



WORLD HEALTH ORGANIZATION
ORGANISATION MONDIALE DE LA SANTE

REVISION/UPDATE OF THE GUIDANCE ON THE SELECTION OF COMPARATOR PHARMACEUTICAL PRODUCTS FOR EQUIVALENCE ASSESSMENT OF INTERCHANGEABLE MULTISOURCE (GENERIC) PRODUCTS

Subsequent to the Thirty-ninth meeting of the WHO Expert Committee on Specifications for Pharmaceutical Preparations the attached list has been mailed for comments to IFPMA. Several responses were received from individual companies which have been included. Thereafter the list was discussed during a consultation held in July 2005. The main recommendation was to update the list in accordance with the recently adopted WHO Model List of Essential Medicines and to include the currently recommend products used within the WHO Prequalification project. Both actions have been taken.

Please address any comments you may have on thereon to Dr S. Kopp, Quality Assurance and Safety: Medicines, Medicines Policy and Standards, World Health Organization, 1211 Geneva 27, Switzerland, fax: (+41 22) 791 4730 , or e-mail: kopps@who.int, with a copy to bonnyw@who.int, **by 30 November 2005**.

© World Health Organization 2005

All rights reserved.

This draft is intended for a restricted audience only, i.e. the individuals and organizations having received this draft. The draft may not be reviewed, abstracted, quoted, reproduced, transmitted, distributed, translated or adapted, in part or in whole, in any form or by any means outside these individuals and organizations (including the organizations' concerned staff and member organizations) without the permission of WHO. The draft should not be displayed on any website.

Please send any request for permission to:

Dr Sabine Kopp, Quality Assurance & Safety: Medicines (QSM), Department of Essential Drugs and Medicines Policy (EDM), World Health Organization, CH-1211 Geneva 27, Switzerland.

Fax: (41-22) 791 4730; e-mails: kopps@who.int; bonnyw@who.int

The designations employed and the presentation of the material in this draft do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement.

The mention of specific companies or of certain manufacturers' products does not imply that they are endorsed or recommended by the World Health Organization in preference to others of a similar nature that are not mentioned.

Errors and omissions excepted, the names of proprietary products are distinguished by initial capital letters.

The World Health Organization does not warrant that the information contained in this draft is complete and correct and shall not be liable for any damages incurred as a result of its use.

INTRODUCTION

The introductory text will be revised in the light of the discussions on the registration requirements to establish interchangeability.

This guidance provides a list of comparator products for equivalence assessment of interchangeable multisource (generic) products. The information on comparator pharmaceutical products was collected by the Secretariat from drug regulatory authorities and pharmaceutical companies. The list has been developed to assist regulatory authorities and pharmaceutical industries in deciding on appropriate comparator products in the context of multisource (generic) marketing authorization. The guidance could also be used for the purpose of procurement of drugs.

The guideline Multisource Pharmaceutical Products: WHO Guideline on registration requirements to establish interchangeability (1) recommends that multisource products need to meet the same quality, safety, and efficacy standards of the corresponding innovator product. It also recommends that quality attributes of a multisource product should be tested against the innovator product for which interchange is intended. [This guidance is currently under revision...]

A list of international comparator pharmaceutical products for equivalence assessment of interchangeable multisource (generic) products¹ is given in Table 1.

INSTRUCTIONS ON THE USE OF THE LIST

1. National regulatory authorities may issue this guidance together with Lists A and B, which should be available to applicants/pharmaceutical companies that plan to develop multisource pharmaceutical products intended to be interchangeable with innovator or other pharmaceutical products of established quality, safety and efficacy.
2. List A provides information about pharmaceutical products from the WHO Model List of Essential Drugs (2), and includes the innovator products (column headed “Trademark”) and the national markets where the manufacturers in question consider that their products’ quality, safety and efficacy are best documented (column headed “Primary market”).
3. Pharmaceutical companies planning to develop an interchangeable multisource pharmaceutical product should determine whether the innovator pharmaceutical product appearing in List A is available on the local market.
4. If the innovator pharmaceutical product is available on the local market, pharmaceutical companies should use this product in equivalence assessment with their multisource product.

¹The list is based on information collected by WHO from drug regulatory authorities and supplemented with that from pharmaceutical companies. It will be periodically updated.

5. If the innovator product is not available on the local market, pharmaceutical companies should obtain from the market a product that is the best representative innovator product from the point of view of its quality, safety and efficacy (see column headed “Primary market” of List A).
6. The type of equivalence assessment of the comparator pharmaceutical product and the multisource product under investigation may vary, depending on local requirements and the availability of resources. Recommendations on the type of equivalence studies to be carried out when such studies are necessary are given in the WHO guidelines on multisource pharmaceutical products (1).
7. For some pharmaceutical products, an innovator product cannot be identified. Examples of these products from the WHO Model List of Essential Drugs (2) appear in List B. For these products, a local, national or regional pharmacopoeia or *The international pharmacopoeia* (3) for both the drug substance and, when available, the product, supplemented by official reference texts, may provide sufficient information and requirements to allow a pharmaceutical company to develop a product of the requisite quality, safety and efficacy. No international comparator product for these pharmaceutical products will be available, and no equivalence assessment can be performed. Also included in List B are pharmaceutical products for which an innovator product can be identified or a market leader product may be available, but for which there is insufficient information available for them to appear in List A, e.g. products for which the originator no longer exists or which cannot be traced. The List A approach can also be applied to these products.
8. When a market leader product is available on the local market but no innovator product can be identified or obtained from the primary market, the market leader product may be used as a comparator product if its quality, safety and efficacy have been established. If this is not the case, the second market leader or compendial standards approach (List B) can be followed. Most of the pharmaceuticals listed are included in the WHO Model List of Essential Drugs (2). In the case of products for which equivalence testing is required, it should be performed in accordance with the WHO guidelines on registration requirements to establish interchangeability of multisource (generic) products (1).

Layout of the list

Pharmaceutical name (1)	Section no. (2)	Dosage forms and strengths (3)	Comparator pharmaceutical products (4)		
			Trademark	Primary market	Manufacturer
albendazole	6.1.1	chtab, 200 mg	Zentel	France	SmithKline Beecham

The list is divided into two parts, as follows:

- *List A* provides information on comparator pharmaceutical products — trademark and primary market — as given by manufacturers of innovator products.

