S) GMP Guides for the manufacturing of the following pharmaceuticals products:-


1. Tablets
2. Capsules
3. Semi-solids

The premise was last inspected on **25-26 January 2012.**


(WAN OTHMAN WAN ISMAIL)
Senior Principal Assistant Director
for Director of Regulatory Pharmacy
National Pharmaceutical Control Bureau
Ministry of Health Malaysia

(This document is valid only for the purpose of product registration in Malaysia only AND WILL BE SUPERCEDED UPON THE ISSUANCE OF A MANUFACTURING LICENSE unless otherwise specified)

Jalan Universiti, P. O. Box 319, 46730 Petaling Jaya, Selangor, Malaysia
Tel.: +603 7883 5400 Fax: +603 7956 2924/7958 1312
<http://www.bpfk.gov.my>


BORANG 2
(Form 2)
PERATURAN-PERATURAN KAWALAN DADAH DAN KOSMETIK 1984
CONTROL OF DRUGS AND COSMETICS REGULATIONS 1984
[Peraturan 12(1)]
[Regulation 12 (1)]
PIHAK BERKUASA KAWALAN DADAH
DRUG CONTROL AUTHORITY
KEMENTERIAN KESIHATAN MALAYSIA
MINISTRY OF HEALTH MALAYSIA

LESEN PENGILANG
MANUFACTURER'S LICENCE

NO. LESEN : **MALLP20151086**
(LICENCE NO.)

Lesen ini diberikan kepada
yang berilmat
(The licensee authorities
of)

IKOP SDN BHD
JALAN SULTAN AHMAD SHAH,
BANDAR INDERA MAHKOTA
25200 Kuantan
PAHANG

untuk mengilang keluaran yang dinyatakan dalam senarai yang dikecualikan pada lesen ini di premis pengilangan yang tertera di bawah dan untuk menjual secara borong atau membeli keluaran tersebut
(to manufacture the products specified in the list attached to this licence at the manufacturing premises mentioned below and to sell by wholesale or to supply the said products)

Nama premis pengilangan
(Name of manufacturing premises)
IKOP SDN BHD

Alamat
(Address)
JALAN SULTAN AHMAD SHAH,
BANDAR INDERA MAHKOTA
25200 Kuantan
PAHANG
MALAYSIA

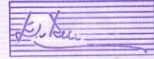
Alamat stor :
(Address of stores):

Lesen ini adalah tertakluk kepada syarat-syarat berikut:
(The licence is subject to the following conditions)
BAGI KELUARAN YANG MANA PERATURAN-PERATURAN INI BERKUATKUASA, PEMEGANG
LESEN DIBENARKAN MENGIKLAN HANYA KELUARAN BERDAFTAR SEPERTI YANG
DILULUSKAN OLEH PIHAK BERKUASA KAWALAN DADAH.
(FOR PRODUCTS TO WHICH THESE REGULATIONS APPLY, THE HOLDER OF THIS LICENCE IS ALLOWED TO
MANUFACTURE ONLY THE REGISTERED PRODUCTS AS APPROVED BY THE DRUG CONTROL AUTHORITY)

(Bersempang di atas kepingan lain yang di lampirkan kepada lesen ini *)
(Continued on another sheet attached to this licence*)

Lesen ini adalah sah dari 16/04/2015 hingga 31/12/2015
(The licence is valid from) (to)

Tarikh: 16/04/2015
(Date):


Pengarah Perkhidmatan Farmasi
(Director of Pharmaceutical Services)

* Potong jika tidak berkenan
(* Delete where not applicable)

No. Lesen dahulu : Tarikh dikeluarkan :
(Previous Licence No.) (Date of issue)



International Islamic University Malaysia

ACKNOWLEDGEMENT

- ANALYTICAL BIO ANALYTICAL RESEARCH LABORATORY, IIUM
- FACULTY OF PHARMACY, IIUM
- IKOP SDN BHD
- RESEARCH MANAGEMENT CENTRE, IIUM
- NPRA
- FUNDING: MOHE, MOF Malaysia.





THANK YOU



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Garden of Knowledge and Virtue

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