- *List B* contains products for which information has not been given by manufacturers of innovator or market leader products or difficulties in providing the information were encountered because the pharmaceutical products have been marketed for a long time.
- (1) Pharmaceutical name: International Nonproprietary Names (INNs) are used to identify the active drug substance as in the WHO Model List of Essential Drugs.
 - (2) Section no.: this corresponds to the WHO Model List of Essential Drugs, and indicates the therapeutic uses/pharmacological effects of the pharmaceutical.
 - (3) Dosage forms and strengths: these correspond to the WHO Model List of Essential Drugs. A strike-through means that no products of the dosage form or strength are available on the market. An entry in bold signifies that a product of the dosage form or strength is available on the market instead of, or in addition to, those in the WHO Model List of Essential Drugs.

The following abbreviations are used:

cap	capsule
chcap	chewable capsule
ctab	chewable tablet
cre	cream
elix	elixir
encotab	enteric coated tablet
eyd	eye drop
eyo	eye ointment
inh	inhalation
inj	injection/injectable solution
lot	lotion
loz	lozenge
multi	multiple
nsp	nasal spray
oilinj	injection in oil
oilsl	oily solution
oilsp	oil suspension
oilspinj	oil suspension injection
oin	ointment
oosl	oral oily solution
osl	oral solution
osp	oral suspension
pes	pessary
pwinj	powder for injection
pwosp	powder for oral suspension
pwsl	powder for solution
respsl	respirator solution
sbtab	tablet sublingual
sctab	scored tablet
sgtab	sugar coated tablet

sl	solution
sr	sustained-released preparation
sup	suppository
syr	syrup
tab	tablet
topsl	solution, topical
vagtab	vaginal tablet
wminj	water-miscible injection

- (4) Comparator pharmaceutical products: “Trademark” and “Primary market” for List A indicate the innovator products and the national markets where the manufacturers in question consider that their products’ quality, safety and efficacy are best documented.

List B, which does not give this information, follows the pharmacopoeial standards approach.

The entry ***** means that additional information on the product must be provided before it can be included in List A.

Additional abbreviations and signs used in this revision, under discussion

[..]	Explanatory notes from the WHO Secretariat on action/update
EML	Model List of Essential Medicines (14 th List, updates)
Pre-qual	entries suggested by colleagues and experts from the prequalification team

Blank page

Table 1
International comparator products for equivalent assessment of interchangeable multisource (generic) products^a

Pharmaceutical Name	Section no.	Dosage Forms, Strengths	Comparator Pharmaceutical Products		
			Trademark	Primary market	Manufacturer
List A					
Abacavir [new entry in EML 2005, Core list and suggested by pre-qual (HIV)]	27.1.1	tab, 300mg (as sulfate) osl, 100mg/5ml (as sulfate)	ZIAGEN		GlaxoSmithKline
Abacavir/ lamivudine/ zidovudine [suggested by pre-qual (HIV)]			TRIZIVIR		GlaxoSmithKline
albendazole	6.1.1	chtab, 200mg On the 14th EML - chtab, 400 mg	ZENTEL	France	SmithKline Beecham
amiloride, hydrochloride	16	tab, 5mg	MIDAMOR	United Kingdom	Merck Sharp &Dohme
[excluded from EML 2005] aminophylline	25.1	tab, (sr), 125mg [Altana comments via IFPMA]	AMINOPHYLLIN [Altana comments via IFPMA]	Germany	Altana Pharma AG [Altana comments via IFPMA]
aminosalicylic acid (p-aminosalicylic acid) [new entry in EML 2005, Compl. list]	6.2.4	tab, 500mg granules, 4 mg in sachet			
amitriptyline, hydrochloride	24.2.1	tab, 25mg	ELAVIL	USA	Zeneca
Amlodipine [new entry in EML 2005, Core list]	12.3	sustained release formulations, tablet 10mg			
amodiaquine [new entry in EML 2005, Core list and suggested by pre-qual (Malaria)]	6.5.3.1	tab, 153 mg, 200 mg (base)	FLAVOQUINE (amodiaquine 200mg tablets)	France	Laboratories Aventis
amoxicillin	6.21	cap, 250, 500mg pwosp, 125mg/5ml	AMOXIL	United Kingdom	SmithKline Beecham

		tab, 250, 500mg			
amphotericin B [suggested by pre-qual (HIV)]			AMPHOCIN FUNGIZONE IV		Pharmacia / Pfizer Squibb
artemether +lumefantrine [new entry in EML 2005, Core list and suggested by pre-qual (Malaria)]	6.5.3.1	tab, 20 mg + 120 mg	RIAMET (Coartem)	Switzerland	Novartis
artesunate [new entry in EML 2005, Compl. List and suggested by pre-qual (Malaria)]	6.5.3.1	tab, 50mg	ARSUMAX	France	Sanofi-Synthelabo
atenolol	12.1 12.2 12.3	tab,50,100mg tab,50,100mg tab,50,100mg	TENORMIN	United Kingdom	Zeneca
atropine, sulfate	21.5	eyd, 0.1, 0.5%, 1%	ATROPIN DISPERSA	Switzerland	Ciba Vision (Novartis)
Azithromycin [new entry in EML 2005, Core list and suggested by pre-qual (HIV)]	6.2.2	cap, 250 mg, 500 mg	ZITHROMAX (osp, 100mg/5ml, 200mg/5ml, 1g in single dose packet; tab, 250mg, 500mg, 600mg; cap, 250mg)		Pfizer
benznidazole	6.5.5	tab, 100mg	RADANIL	Argentina, Brazil, Switzerland	Roche
biperiden, hydrochloride	9	tab, 2mg	AKINETON	Germany	Desma GmbH [Abbott comments via IFPMA]
bleomycin [suggested by pre-qual (HIV)]			BLENOXANE		Bristol-Myers Squibb
calcium folinate [new entry in EML 2005, Compl. list] [excluded from EML 2005] captopril	8.2 12.3	tab, 15mg sctab, 25mg	CAPOTEN	USA	Bristol-Myers Squibb
carbamazepine	5	sctab, 100, 200mg (sr)	TEGRETOL	Switzerland	Novartis

cefixime [new entry in EML 2005, Core list and suggested by pre-qual (HIV)]	6.2.1	cap, 400mg (Does SUPRAX has this dosage form and dosage?)	SUPRAX		Rhone-Poulenc Rorer
ceftriaxone [suggested by pre-qual (HIV)]			ROCEPHIN		Roche Pharma
chlorambucil [new entry in EML 2005, Compl. list]	8.2	tab, 2mg			
chloramphenicol	6.2.2	cap, 250mg	CHLOROMYCETIN	USA	Parke-Davis
chloramphenicol, sodium succinate	6.2.2	oilspinj, 0.5g/2ml On the 14th EML - oilspinj 0.5g/ml	CHLOROMYCETIN SODIUM SUCCINATE	USA	Parke-Davis/Parkedale
chloroquine, phosphate	6.5.3	tab, 25mg, 100mg, ^b 150mg, ^{b, c} 500mg On the 14th EML - only tab, 100mg, 150mg	ALAREN PHOSPHATE	USA	Sanofi Winthrop
chlorphenamine, hydrogen maleate	3	tab, 4mg	CHLORTRIMETON	USA	Schering-Plough
chlorpheniramine [suggested by pre-qual (HIV)]					
ciclosporin	8.1	cap, 25mg	SANDIMMUN	Switzerland	Novartis
[excluded from EML 2005] cimetidine	17.1	tab, 200mg	TAGAMET	France	SmithKline Beecham
ciprofloxacin, hydrochloride	6.22	tab, 250mg On the 14th EML - also tab, 500mg	CIPROBAY (tab, 250mg, 500mg, 750mg; osp, 5%) CIPRO [suggested by pre-qual (HIV)] (tab, 250mg, 500mg, 750mg; osp, 5%, 10%)	Germany	Bayer <u>HealthCare</u> [Bayer comments via IFPMA]
clarithromycin[suggested by pre-qual (HIV)]			BIAXIN KLARICID		Abbott Laboratories Abbott Laboratories

clindamycin [new entry in EML 2005, Compl. list and suggested by pre-qual (HIV)]	6.2.2	cap, 150mg	CLEOCIN (cap, 75mg, 300mg also available)		Pharmacia & Upjohn
clofazimine	6.2.3	cap, 50mg, 100mg	LAMPRENE	Switzerland	Novartis

Table 1 (continued)

Pharmaceutical Name	Section no.	Dosage Forms, Strengths	Comparator Pharmaceutical Products		
			Trademark	Primary market	Manufacturer
clomifene, citrate	18.6	tab, 50mg	CLOMID	USA	Hoechst Marion Roussel
Clomipramine, hydrochloride	24.4	cap, 10mg, 25mg	ANAFRANIL	Switzerland	Novartis
[excluded from EML 2005] clonazepam	5	sctab, 500µg	RIVOTRIL	Switzerland	Roche
clotrimazole [new entry in EML 2005, Core list]	6.3	vagtab, 100mg, 500mg vagcre, 1%, 10%			
cloxacillin, sodium	6.2.1	cap, 500mg pwosl, 125mg/5ml On the 14th EML - also cap, 1g	PENSTAPHON TEGOPEN	Belgium USA	Bristol-Myers Squibb
cyclophosphamide	8.2	tab, 25, 50mg On the 14th EML - only tab, 25mg	ENDOXANA	United Kingdom	ASTA Medica
cycloserine [new entry in EML 2005, Compl. list]	6.2.4	tab, 250mg cap, 250mg			
dapsone	6.2.3	tab, 25 mg , 50mg, 100mg	DAPSONE	USA	Jacobus
[excluded from EML 2005] desmopressin, acetate	10.2	nsp, 10µg metered dose	DDAVP	USA	Ferring
dexamethasone	3 18.1	tab, 500µg, 4mg tab, 500µg, 4mg On the 14th EML - only inj,	DECADRON	USA	Merck Sharp&Dohme

		4mg/ml			
diazepam	24.3	sctab, 2mg, 5mg On the 14th EML - also tab, 5mg	VALIUM	USA	Roche
didanosine (ddl) [new entry in EML 2005, Core list and suggested by pre-qual (HIV)]	27.1.1	buffered chewable, dispersible tablets 25 mg, 50 mg, 100 mg, 150 mg, 200 mg unbuffered enteric coated capsule 125 mg, 200 mg, 250 mg, 400 mg buffered powder for oral solution 100 mg, 167 mg, 250 mg (Does VIDEX have all these dosage forms?)	VIDEX		Bristol-Myers Squibb
[excluded from EML 2005] doxazosin mesilate	12.3	tab, 1mg, 2mg, 4mg	CALDURA	Germany	Pfizer
doxycycline, hyclate	6.22	cap, 100mg tab, 100mg On the 14th EML -hydrochloride instead of hyclate	VIBRAMYCIN	Germany	Pfizer
efavirenz (EFV or EFZ) [new entry in EML 2005, Core list and suggested by pre-qual (HIV)]	27.1.2	cap, 50 mg, 100 mg, 200 mg osl, 150mg/5ml	SUSTIVA (tab, 600 mg also available) STOCRIN (tab, 600 mg also available)		Bristol-Myers Squibb Merck
enalapril [new entry in EML 2005, Core list]	12.3 12.4	tab, 2.5mg tab, 2.5mg			
epinephrine, hydrochloride	21.5	eyd, 2%	SUPRARENIN	Germany	Hoechst Marion Roussel
ergocalciferol	27	cap, 1.25mg (50000IU) osl, 250µg/ml (10000IU/ml) tab, 1.25mg (50000IU)	DRISDOL	USA	Sanofi
					[Has been terminated by us

					worldwide Schering comments, Germany]
ethinylestradiol (deleted from Comparator Products' List (see above) but included in the 14th EML)	18.4	tab, 10µg, 50µg			
ethinylestradiol+ levonorgestrel	18.31	tab, 30µg +150µg, 50µg + 250µg On the 14th EML - only tab, 30µg +150µg	NORDETTE-21	USA	Wyeth-Ayerst
ethionamide [new entry in EML 2005, Compl. list]	6.2.4	tab, 125mg, 250mg			
ethosuximide	5	cap, 250mg syr, 250mg/5ml	ZARONTIN	USA	Parke-Davis
etoposide	8.2	cap, 100mg inj, 20mg/ml, 50mg/ml	VEPESID	Netherlands USA	Bristol-Myers Squibb
fluconazole [new entry in EML 2005, Core list and suggested by pre-qual (HIV)]	6.3	cap, 50 mg osp, 50 mg/5ml	DIFLUCAN (tab, 50mg, 100mg, 150mg, 200mg; osp, 10mg/ml, 40mg/ml (after reconstitution))		Pfizer
flucytosine	6.3	cap, 250mg	ANCOBON	USA	ICN Pharmaceuticals
[excluded from EML 2005]	18.1	tab, 100µg	FLORINEF	USA	Bristol-Myers Squibb
fludrocortisone, acetate					
fluorouracil	13.5	oin, 5%	EFUDIX	USA	Roche
fluphenazine, decanoate	24.1	depot inj, 25mg/1ml	PROLIXIN DECANOATE	USA	Bristol-Myers Squibb
fluphenazine, enanthate	24.1	depot inj, 25mg/1ml	PROLIXIN ENANTHATE	USA	Bristol-Myers Squibb
folinic acid [suggested by pre-qual (HIV)]			REFOLINON		Pharmacia &Upjohn
furosemide	16	tab, 40mg	LASIX	Germany	Hoechst Marion Roussel
ganciclovir [suggested by pre-qual (HIV)]			CYTOVENE		Roche Pharma
glyceryl trinitrate	12.1	s tab, 500µg; chcap, 800µg	NITROGLYCERIN	Switzerland	Novartis

		On the 14th EML - still sbtab, 500 µg	WANDER		
griseofulvin	6.3	cap, 125mg, 250mg tab, 125mg, 250mg	GRISACTIN FULCIN	USA USA	Zeneca
haloperidol	24.1	tab, 2mg, 5mg	HALDOL	Belgium	Janssen
hydralazine, hydrochloride	12.3	tab, 25mg, 50mg pwinj, 20mg	APRESOLINE	Netherlands United Kingdom	Novartis
hydrochlorothiazide	12.3 16	tab, 25mg tab, 25mg, 50mg On the 14th EML - only sctab, 25mg	HYDROSALURIC	United Kingdom	Merck Sharp & Dohme
ibuprofen	2.1	tab, 200mg On the 14th EML - also tab, 400mg	NUROFEN	United Kingdom	Boots
idoxuridine	21.1	eyd, 0.1% eyo, 0.2%	HERPLEX	USA	Allergan
imipenem monohydrate + cilastin (sodium)	6.2.1	pwinj, 250mg +250mg, 500mg + 500mg pwinj, 500mg +500mg	TIENAM	Italy	Merck Sharp & Dohme
indinavir (IDV) [new entry in EML 2005, Core list and suggested by pre-qual (HIV)]	27.1	cap, 200 mg, 333 mg, 400 mg (as sulfate)	CRIXIVAN (cap, 100mg also available)		Merck & Co.
insulin injection (soluble)	18.5	inj, 40IU/ml, 80 IU/ml , 100IU/ml inj, 40IU/ml , 80 IU/ml , 100IU/ml inj, 40IU/ml , 80 IU/ml , 100IU/ml On the 14th EML - inj, 40IU/ml, 100IU/ml	ACTRAPID ACTRAPID NOVOLIN R	Germany Zimbabwe Japan, USA	Novo Nordisk
intermediate-acting insulin (as compound insulin zinc suspension)	18.5	inj, 40IU/ml, 80IU/ml, 100IU/ml On the 14th EML - only inj,	HUMULIN L	USA	Eli Lilly

		40IU/ml, 100IU/ml			
intermediate-acting insulin (as isophane insulin)	18.5	inj, 40IU/ml, 80IU/ml, 100IU/ml	HUMULIN N	USA	Eli Lilly
??? iodine [new entry in EML 2005, Core list]	27	iodized oil, 0.5 ml (240 mg iodine), 1 ml (480 mg iodine) in ampoule (oral or injectable) 0.57 ml, (308 mg iodine) in dispenser bottle cap, 200 mg			
ipratropium bromide	25.1	inh, 20ug/metered dose	ATROVENT	USA	Boehringer Ingelheim
[excluded from EML 2005]	10.1	inj, equiv. to 50mg. iron/ml	INFED	USA	Shein Pharmaceuticals
iron dextran					
isosorbide dinitrate	12.1	sblltab, 5mg	ISORDIL	USA	Wyeth-Ayerst
itraconazole [suggested by pre-qual (HIV)]			SPORANOX		Janssen Pharmaceutica
ivermectin	6.1.2	sctab, 6mg On the 14th EML - also sctab, 3mg	MECTIZAN/STROMECTOL	Netherlands	Merck Sharp & Dohme
[excluded from EML 2005]	6.3	osp, 100mg/5ml tab, 200mg	NIZORAL	Belgium	Janssen
ketoconazole					
lamivudine (3TC) [new entry in EML 2005, Core list and suggested by pre-qual (HIV)]	27.1.1	tab, 150mg osl, 50 mg/5ml	EPIVIR (tab, 300mg also available)		GlaxoSmithKline
lamivudine/ zidovudine [suggested by pre-qual (HIV)]			COMBIVIR		GlaxoSmithKline
levamisole, hydrochloride	6.1.1 8.2	tab, 50mg, 150mg tab, 50mg	ERGAMISOL	Belgium	Janssen
levodopa + carbidopa	9	tab, 100mg +10mg , 250mg + 50mg On the 14th EML - tab, 100mg	SINEMET	Italy	Merck Sharp&Dohme

		+ 10mg, 250mg + 25mg			
levofloxacin [new entry in EML 2005, Compl. list]	6.2.4	tab, 250mg, 500mg			
levonorgestrel	18.3.1	tab, 30µg On the 14th EML - also tab, 750µg (pack of two), 1,5mg	MICROVAL	Germany	Wyeth-Ayerst
lithium carbonate	24.2.2	cap, 300mg tab, 300mg	QUILONUM	Germany	SmithKlaine Beecham
loperamide [suggested by pre-qual (HIV)]					
lopinavir + ritonavir (LPV/r) [new entry in EML 2005, Core list and suggested by pre-qual (HIV)]	27.1	cap, 133.3 mg + 33.3 mg osl, 400mg + 100mg/5ml	KALETRA		Abbott Laboratories
mebendazole	6.1.1	chtab, 100mg, 500mg	VERMOX	Belgium	Janssen
Medroxyprogesterone acetate	18.3.1 18.7	inj, 150mg/ml, depot tab, 5mg	DEPO-PROVERA PROVERA	USA	Pharmacia-Upjohn
mefloquine, hydrochloride	6.5.3	tab, 250mg	LARIAM	Switzerland	Roche
methadone [new entry in EML 2005, Compl. List]	24.5	osl, 5mg/5ml, 10mg/5ml concentrate for osl, 5mg/ml, 10mg/ml (hydrochloride)			
methyl dopa	12.3	tab, 250mg	ALDOMET	Spain	Merck Sharp & Dohme
metoclopramide, hydrochloride	17.2	tab, 10mg	PRIMPERAN	France	Synthelabo
miconazole, nitrate	13.1	cre, 2% oin, 2%	DAKTARIN	Belgium	Janssen
mifepristone - misoprostol [new entry in EML 2005, Compl. list]	22.1	tab, 200mg - tab, 200mcg			
misoprostol [new entry in	22.1	vagtab, 25mcg			

EML 2005, Compl. list] [excluded from EML 2005] nalidixic acid	6.2.2	tab, 500mg cap, 500mg	NEGGRAN	USA	Sanofi Winthrop
nelfinavir (NFV) [new entry in EML 2005, Core list and suggested by pre-qual (HIV)]	27.1	tab, 250mg (as mesilate) oral powder 50mg/g	VIRACEPT (tab, 625mg also available)		Pfizer Roche
neostigmine, bromide	20	tab, 15mg	PROSTIGMIN	Germany	Roche
nevirapine (NVP) [new entry in EML 2005, Core list and suggested by pre-qual (HIV)]	27.1.2	tab, 200 mg osp, 50 mg/5-ml (Does VIRAMUNE have these dosage forms/dosages?)	VIRAMUNE		Boehringer Ingelheim
niclosamide	6.1.1	chtab, 500mg	YOMESAN	Germany	Bayer <u>HealthCare</u> [Bayer comments via IFPMA]
nifedipine	12.3	cap, 5mg, 10mg tab 20mg, 30mg, 60mg (sr) ¹ tab 30mg, 60mg (sr) ² tab 10mg, 20mg, 40mg (sr) ³ [Bayer comments via IFPMA] On the 14th EML - immediate release cap, 10mg	ADALAT 5/10 ADALAT XL ADALAT EINS 30/60 ADALAT CR 10/20/40 [Bayer comments via IFPMA]	Germany Canada Germany Japan [Bayer comments via IFPMA]	Bayer <u>HealthCare</u> [Bayer comments via IFPMA]
nifurtimox	6.5.5	tab, 30mg, 120mg, 250mg On the 14th EML - still also tab, 250mg	LAMPIT	Honduras [Bayer comments via IFPMA]	Bayer HealthCare [Bayer comments via IFPMA]
nitrofurantoin	6.2.2	tab, 100mg	FURADANTIN	Ireland, United Kingdom	Proctor & Gamble
norethisterone, enantate	18.3.1	oilsl, 200mg/ml	NORISTERAT	Mexico, South Africa	Schering
nystatin	6.3	loz, 100000IU pes, 100000IU tab, 100000IU, tab, 500000IU	NYSTAN MYCOSTATINE	United Kingdom France France USA	Bristol-Myers Squibb

¹ Controlled release GITS - Gastro-Intestinal Therapeutic System

² Controlled release once daily CC - Coat Core

³ Controlled release once daily CC - Coat Core

		vagtab, 100000IU On the 14th EML - still pes, 100000 IU instead of vagtab, 100000IU		France	
ofloxacin [new entry in EML 2005, Compl. list and suggested by pre-qual (TB)]	6.2.4	tab, 200mg, 400mg	TARIVID (200mg tablets)	Germany	Aventis Pharma
oxamniquine	6.1.3	cap, 250mg syr, 250mg/5ml	MANSIL / VANSIL	Brazil	Pfizer
paracetamol	2.1	sup, 400mg , 125mg, 250mg, 500mg, 1000 mg On the 14th EML - only sup, 100mg	BEN-U-RON	Germany	Bene
penicillamine	4.2	cap, 250mg tab, 250mg	CUPRIMINE DEPEN	USA	Merck Sharp & Dohme Carter-Wallace
pentamidine [new entry in EML 2005, Compl. List and suggested by pre-qual (HIV)]	6.5.4	tab, 200mg, 300mg (Does PENTACARINAT has this dosage form/ dosages?)	PENTACARINAT		Aventis Pharma
phenobarbital	5	tab, 15-100mg	LUMINAL (100mg) LUMINALETTEN (15mg)	Germany	Desitin
phenoxymethylpenicillin, potassium	6.2.1	pwosp, 250mg/5ml tab, 250mg	V-CILLIN K	USA	Eli Lilly
phenytoin, sodium	5	cap, 25mg , 30mg, 50mg , 100mg tab, 25mg , 50mg, 400mg On the 14th EML - cap, 25mg, 50mg, 100mg; tab, 25mg, 50mg, 100mg	DILANTIN KAPSEALS DILANTIN INFATABS	USA	Parke-Davis
phytomenadione	10.2	tab, 10mg	KONAKION	Switzerland	Roche
??? potassium ferric hexacyanoferrate (II)2H2O (Prussian blue) [new entry in EML 2005,	4.2	powder for oral administration			

Core list]					
praziquantel	6.1.1 6.1.3	, 600mg tab, 600mg [Bayer comments via IFPMA] On the 14th EML - also tab, 150mg still included	BILTRICIDE	Germany	Bayer HealthCare [Bayer comments via IFPMA]
prednisolone	3 8.3 18.1	tab, 5mg [Is available from Schering AG only as 5mg tablet . Schering comments, Germany]	SCHERISOLON	Columbia, [Still marketed only in Columbia. Schering comments, Germany]	Schering
	21.2	eyd, 0.5% On the 14th EML - tab, 1mg, 5mg, 25mg; eyd, 0.5%	ULTRACORTENOL	Germany	Ciba Vision (Novartis)
procainamide, hydrochloride	12.2	tab, 250mg, 500mg On the 14th EML - only inj, 100mg/ml	PRONESTYL	USA	Bristol-Myers Squibb
procarbazine, hydrochloride	8.2	cap, 50mg	NATULAN	Switzerland	Roche
proguanil, hydrochloride	6.5.3	tab, 100mg	PALUDRINE	United Kingdom	Zeneca
propranolol, hydrochloride	7.2 –	tab, 20mg, 40mg tab, 10mg, 40mg On the 14th EML - only tab, 20mg, 40mg	INDERAL	Japan United Kingdom	Zeneca
pyrantel, embonate	6.1.1	chtab, 250mg osp, 50mg/ml	COMBANTRIN	Germany	Pfizer
pyrazinamide	6.2.4	tab, 400mg , 500 mg tab, 400mg [suggested by pre- qual (TB)] On the 14th EML - tab, 400mg	ZINAMIDE (Pyrazinamide 500mg) 500mg Pyrazinamide [suggested by pre-qual (TB)]	United Kingdom Alternative: South Africa [suggested by pre-qual (TB)]	Merck Sharp&Dohme Alternative: Rolab [suggested by pre-qual (TB)]
pyridostigmine, bromide	20	tab, 60mg	MESTINON	Switzerland	Roche
pyrimethamine [new entry in EML 2005, Core list and suggested by pre-	6.5.4	tab, 25 mg	DARAPRIM (25 mg scored tablets)		GlaxoSmithKline

qual (HIV)]					
ranitidine [new entry in EML 2005, Core list]	17.1	tab, 150 mg (as hydrochloride) osl, 75mg/5ml			
rifabutin [suggested by pre-qual (HIV)]			MYCOBUTIN		Pharmacia & Upjohn / Pfizer
rifampicin	6.2.3 6.2.4	cap, 150mg, 300mg tab, 150mg, 300mg cap, 150mg, 300mg tab, 150mg, 300mg	RIFADIN RIMACTANE (tab, 150mg) [suggested by pre-qual (TB)]	Italy Switzerland	Gruppo Lepetit Novartis
rifampicin+isoniazid	6.2.4	tab, 150mg + 100mg, 300mg + 150mg On the 14th EML - tab, 60mg + 30mg; 150mg + 75mg; 300mg + 150mg; 60mg + 60mg; 150mg +150mg	RIFINAH	Italy	Gruppo Lepetit
rifampicin + isoniazid + pyrazinamide	6.2.4	tab, 150mg + 75mg + 400mg, 150mg +150mg +500mg On the 14th EML - also tab, 60mg + 30mg + 150mg	RIFATER	Italy	Hoechst Marion Roussel
rifampicin + isoniazid + pyrazinamide + ethambutol [new entry in EML 2005, Core list]	6.2.4	tab, 150 mg + 75 mg + 400 mg + 275 mg			
ritonavir (r) [new entry in EML 2005, Core list and suggested by pre-qual (HIV)]	27.1	capsule, 100 mg osl, 400mg/5ml	NORVIR		Abbott Laboratories
saquinavir (SQV) [new entry in EML 2005, Core list and suggested by pre-qual (HIV)]	27.1	cap, 200mg	FORTOVASE INVIRASE (tab, 500mg also available)		Roche Pharma Roche Pharma
silver sulfadiazine	13.2	cre, 1%/500g	SILVADENE	USA	Hoechst Marion Roussel
spectinomycin [suggested			TROBOCIN		Pharmacia & Upjohn

by pre-qual (HIV)]					
stavudine (d4T) [new entry in EML 2005, Core list and suggested by pre-qual (HIV)]	27.1.1	cap, 15mg, 20mg, 30mg, 40mg powder for oral solution 5mg/5ml	ZERIT		Bristol-Meyers Squibb
sulfadoxine + pyrimethamine	6.5.3	tab, 500mg + 25mg	FANSIDAR	Switzerland	Roche
sulfamethoxazole + trimethoprim	6.2.2	osp, 200mg + 40mg/5ml tab, 100mg + 20mg, 400mg + 80mg	BACTRIM	Switzerland	Roche
sulfasalazine	17.4	tab, 500mg On the 14th EML - also sup, 500mg	AZULFIDINE	USA	Pharmacia-Upjohn
tamoxifen, citrate	8.3	tab, 10mg, 20mg	NOLVADEX	United Kingdom	Zeneca
tenofovir disoproxil fumarate [suggested by pre-qual (HIV)]			VIREAD		Gilead Sciences
testosterone, enantate	18.2	inj, 200mg/ml, 250mg/ml [Is available as a 250mg/ml dosage. The 200mg/ml dosage is not manufactured by us. Schering comments, Germany] On the 14th EML - only inj, 200mg/ml	TESTOVIRON DEPOT [Schering comments, Germany]	Argentina, Germany, Mexico	Schering
[excluded from EML 2005] theophylline	25.1	tab, 100mg , 125mg , 200mg, 250mg, 300mg, 375mg, 500 mg [Altana comments via IFPMA]	EUPHYLONG	Germany	Altana Pharma AG [Altana comments via IFPMA]
timolol, maleate	21.4	sl (eyd), 0.25%, 0.5% (sol) eyd, 0.25%, 0.5% (unit dose) gel (eyd), 0.25%, 0.5% On the 14th EML - only sl (eyd) 0.25%, 0.5%	TIMOPTOL Ophthalmic Solution TIMOPTOL Oculdose TIMOPTOL LP	France	Merck Sharp&Dohme
[excluded from EML	–	tab, 500mg	RASTINON	Germany	Hoechst Marion Roussel

2005] tolbutamide					
triclabendazole	6.1.3	tab, 250mg	EGATEN	Egypt	Novartis
tropicamide	14.1	eyd, 0.5%	MYDRIACYL	United Kingdom	Alcon
verapamil, hydrochloride	12.1 12.2	tab, 40mg, 80mg (sr) tab, 40mg, 80mg (sr)	ISOPTIN	Germany	Abbott GmbH & Co. KG [Abbott comments via IFPMA]
??? zinc sulfate [new entry in EML 2005, Core list]	17.5.2	tab or syr in 10mg per unit dosage forms			
List B					
acetazolamide	21.4	tab, 250mg	*****		
acetylsalicylic acid	2.1 7.1 12.5	sup, 50-150mg tab, 100-500mg tab, 300-500mg tab, 100mg	***** ***** ***** *****		
aciclovir	6.4.1	tab, 200mg	***** ZOVIRAX [suggested by pre-qual (HIV)] (cap, 200mg; tab, 400mg, 800mg; osp, 200mg/5ml available)		GlaxoSmithKline
aciclovir (sodium)	6.4.1	pwinj, 250mg	***** ZOVIRAX [suggested by pre-qual (HIV)] (pwinj, 500mg, 1000mg available)		GlaxoSmithKline
allopurinol	2.3	tab, 100mg	*****		
aluminum hydroxide	17.1	osp, 320mg/5ml tab, 500mg			
amoxicillin + clavulanic acid	6.2.1	tab, 500 + 125mg	*****		
ascorbic acid	27	tab, 50mg			
[excluded from EML 2005]	17.5	tab, 1mg	*****		
atropine, sulfate					
azathioprine	8.1	tab, 50mg	*****		

beclometasone, dipropionate	25.1	inh, 50µg/dose On the 14th EML - also inh, 250µg/dose	*****		
benzoic acid +salicylic acid	13.1	cre, 6% + 3% oin, 6% + 3%			
benzoyl peroxide	13.5	cre, 5% lot, 5%			
benzyl benzoate	13.6	lot, 25%			
betamethasone, valerate	13.3	cre, 0.1% oin , 0.1%	***** *****		
calamine lotion	13.3	lot			
[excluded from EML 2005] chloral hydrate	1.3	syr, 200mg/5ml			
chloramphenicol, palmitate	6.2.2	osp, 150mg/5ml	*****		
chloroquine, phosphate	6.5.3	syr, 50mg/5ml ^{b, c}	*****		
chloroquine, sulfate	6.5.3	syr, 50mg/5ml ^{b, c} tab, 100mg, ^b 150mg ^{b, c}			
chlorpromazine, hydrochloride	24.1	syr, 25mg/5ml tab, 100mg	***** *****		
coal tar	13.5	topsl, 5%			
codeine, phosphate	2.2 17.7.2	tab, 30mg tab, 30mg	***** *****		
[excluded from EML 2005] colchicine	2.3	tab, 500µg	*****		
[excluded from EML 2005] cromoglicic acid, sodium	25.1	inh, 20mg/dose	*****		
[excluded from EML 2005] dextromethorphan	25.2	osl, 3.5mg/5ml	*****		
diethylcarbamazine, dihydrogen citrate	6.1.2	tab, 50mg On the 14th EML - also tab,	*****		

		100mg			
[excluded from EML 2005] diethyltoluamide	6.6	topsl, 50%, 75%			
[excluded from EML 2005] digitoxin	–	tab, 50µg, 100µg	*****		
digoxin	12.4	osl, 50µg/ml tab, 62.5µg, 250µg	***** *****		
diloxanide, furoate	6.5.1	tab, 500mg	*****		
dimercaprol	4.2	oilinj, 50mg/ml	*****		
dithranol	13.5	oin, 0.1-2%	*****		
[excluded from EML 2005] ergometrine, hydrogen maleate	22.1	tab, 200µg	*****		
[excluded from EML 2005] ergotamine, tartrate	7.1	tab, 1mg			
erythromycin, ethyl succinate	6.2.2	cap, 250mg pwosp, 125mg tab, 250mg	***** ***** *****		
erythromycin, stearate	6.2.2	cap, 250mg pwosp, 125mg tab, 250mg	***** ***** *****		
ethambutol, hydrochloride	6.2.4	tab, 100-400mg	***** Myambutol (400mg Ethambutol) [suggested by pre-qual (TB)]		Ledere Arzneimittel GmbH & Co
ethinylestradiol + norethisterone	18.3.1	tab, 35µg+1.0mg	*****		
ferrous salt, sulfate	10.1	osl, equiv. to 25mg iron/ml tab, equiv. to 60mg iron			
ferrous salt (sulfate) +	10.1	tab, equiv. to 60mg iron +			

folic acid		250µg folic acid On the 14th EML - tab, equiv. to 60mg iron + 400µg folic acid			
folic acid	10.1	tab, 1mg, 5mg	*****		
gentamicin, sulfate	21.1	eyd, 0.3%	*****		
glibenclamide	18.5	tab, 2.5, 5mg	*****		
glibenclamide	18.5	tab, 2.5, 5mg	*****		
hydrocortisone, acetate	13.3	cre, 1%	*****		
		oin, 1%	*****		
	17.4	supp, 25mg	*****		
[excluded from EML 2005]	-	sl, 3%			
hydrogen peroxide					
iopanoic acid	14.2	tab, 500mg	*****		
[excluded from EML 2005]	4.1	syr, 0.14%, as emetine			
ipecacuanha					
isoniazid	6.2.4	tab, 100-300mg	***** ISOZID (100mg isoniazid) [suggested by pre- qual (TB)]	Germany	Fatol
isoniazid + ethambutol	6.2.4	tab, 150mg + 400mg	***** Use appropriate combination of MYAMBUTOL (ethambutol) & ISOZID (isoniazid) [suggested by pre-qual (TB)]		
levothyroxine, sodium	18.8	tab, 50µg, 100µg	*****		
magnesium hydroxide	17.1	osp, equiv. to 550mg/10ml			
mercaptopurine	8.2	tab, 50mg	*****		
metformin	18.5	tab, 500mg	*****		
DL-methionine	4.2	tab, 250mg	*****		
methotrexate, sodium	8.2	tab, 2.5mg	*****		
[excluded from EML 2005]	-	tab, 100mg	*****		
metrifonate					
metronidazole	6.2.2	sup, 500mg, 1g	*****		

	6.5.1	tab, 200-500mg tab, 200-500mg	***** *****		
metronidazole, benzoate	6.5.1	osp, 200mg/5ml	*****		
morphine, hydrochloride	2.2	osl, 10mg/5ml			
morphine, sulfate	2.2	osl, 10mg/5ml tab, 10mg			
neomycin, sulfate + bacitracin zinc	13.2	oin, 5mg + 500IU	*****		
nicotinamide	27	tab, 50mg			
norethisterone	18.7	tab, 5mg	*****		
paracetamol	2.1	syr, 125 mg/5ml tab, 100-500mg			
	7.1	tab, 300-500mg			
permethrin	13.6	lot, 1% On the 14th EML - also cre, 5%			
[excluded from EML 2005]	2.2	tab, 50mg, 100mg	*****		
pethidine, hydrochloride					
phenobarbital	5	elix, 15mg/5ml	*****		
pilocarpine, hydrochloride or nitrate	21.4	Sl (eyd), 2%, 4%	*****		
podophyllum resin	13.5	topsl, 10-25%			
potassium iodide	18.8	tab, 60mg			
primaquine, diphosphate	6.5.3	tab, 7.5, 15mg	*****		
promethazine, hydrochloride	1.3	elix, 5mg/5ml syr, 5mg/5ml	***** *****		
	17.2	elix, 5mg/5ml syr, 5mg/5ml tab, 10mg, 25mg	***** ***** *****		
propylidone	14.2	oilsp, 500-600mg/ml	*****		
propylthiouracil	18.8	tab, 50mg	*****		
pyridoxine, hydrochloride	27	tab, 25mg			
quinidine, sulfate	12.2	tab, 200mg	*****		

quinine, bisulfate	6.5.3	tab, 300mg			
quinine, sulfate	6.5.3	tab, 300mg			
[excluded from EML 2005] reserpine	12.3	tab, 100µg, 250µg	*****		
retinol, palmitate	27	cap, 200000IU (110mg) oosl, 100000IU/ml sgtab, 10000IU (5.5mg) wminj, 100000IU/2ml (55mg)			
riboflavin	27	tab, 5mg			
salbutamol, sulfate	22.2 25.1	tab, 4mg inh, 100µg/dose respsl, 5mg/ml syr, 2mg/5ml tab, 2mg, 4mg On the 14th EML - only tab, 4mg	***** ***** ***** ***** *****		
salicylic acid	13.5	topsl, 5%			
senna (sennoside)	17.6	tab, 7.5mg			
[excluded from EML 2005] silver nitrate	21.1	sl (eyd), 1%			
sodium fluoride	27	any			
spironolactone	16	tab, 25mg	*****		
sulfadiazine	6.2.2	tab, 500mg	***** MICROSULFON [suggested by pre-qual (HIV)]		
[excluded from EML 2005] sulfadimidine	-	osp, 500mg/5ml tab, 500mg	***** *****		
tetracaine, hydrochloride	21.3	sl (eyd), 0.5%	*****		
tetracycline, hydrochloride	21.1	eyo, 1%	*****		
thiamine, hydrochloride	27	tab, 50mg			
[excluded from EML 2005]	6.2.4	tab, 50mg + 100mg, 150 + 300mg	*****		

thioacetazone+isoniazid					
trimethoprim	6.2.2	tab, 100mg, 200mg	*****		
urea	13.5	cre, 10% oin, 10%			
valproic acid, sodium	5	encotab, 200mg, 500mg	*****		
warfarin, sodium	10.2	tab, 1mg, 2mg, 5mg	*****		
zidovudine	6.4.2	cap, 100mg, 250mg osl, 50mg/5ml On the 14th EML - also tab, 300mg; osl or syr, 50mg/5ml	*****RETROVIR[suggested by pre-qual (HIV)] (tab, 300mg; cap, 100mg; syr, 50mg/5ml available) *****		GlaxoSmithKline
[excluded from EML 2005] zinc oxide	—	cre oin			

^a For instructions on the of the list, see pages 5-7

^b For curative treatment

^c For prophylaxis

Blank page

Updated Information from Bayer HealthCare

For Nifedipine we suggest to include controlled released products as a substitute for Adalat T 10 (no longer marketed). Adalat controlled-release tablets are formulated to provide nifedipine at an approximately constant rate over 24 hours, thereby providing sustained blood pressure control over the full dosing interval (Mancia G et al. J Hypertension 2002;20:545-553). Furthermore, in patients with chronic stable angina the number of anginal episodes was significantly reduced, over the full 24 hour period (Parmley WW et al. JACC 1992;19(7):1380-9).

Obsolete information is crossed out. Please see specific comments on pages 7, 10, & 11.

In the second list with no originator names "acetylsalicylic acid" is listed which of course is originated by Bayer. We have all forms except suppositories.

Updated Information from Abbott Laboratories, USA

Table 1, International comparator products for equivalence assessment of interchangeable multisource (generic) products, should be revised with regard to:

biperiden, hydrochloride, 2 mg tablet, Akineton, Germany, Desma GmbH (NO LONGER KNOLL)

verapamil, hydrochloride, 40 and 80 mg tablet, Isoptin, Germany, Abbott GmbH & Co. KG (NO LONGER KNOLL) Please see specific comments on page 7 & 12.

Updated Information from Altana Pharma AG

The information concerns the following products: aminophylline and theophylline.

- 1) In both cases the current entries (column manufacturer) "BYK Gulden Lomberg", respectively "BYK-Gulden" are to be replaced by "ALTANA Pharma AG".*
- 2) Regarding aminophylline, a) the trademark is Aminophyllin (with 2 "L") and b) only the 125 mg dosage form is available (please delete 100 mg and 200 mg).*
- 3) Regarding theophylline, following dosage forms are correct: 125 mg, 200 mg, 250 mg, 300 mg, 375 mg and 500 mg. Please see specific comments on page 7 & 12.*

Acknowledgements

Acknowledgement was made by the WHO Secretariat to the following people, for their valuable contributions to the discussions: International Federation of Pharmaceutical Manufacturers Associations (IFPMA), Geneva, Switzerland.

[To be updated]

References

1. Multisource (generic) pharmaceutical products: guidelines on registration requirements to establish interchangeability. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations. Thirty-fourth report. Geneva, World Health Organization, 1996, Annex 9 (WHO Technical Report Series, No. 863).
2. The use of essential drugs. Eighth report of the WHO Expert Committee on Specifications for Pharmaceutical Preparations (including the revised Model List of Essential Drugs). Geneva, World Health Organization, 1998 (WHO Technical Report Series, No. 882).
3. The International Pharmacopoeia, 3rd ed. Vol. 1. General methods of analysis; Vol. 2. Quality specifications; Vol. 3. Quality specifications; Vol 4. Tests, methods, and general requirements. Quality specifications for pharmaceutical substances, excipients, and dosage forms. Geneva, World Health Organization, 1979–1994.